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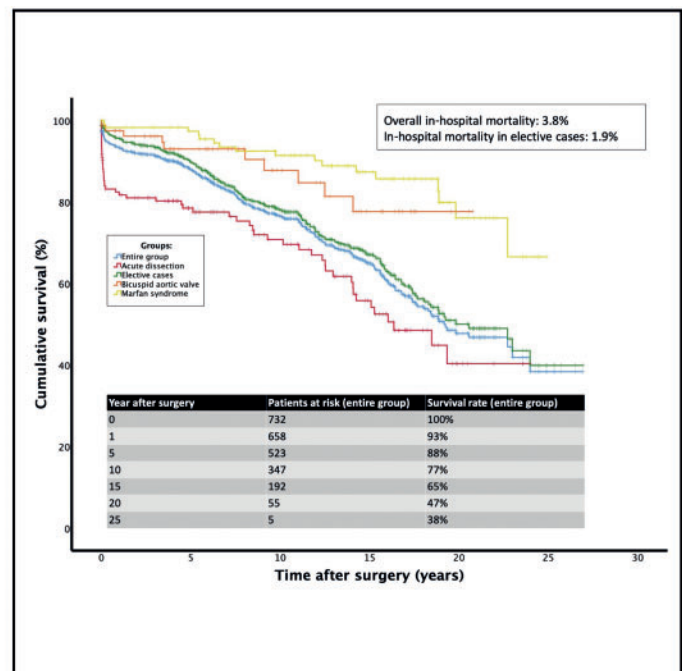
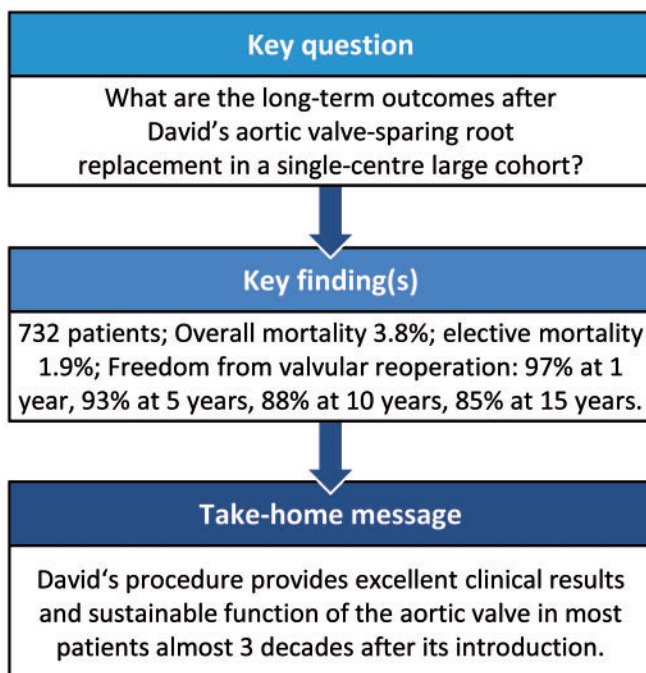
Aortic valve-sparing root replacement with Tirone E. David's reimplantation technique: single-centre 25-year experience

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Abstract

OBJECTIVES: Tirone E. David described aortic valve-sparing root reimplantation (AVSRR) almost 30 years ago. At our centre, we adopted this operation in 1993, and since then, we have performed >700 operations over a time period of >25 years. In this report, we present our single-centre experience.

METHODS: Between 1993 and 2019, a total of 732 patients underwent AVSRR at our centre. The mean age was 53 ± 15 and 522 (71%) were male. Marfan syndrome was present in 117 (16%) patients and bicuspid aortic valve in 81 (11%). The indication for surgery was aortic root aneurysm in 588 (80%) patients and acute aortic dissection in 144 (20%) patients.

RESULTS: Mini-sternotomy was performed in 74 (10%) patients. A straight tube graft (David I) was used in 677 (92%) and a Valsalva-graft in 55 (8%) patients. Cusp plasty was done in 83 (11%) patients. Concomitant cardiac procedures were performed in 438 (60%) patients. Overall in-hospital mortality was 3.8% ($n=29$) and 1.9% ($n=11$) in elective cases. Postoperative echocardiography was available for 671

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patients and showed aortic insufficiency (AI) $\leq 1^\circ$ in 647 (96%) patients. The mean follow-up time was 10 ± 6.7 years and comprised a total of 7307 patient-years. The 1-, 5-, 10- and 15-year survival rates were: 93%, 88%, 77% and 65%, respectively. The rates for freedom from valve-related reoperation at 1, 5, 10 and 15 years after initial surgery were 97%, 93%, 88% and 85%, respectively. Cox regression analysis identified age [odds ratio (OR) = 0.975, 95% confidence interval (CI) = 0.955–0.995, $P = 0.016$], hyperlipidaemia (OR = 1.980, 95% CI = 1.175–3.335, $P = 0.010$), preoperative level of left ventricular ejection function (OR = 1.749, 95% CI = 1.024–2.987, $P = 0.041$) and postoperative degree of AI (OR = 1.880, 95% CI = 1.532–2.308, $P \leq 0.001$) as risk factors for the future AI or reoperation.

CONCLUSIONS: David procedure can be performed extremely safely, with low risks for perioperative morbidity and mortality, both in elective situations via minimally invasive access and in emergent settings for acute aortic type A dissection. Regarding long-term outcome, David's AVSRR seems to provide excellent clinical results and sustainable function of the aortic valve in the majority of patients almost 3 decades after its introduction.

Keywords: Aortic valve-sparing root replacement • David procedure • Reimplantation procedure

ABBREVIATIONS

AI	Aortic insufficiency
AVSRR	Aortic valve-sparing root reimplantation
CI	Confidence interval
OR	Odds ratio

INTRODUCTION

Tirone E. David introduced his technique of aortic valve-sparing root reimplantation (AVSRR) in 1992, almost 30 years ago [1]. At this time, this procedure was almost 'experimental' and nothing was known about the long-term performance of the reimplanted aortic valve. Now, almost 30 years later, the former 'experimental' procedure has evolved into a generally accepted and widely performed approach to replace the aortic root and simultaneously to preserve the native aortic valve. Tirone E. David's technique has to be considered one of the most innovative operations in reconstructive aortic root surgery of the recent decades.

Aortic valve-sparing surgery avoids the disadvantages of composite root replacement, including the need for life-long anticoagulation with associated risks of thromboembolism and haemorrhage as in mechanical valve conduits [2] or prosthetic leaflet degeneration with the need for reoperation as in tissue valve conduits [3]. Furthermore, the risk for endocarditis is lower after valve-sparing surgery when compared to composite root replacement [4].

However, there are also potential disadvantages of AVSRR: longer aortic cross-clamp times due to the complexity of the procedure, intraoperative conversion to composite root replacement or late failure of the reimplanted aortic valve with the need for reoperation.

Initially, AVSRR was performed by using a straight Dacron tube graft and was applied only to young patients with aortic aneurysms and normal cusps [5]. With growing evidence on the performance of the reimplanted valve and confidence in this operation, the indications for AVSRR were expanded, and nowadays, this procedure is applied in patients with acute aortic dissection or bicuspid aortic valves [6]. Over time, various modifications to the original operation have been made, which have been classified by Demers and Miller [7].

At our centre, we have adopted AVSRR early on in 1993, only 1 year after the description and publication of Tirone E. David's technique. Due to the early adoption of this operation and our confidence in this procedure, we were able to perform this

operation in a multitude of cases and settings [8–12]. This study reports and summarizes our current experience with AVSRR over a time period of >25 years.

METHODS

Ethical statement

This is a retrospective study with follow-up. Our institution does not require institutional review board approval for retrospective studies. Thus, this study was in line with our institution's ethical policies and standards.

Study design

Between 1993 and 2019, a total of 732 patients underwent AVSRR at our centre. We conducted a retrospective analysis with follow-up. Hospital records were analysed to extract data.

Preoperative assessment and surgical technique

All patients in this study underwent AVSRR. A detailed description of our surgical technique is found in previous publications [13]. The detailed surgical technique is presented in the [Supplementary Material](#).

Of note, we perform AVSRR not only in patients with tricuspid but also bicuspid aortic valves. The bicuspid aortic valve is classified according to the Sievers classification system [14]. In the present study, 81 patients (11%) had a bicuspid aortic valve.

Postoperative follow-up

Echocardiography was performed postoperatively. Individual consent was obtained from patients to allow for follow-up examination. Follow-up was done according to common guidelines [15]. Patients were contacted by telephone and/or seen in our clinic. Primary care physicians and/or cardiologists were contacted and examination results with echocardiography data were obtained.

Statistical analysis

Data analysis was performed using SPSS 26 Statistics software (IBM Corp. Released 2019. IBM SPSS Statistics for Windows, Version 26.0; IBM Corp., Armonk, NY, USA). Normal distribution

of variables was analysed with the Kolmogorov–Smirnov test. Normally distributed continuous variables are stated as mean \pm standard deviation, while continuous variables without normal distribution are stated as median + range. Continuous variables were analysed with Fisher's exact test, while categorical variables were compared with t-test. Univariable analysis was performed to analyse association between variables and the combined end point of aortic valve-related reoperation or aortic insufficiency (AI) $>II^\circ$. These results can be found in the [Supplementary Material](#). Next, variables were entered into the Cox regression analysis. Kaplan–Meier analysis was used for the evaluation of both survival and reoperation of the aortic valve, and the log-rank test was used to test for differences. A value of $P < 0.05$ was considered statistically significant.

RESULTS

Patient demographics and early outcome

The patient demographics are found in Table 1. The mean age was 53 ± 15 and 522 (71%) were male. Marfan syndrome was present in 117 (16%) patients and the mean age of these patients was 33 ± 13 years. Bicuspid aortic valve was present in 81 (11%).

Variable	Value
Demographic data	
Demographic data ($n = 732$)	
Age (years), mean \pm SD	53 ± 15
Male, n (%)	522 (71)
Weight (kg), mean \pm SD	82 ± 16
Height (cm), mean \pm SD	177 ± 10
BMI (kg/m^2), mean \pm SD	26 ± 4
Medical history ($n = 732$), n (%)	
Diabetes	33 (5)
Hyperlipidaemia	179 (24)
Arterial hypertension	448 (61)
Coronary artery disease	131 (18)
COPD	40 (5)
Kidney disease	30 (4)
Stroke	4 (1)
Marfan syndrome	117 (16)
Previous cardiac surgery	36 (5)
Bicuspid aortic valve	81 (11)
Echocardiography	
AI ($n = 670$), n (%)	
AI 0° or $0\text{--}I^\circ$	57 (9)
AI I° or $I\text{--}II^\circ$	137 (20)
AI II° or $II\text{--}III^\circ$	235 (35)
AI III° or $III\text{--}IV^\circ$	224 (33)
AI IV°	17 (3)
Left ventricular ejection fraction ($n = 563$)	
Mean LVEF (%), mean \pm SD	61 ± 10
Normal or slightly reduced LVEF, n (%)	490 (87)
Moderately reduced LVEF, n (%)	69 (14)
Severely reduced LVEF, n (%)	4 (1)
Indication	
Indication for surgery ($n = 732$), n (%)	
Aortic aneurysm	588 (80)
Acute aortic dissection	144 (20)

AI: aortic insufficiency; BMI: body mass index; COPD: chronic obstructive pulmonary disease; LVEF: left ventricular ejection fraction; SD: standard deviation.

The indication for surgery was aortic root aneurysm in 588 (80%) patients and acute aortic dissection in 144 (20%) patients. All of the patients with acute aortic dissection underwent emergent surgery.

The intraoperative data are given in Table 2. Minimally invasive access via upper hemi-sternotomy was performed in 74 (10%) elective patients. A straight tube graft (David I) was used in 677 (92%) and a Valsalva-graft in 55 (8%) patients. Cusp plasty via central cusp plication was done in 83 (11%) patients. Concomitant cardiac procedures were performed in 438 (60%) patients. There were 18 cases (2%) requiring intraoperative conversion to conventional root replacement.

The early postoperative outcome is shown in Table 2. Permanent neurological injury occurred in 27 patients (4%). The rate for neurological complications in patients with acute aortic

Table 2: Intraoperative and early postoperative data

Variable	Value
Intraoperative data ($n = 732$)	
Times, mean \pm SD	
Cardiopulmonary bypass time (min)	197 ± 65
Aortic cross-clamp time (min)	133 ± 65
Cerebral perfusion time (min)	42 ± 40
Access, n (%)	
Minimally invasive access	74 (10)
Full sternotomy	658 (90)
Prosthesis	
Straight tube graft, n (%)	677 (92)
Graft with preformed sinus of Valsalva, n (%)	55 (8)
Average graft size (mm), mean \pm SD	28 ± 2
Cusp plasty, n (%)	
1 cusp	46 (6)
2 cusps	32 (4)
3 cusps	5 (1)
Concomitant cardiac procedures, n (%)	
Cases with concomitant surgery	438 (60)
Mitral valve repair/replacement	35 (5)
Coronary artery bypass grafting	134 (18)
Proximal aortic arch replacement	163 (22)
Total aortic arch replacement (incl. FET)	113 (15)
Other procedures	30 (4)
Early postoperative outcome ($n = 732$)	
Ventilation time (h), median (IQR)	13 (0–1981)
Prolonged ventilation >72 h, n (%)	64 (9)
Tracheostomy, n (%)	25 (3)
New dialysis, n (%)	23 (3)
Stroke, n (%)	27 (4)
Rethoracotomy for bleeding, n (%)	52 (7)
ICU stay (days), median (IQR)	1 (0–57)
Overall in-hospital mortality, n (%)	29 (3.8)
In-hospital mortality of elective cases, n (%)	11 (1.9)
Overall 30-day mortality, n (%)	25 (3.4)
30-Day mortality for elective cases, n (%)	10 (1.7)
Postoperative echocardiography	
AI ($n = 671$), n (%)	
AI 0° or $0\text{--}I^\circ$	515 (77)
AI I°	132 (20)
AI $I\text{--}II^\circ$ or II°	24 (4)
Other data, mean \pm SD	
Max. (mmHg)	13 ± 7
Mean (mmHg)	7 ± 4
Aortic valve opening area (cm^2)	2.7 ± 1
LVEF (%)	55 ± 12

AI: aortic insufficiency; FET: frozen elephant trunk; ICU: intensive care unit; IQR: interquartile range; LVEF: left ventricular ejection fraction; SD: standard deviation.

type A dissection was 9% ($n=13$), and only 2% ($n=14$) in electively operated patients. Overall in-hospital mortality was 3.8% ($n=29$) and 1.9% ($n=11$) in elective cases. The reasons for death in elective cases were cardiac failure ($n=6$), septic multiorgan failure ($n=3$) and cerebral injury ($n=2$). Postoperative echocardiography was available for 671 patients and showed AI $\leq 1^\circ$ in 647 (96%) patients. The mean transaortic maximum gradient was 13 ± 7 , and the average mean gradient was 7 ± 4 mmHg.

Long-term outcome

Late outcome is shown in Table 3. The mean follow-up time was 10 ± 6.7 years and comprised a total of 7307 patient-years. The follow-up completion rate was 98%. The Kaplan–Meier curves for long-term survival is found in Fig. 1. The 1-, 5-, 10- and 15-year survival rates for the entire cohort were 93%, 88%, 77% and 65%, respectively.

During follow-up, 78 patients required reoperation of the aortic valve. The reasons for reoperation in these 78 patients were: severe aortic valve insufficiency in 45 patients, severe aortic valve stenosis in 4 patients, combined aortic valve stenosis and insufficiency in 6 patients, prosthetic infection/endocarditis in 7 patients and unknown reasons in 16 patients. The Kaplan–Meier curves for freedom from aortic valve-related reoperation are found in Fig. 2. The rates for freedom from valve-related

reoperation at 1, 5, 10 and 15 years after initial surgery for the entire group were 97%, 93%, 88% and 85%, respectively.

Follow-up echocardiography was obtained for 646 event-free patients, i.e. those patients who did not require aortic valve-related reoperation. This resulted in a completion rate of 99%. The majority of patients ($n=493$, 76%) showed AI $\leq 1^\circ$. The mean left ventricular ejection fraction was $56 \pm 9\%$.

Risk factor analysis

We performed a risk factor analysis to identify variables linked to the combined end point of either AI $> 11^\circ$ or aortic valve-related reoperation. Cox regression analysis was performed (Table 4) and showed that age [odds ratio (OR) = 0.975, 95% confidence interval

Table 3: Late outcome	
Variable	Value
Late clinical outcome	
Follow-up information	
Completion rate, n (%)	717 (98)
Follow-up time (years), mean \pm SD	10 ± 6.7
Cumulative patient-years	7307
Total death events, n (%)	228 (31)
Total reoperations at aortic valve, n (%)	78 (11)
Survival rates at (%)	
1 year	93
5 years	88
10 years	77
15 years	65
20 years	47
25 years	38
Freedom from aortic valve-related reoperation at (%)	
1 year	97
5 years	93
10 years	88
15 years	85
20 years	81
25 years	81
Follow-up echocardiography ^a	
Time to echocardiography (years), mean \pm SD	
8.3 ± 6	
AI ($n=646$, 99%), n (%)	
AI 0° or 0-I°	358 (55)
AI I°	135 (21)
AI I-II° or II°	78 (12)
AI II-III°	5 (1)
AI III°	4 (1)
Other data, mean \pm SD	
Max. (mmHg)	16 ± 15
Mean (mmHg)	9 ± 8
LVEF (%)	56 ± 9

AI: aortic insufficiency; LVEF: left ventricular ejection fraction; SD: standard deviation.

^aOf event-free patients.

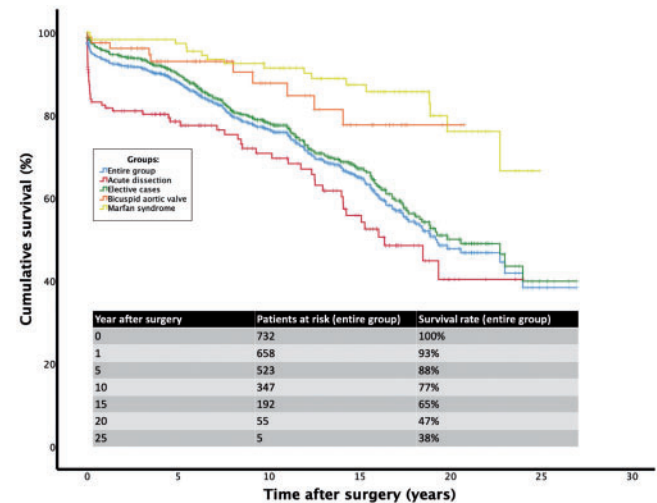


Figure 1: Survival. The figure shows the Kaplan–Meier survival curves for patients who underwent David procedure with the following groups: entire cohort (blue), acute aortic dissection type A (red), elective cases (green), bicuspid aortic valve (orange) and Marfan syndrome (yellow). Time origin on x-axis denotes day of surgery.

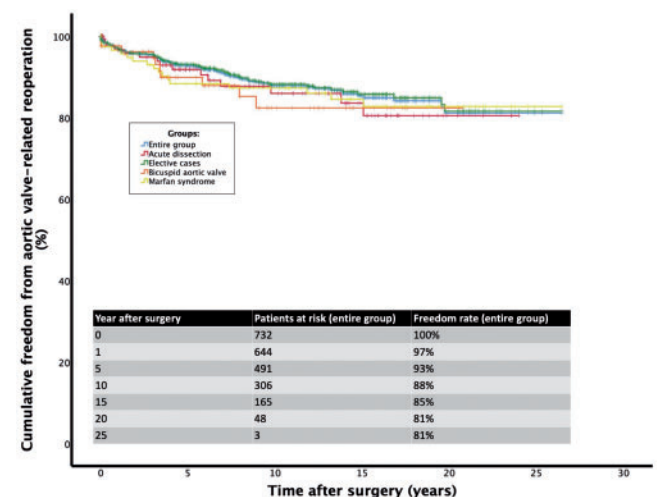


Figure 2: Freedom from aortic valve-related reoperation. The figure shows the Kaplan–Meier curves for freedom from aortic valve-related reoperation after David procedure with the following groups: entire cohort (blue), acute aortic dissection type A (red), elective cases (green), bicuspid aortic valve (orange) and Marfan syndrome (yellow). Time origin on x-axis denotes day of surgery.

Table 4: Risk factor analysis

Variable	OR	95% CI	P-value
Risk factors for reoperation/ aortic insufficiency >II°			
Age	0.975	0.955–0.995	0.016
Hyperlipidaemia	1.980	1.175–3.335	0.010
Postoperative residual aortic insufficiency	1.880	1.532–2.308	<0.001
Preoperative LVEF	1.749	1.024–2.987	0.041

CI: confidence interval; LVEF: left ventricular ejection fraction; OR: odds ratio.

(CI) = 0.955–0.995, $P = 0.016$), hyperlipidaemia (OR = 1.980, 95% CI = 1.175–3.335, $P = 0.010$), preoperative class of left ventricular ejection function (OR = 1.749, 95% CI = 1.024–2.987, $P = 0.041$) and postoperative degree of AI (OR = 1.880, 95% CI = 1.532–2.308, $P \leq 0.001$) were risk factors for the combined end point.

DISCUSSION

The present study represents probably the largest single-centre cohort of patients who underwent Tirone E. David's AVSRR, with one of the longest follow-up times. This study demonstrates that AVSRR can be performed extremely safely, with low risks for perioperative morbidity and mortality in both elective and emergent settings for acute dissection. With regard to the long-term outcome, AVSRR seems to provide excellent clinical results and sustainable function of the aortic valve in the majority of patients almost 3 decades after its introduction.

Early outcome

The overall in-hospital mortality was relatively low (3.8%). However, the early outcome has to be seen in the light of the patient demographics and indications for surgery.

In our study, one-fifth of the total study population had emergent surgery for acute type A aortic dissection. The in-hospital mortality for the remaining elective cases was 1.9%. This number is acceptable for aortic root replacement especially since many patients underwent additional cardiac procedures. Therefore, we think that these numbers underline the statement that AVSRR is safe. We think that in experienced centres, AVSRR does not pose a higher perioperative risk than conventional composite root replacement. Of course, careful patient selection is mandatory. High-risk patients (e.g. severely reduced left ventricular function) may benefit from a quick conventional operation without the potential risk of conversion from AVSRR to Bentall procedure.

As mentioned before, one-fifth of the whole study population was operated on emergently for acute type A aortic dissection. A recent publication by the German Registry for Acute Aortic Dissection Type A analysed >2000 patients and found a 30-day mortality rate of 16.9% [16]. The early mortality rate in this study is clearly lower and underlines that AVSRR can be applied in emergent settings for acute dissection. Clearly, and as we have pointed out before, AVSRR is usually applied to selected patients if performed in emergent settings for acute aortic dissection [10, 17]. Ideally, AVSRR is performed in young and stable dissection

patients. Unstable patients might benefit more from a quick operation. In acute type A aortic dissection, the primary goal remains to bring the patients out of the operating room alive.

Early complications were also extremely low. Permanent neurological injury occurred in 27 patients, which represents 4% of the entire group. The rate for neurological complications in patients with acute aortic type A dissection was 9% ($n = 13$), and only 2% ($n = 14$) in electively operated patients. This demonstrates that AVSRR can be performed with low neurological complications in elective patients.

The overall rethoracotomy rate was 7% in our study. This may seem higher than expected at first, but again, we would like to emphasize that one-fifth of all patients in this study underwent emergent operations for aortic dissection, and many received additional total aortic arch replacement. The rethoracotomy was 6% for elective cases and 14% for emergent cases for aortic dissection. Having this in mind, the overall rate is acceptable in our opinion and comparable to the rethoracotomy rate of other groups. For instance, Tirone E. David's 20-year experience with his technique reported a rethoracotomy rate of 8.7–9.6% [6].

The early- and long-term performance of the reimplanted aortic valve is highly dependent on the initial success of the reconstruction. Nearly all patients (96%) left the hospital with AI \leq I°. Over a time period of >25 years, we have undergone a learning curve of AVSRR [18]. We always re-evaluate and try to improve our surgical technique. Nowadays, it is our policy not to tolerate moderate AI after repair. If moderate AI is present after repair, it is the policy to reclamp and to either achieve a better repair or convert to composite aortic root replacement.

Long-term outcome

In our opinion, one of this study's strengths is its long-time follow-up of more with >25 years of experience. As to our knowledge, only Tirone E. David's experience has a longer follow-up period. We think that the large sample size and long follow-up time are the key to obtain valid results and in turn draw right conclusions.

The Kaplan-Meier survival curve of the entire population spans >25 years. Long-term survival seems to be excellent during the early years, but after 15–25 years, survival drops further. In our opinion, this does not imply worse outcome of AVSRR, but rather represents the natural course of many patients. One has to remember that this study overlooks a time period of more than 25 years, and the mean age of our patients at the time of surgery was 53 years. In turn, it is expected that some patients, especially the older ones, will cease eventually. This natural course is also underlined by the fact that younger patients of this study, as represented by patients with Marfan syndrome or bicuspid aortic valve, have superior long-term survival. Tirone E. David reports survival rates of 78% and 72% at 15 and 20 years, respectively. This seems to be more admirable at first; however, his patient cohort is also significantly younger. The mean age of David's group is 46 years at the time of surgery [6], while the mean age of our patients was 53 years. The older age at the time of operation also explains the lower long-term survival rates. Furthermore, the rate of patients with acute type A aortic dissection was two- to three-fold as high as in David's cohort. As patients with type A dissection have a higher chance for future aortic-related events and operations, their life expectancy is limited.

The long-term performance of the reimplanted aortic valve is of major importance when performing AVSRR. In our study, a total of 78 reoperations at the aortic valve were necessary, resulting in freedom from reoperation rates of 97%, 93%, 88%, 85%, 81% and 81% at 1, 5, 10, 15, 20 and 25 years, respectively. These numbers are comparable to the results of other centres, although slightly lower than in Tirone E. David's series. Recently, Tirone E. David published an update on his cohort and reported an increasing rate of AI over time [19]. When looking at our data, we have to keep in mind that our study is not a single-surgeon experience but represents the outcome of 24 different surgeons. Every surgeon undergoes a learning curve, which will have an impact on the outcome [18]. In the light of the previous comments, we think that the long-term results of the reimplanted aortic valves in this study are acceptable and AVSRR provides excellent clinical results and sustainable function of the aortic valve in the majority of patients almost 3 decades after its introduction.

When looking at the different patient subgroups in the Kaplan–Meier survival curves, one observes a lower mortality in the long term in Marfan patients and patients with bicuspid aortic valves. This can be explained by the younger age at the time of operation in these 2 subgroups. We have reported our experience of these 2 patient groups previously [8, 11]. Besides long-term survival, it is also important to note that the durability of the reimplanted aortic valve in these 2 subgroups is not majorly worse than in other patients. Especially, in Marfan patients, the long-term performance is absolutely comparable to patients without connective tissue disorders [8]. As we have previously shown, acceptable results in terms of aortic valve durability can also be achieved in patients with bicuspid aortic valve [11]. However, in these patients, very careful patient selection is key to the satisfactory results [20]. The usage of David procedure in emergent situations for aortic dissection has been criticized in the past. However, previous studies have proven the non-inferiority of AVSRR to common techniques such as the Bentall procedure in emergent settings for dissection [17]. The Kaplan–Meier survival graph implies a higher mortality during the early postoperative period in AADA patients, which is clearly attributed to the aortic dissection and its great immediate risk. However, in the following course, the survival curve of the dissection patients is absolutely parallel to the curve of the elective patients, indicating no significant difference between the 2 different groups. We think it is important to note that AVSRR can be used in emergent settings for aortic dissection without having impaired long-term outcome in terms of survival and valve performance. Clearly, the primary goal in operations for aortic dissection, the primary goal remains to bring out the patient alive. However, in young and stable dissection patients, AVSRR is a possible surgical approach.

Risk factor analysis

The Cox regression analysis identified age as a risk factor for the combined end point of aortic valve insufficiency > II° or reoperation of the aortic valve. This is not an unexpected finding, as older patients will not require any further operation due to their limited life expectancy. Hyperlipidaemia was identified as a risk factor as well. This was an unexpected finding, and we could hypothesize that the lipid deposition in the cusp tissue will lead to progressive sclerosis with subsequent aortic valve dysfunction. Furthermore, both the preoperative degree of left ventricular ejection function and postoperative degree of AI were identified

as independent risk factors for the combined end point. This is in line with the results of de Kerchove *et al.* [21], who published previously that reduced left ventricular function and residual AI are predictors of future AI. This underlines the importance of an optimal intraoperative repair result of the aortic valve.

Limitations

This is a retrospective study, with all potential bias linked to this kind of study. Furthermore, there might be selection bias, as the final decision whether to proceed with composite root replacement or AVSRR is made by the operating surgeon. In this study, we reported 672/732 postoperative echocardiography results. Although we strongly think that postoperative echocardiography is mandatory after AVSRR, we could not gather all of these reports due to the retrospective nature of this study. Furthermore, we cannot exclude that some patients who died during follow-up died from aortic valve-related causes.

CONCLUSIONS

This study represents probably the largest single-centre cohort of patients who underwent Tirone E. David's AVSRR, with one of the longest follow-up times. AVSRR can be performed extremely safely, with low risks for perioperative morbidity and mortality. With regard to the long-term outcome, AVSRR seems to provide excellent clinical results and sustainable function of the aortic valve in the majority of patients almost 3 decades after its introduction.

SUPPLEMENTARY MATERIAL

Supplementary material is available at *EJCTS* online.

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Conflict of interest: none declared.

Author contributions

Erik Beckmann: Conceptualization; Data curation; Formal analysis; Investigation; Methodology; Software; Supervision; Validation; Visualization; Writing—original draft. **Andreas Martens:** Conceptualization; Investigation; Methodology; Visualization; Writing—original draft. **Heike Krüger:** Data curation; Methodology; Supervision; Validation. **Wilhelm Korte:** Conceptualization; Investigation; Methodology; Software. **Tim Kaufeld:** Data curation; Formal analysis; Software; Validation. **Alissa Stettinger:** Data curation; Formal analysis; Investigation; Validation. **Axel Haverich:** Conceptualization; Funding acquisition; Methodology; Project administration; Resources; Supervision. **Malakh Lal Shrestha:** Conceptualization; Investigation; Project administration; Resources; Supervision; Writing—review & editing.

Reviewer information

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