A progress report on reimplantation of the aortic valve

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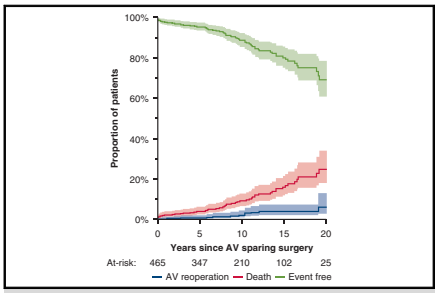
ABSTRACT

Objective: To examine the late outcomes of reimplantation of the aortic valve (RAV) in patients followed prospectively since surgery.

Methods: All 465 patients who had RAV from 1989 to 2018 were followed prospectively with periodic clinical and echocardiographic assessments. Mean follow-up was 10 ± 6 years and 98% complete.

Results: Patients' mean age was 47 ± 5.1 years, and 78% were men. The aortic root aneurysm was associated with Marfan syndrome in 164 patients, Loeys–Dietz syndrome in 13, bicuspid aortic valve (BAV) in 67, and type A aortic dissection in 33. Aortic insufficiency (AI) was greater than mild in 298 patients. Concomitant procedures were performed in 105 patients. There were 5 operative and 51 late deaths. At 20 years, 69.1% of patients were alive and free from aortic valve reoperation, and the cumulative probability of aortic valve reoperation with death as a competing risk was 6.0%, and the cumulative probability of developing moderate or severe AI was 10.2%. Only time per 1-year interval was associated with the development of postoperative AI by multivariable analysis (hazard ratio, 1.06; 95% confidence interval, >1.02-1.10; $P = .006$). Gradients across preserved BAV increased in 5 patients, and 1 required reoperation for aortic stenosis. Distal aortic dissections occurred in 22 patients, primarily in those with associated genetic syndromes.

Conclusions: RAV provides excellent long-term results, but there is a progressive rate of AI over time, and patients with BAV may develop aortic stenosis. Patients with genetic syndromes have a risk of distal aortic dissections. Continued surveillance after RAV is necessary. (J Thorac Cardiovasc Surg 2021;161:890-99)



Estimates of pertinent events after reimplantation of the aortic valve.

CENTRAL MESSAGE

Reimplantation of the aortic valve to treat patients with aortic root aneurysm provides excellent long-term results with slow but progressive aortic valve dysfunction.

PERSPECTIVE

This study provides new insights on late events after reimplantation of the aortic valve. Aortic valve function deteriorates slowly over the years and it may be worse in patients with bicuspid aortic valves. Furthermore, there is a risk of distal aortic dissections in patients with associated genetic syndromes and continued surveillance is necessary.

See Commentaries on pages 900, 901, and 903.

Reimplantation of the aortic valve (RAV) into a tubular Dacron graft was developed in 1989 as method to preserve the native aortic valve (AV) in patients with aortic root aneurysm and normal aortic cusps with or without aortic insufficiency (AI).[1] RAV has been successfully applied to patients with bicuspid aortic valves (BAV), but the late follow-up is not as long as for tricuspid AV.[2] The importance of using a prosthesis with aortic sinuses for RAV remains controversial.[3,4] Studies on longitudinal outcomes of RAV have failed to show that these prostheses improve AV function or durability of the procedure.[5,6] We tailored a tubular Dacron graft at the nadir of the aortic annulus and in between commissures at the level of the sinotubular

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Abbreviations and Acronyms
AI = aortic insufficiency
AV = aortic valve
BAV = bicuspid aortic valve
CI = confidence interval
HR = hazard ratio
IQR = interquartile range
RAV = reimplantation of the aortic valve

junction to fashion aortic sinuses in a number of patients and could find no difference in outcomes up to 15 years of follow-up.[6] We have reverted to implanting the AV into a straight tubular Dacron graft without fashioning sinuses unless necessary to approximate 2 adjacent commissures to improve cusp coaptation. We have been following our patients who had RAV in our hospital, and this paper is a progress report on late clinical outcomes and AV valve function.

METHODS

From August 3, 1989, to December 31, 2018, 465 consecutive patients with aortic root aneurysm had RAV by 3 attending surgeons at Toronto General Hospital. Tables 1 and 2 summarize the clinical profile and operative data. Postoperative transthoracic echocardiograms were obtained before discharge from hospital and every 2 to 5 years in most patients. The median (interquartile range [IQR]) number of echocardiograms for each patient was 4 [3, 6] over the course of their follow-up. Overall, the average number of echocardiograms per patient-year of follow-up was 0.47 echo per patient-year of follow-up. Eleven patients (most nonresidents) were lost to follow-up from 1 to 12 years after surgery. The mean follow-up was 10 ± 6 years and ranged from 1 to 28 years. Only 25 patients were alive and free from reoperation beyond 20 years. This study was approved by the Review Ethics Board of University Health Network, and consent was required from all patients.

Statistical Analysis

Baseline clinical and surgical characteristics as well as perioperative and long-term outcomes were summarized using descriptive statistics. Continuous variables were summarized in terms of median and IQR. Dichotomous and polytomous variables were summarized in terms of frequencies and proportions. Peak and mean systolic gradients in patients with BAV were described using median and IQR. Survival estimates were obtained using the Kaplan–Meier method. The proportion of patients with a reoperation of the AV were estimated using a competing risk model with death as a competing risk. The proportion of patients with either thromboembolism or endocarditis were estimated using competing risk models with death or AV reoperation as a competing risk. AI grade was assessed using postoperative transthoracic echocardiograms. The probability of recurrent moderate or severe AI was estimated using partly conditional mean models because the longitudinal data were truncated by death or reoperation in the AV.[7] The partly conditional mean model was implemented using independent estimation equations (independence estimating equation or generalized estimating equation with independent covariance) with robust sandwich estimators for standard errors. For subjects who had AV reoperation, only echocardiograms done before the reoperation were included in the analysis. Univariable risk factor analysis was performed using Cox regression for all-cause mortality and AV reoperation, and independent estimating equations for postoperative moderate/severe AI. Hazard ratios

TABLE 1. Clinical characteristics of 465 patients who underwent reimplantation of the aortic valve

Median age, y (IQR)	46 (34, 57)
<21	16 (3.4)
21-40	151 (32.4)
41-60	213 (45.8)
61-80	84 (18.0)
>80	1 (0.2)
Sex: men	365 (78.5)
Year of surgery	
1989-2000	66 (14.1)
2001-2010	229 (49.3)
2011-2018	170 (36.6)
Electrocardiogram	
Sinus rhythm	448 (96.3)
Atrial fibrillation	16 (3.4)
Heart block/pacemaker	1 (0.2)
Previous cardiac surgery	
Ross procedure	2 (0.4)
Mitral valve repair	4 (0.9)
Other (including 1 heart transplant)	10 (2.1)
Marfan syndrome	165 (35.4)
Loeys–Dietz syndrome	12 (2.6)
Associated disorders	
Diabetes mellitus	19 (4.1)
Hypertension	173 (37.2)
Hyperlipidemia	104 (22.3)
COPD (FEV1<1)	8 (1.7)
Previous stroke	11 (2.3)
Peripheral vascular disease	6 (1.3)
Renal failure (dialysis)	5 (1.1)
Remote infective endocarditis	5 (1.1)
Coronary artery disease	46 (9.9)
Type A aortic dissection	33 (7.1)
New York Heart Association functional class	
Class I	315 (67.7)
Class II	101 (21.7)
Class III	24 (5.1)
Class IV	25 (5.3)
Left ventricular ejection fraction	
≥60%	324 (69.6)
40%-59%	113 (24.3)
20%-39%	24 (5.1)
Unknown	4 (0.8)
Aortic insufficiency	
None, trivial and mild	136 (29.2)
Moderate or severe	295 (63.4)
Unknown	34 (7.3)
Mitral regurgitation (moderate/severe)	31 (6.6)
Tricuspid regurgitation (moderate/severe)	2 (0.4)
Atrial septal defect	25 (5.3)
Ventricular septal defect	3 (0.6)

(Continued)

TABLE 1. Continued

Aortic valve morphology	
Tricuspid aortic valve	396 (85.1)
Bicuspid aortic valve	67 (14.4)
Pulmonary autograft	2 (0.4)
Aortic root diameter, mm, median (IQR)	52 (50, 55)
Aortic annulus diameter, mm, median (IQR)	29 (26, 33)

Percentages are shown in parentheses unless indicated as IQR. *IQR*, Interquartile range; *COPD*, chronic obstructive pulmonary disease; *FEV1*, forced expiratory volume in 1 second.

(HRs) and odds ratios are reported as appropriate along with 95% confidence intervals (CIs). All pertinent variables in Tables 1 and 2 were examined. Variables with univariable *P* value less than .25 were tested in multivariable models when appropriate. Only variables that remained significant in multivariable models were retained in the final model. Analyses were performed using SAS 9.4 (SAS Institute, Cary, NC) and R version 3.5.3 (R Foundation for Statistical Computing, Vienna, Austria).

RESULTS

Operative Outcomes

The operative mortality was 1% (5 patients). Postoperative complications are listed in Table 3.

Late Mortality

There were 51 late deaths with documented cause as follows: 4 sudden, 5 stroke, 2 myocardial infarction, 2 heart and renal failure, 6 complications of dissection or new aortic aneurysms, 1 unknown, and 31 noncardiovascular. The cumulative proportion of deaths from any cause at 20 years was 24.8% (95% CI, 18.1%-34.1%; Figures 1 and 2 and Table 4). Although age by 5-year increments, functional classes III and IV, left ventricular ejection fraction <60%, coronary artery disease, hypertension, and aortic clamp and cardiopulmonary bypass times were associated with increased mortality by univariable analysis, only age by 5-year increments was significant by

TABLE 2. Operative data

Reimplantation of the aortic valve	465 (100)
Size of graft, mm, median (IQR)	30 (28, 32)
Aortic cusp plication	178 (38.2)
Free margin reinforcement with Gore-Tex	111 (23.8)
Creation of neo-aortic sinuses	153 (32.9)
Mitral valve repair	38 (8.1)
Mitral valve replacement	1 (0.2)
Tricuspid annuloplasty	2 (0.4)
Coronary artery bypass	46 (9.9)
Replacement of aortic arch/hemiarch	52 (11.2)
Closure of atrial septal defect	25 (5.3)
Closure of ventricular septal defect	3 (0.6)
Maze procedure	7 (1.5)
Repair of abdominal aortic aneurysm	1 (0.3)
Cardiopulmonary bypass time, min (IQR)	137 (118-163)
Aortic clamping time, mm (IQR)	113 (98-135)

Percentages are shown in parentheses unless indicated as IQR. *IQR*, Interquartile range.

TABLE 3. Perioperative outcomes

Operative deaths	5 (1)
Ventilation time, h, median (IQR)	5 [4, 9]
Intensive care unit stay, h, median (IQR)	24 [21, 47]
Hospital stay, d, median (IQR)	6 [5, 8]
Reoperations before discharge	
Bleeding/tamponade/arrest	34 (7.3)
Bentall	1 (0.2)
Mitral valve repair (1 perforation; 1 SAM)	2 (0.4)
Repair of ruptured liver after arrest	1 (0.2)
Sternal infection	1 (0.2)
Myocardial infarction	5 (1.0)
Insertion of permanent pacemaker	9 (1.9)
Postoperative new atrial fibrillation	109 (23.4)
Transient ischemic attack	2 (0.4)
Stroke	3 (0.6)
Sepsis with positive blood culture	9 (1.9)
Transfusion of blood products	233 (50.1)

Percentages are shown in parentheses unless indicated as IQR. *IQR*, Interquartile range; *SAM*, systolic anterior motion of the mitral valve.

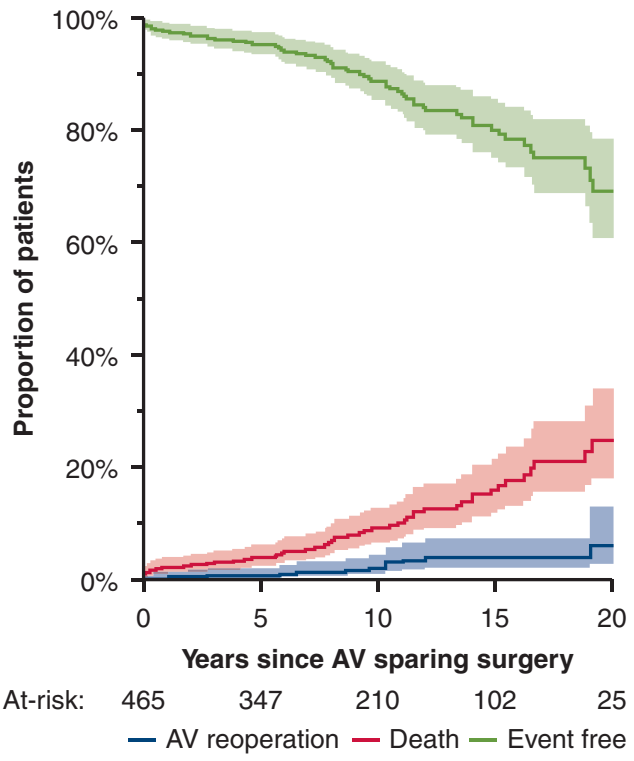


FIGURE 1. Estimates of pertinent events after reimplantation of the aortic valve.

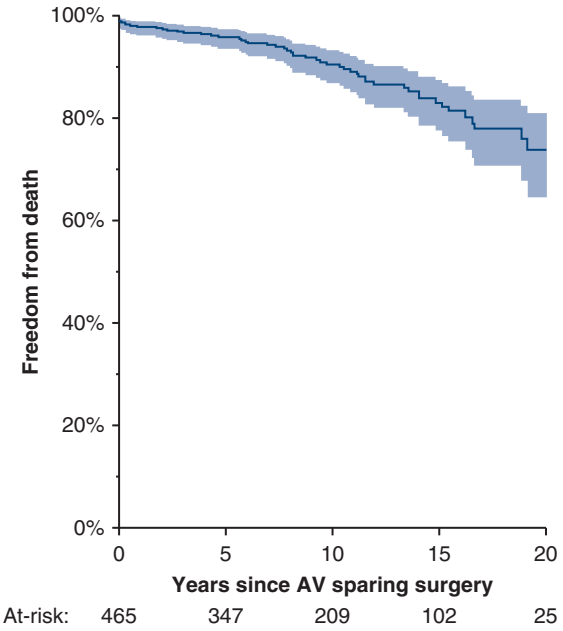


FIGURE 2. Survival following reimplantation of the aortic valve. Estimated survival at 20-year was 75.1% [63.7, 91.4%]. *AV*, Aortic valve.

multivariable analysis (HR, 1.32; 95% CI, 1.18-1.47; $P < .001$). Figure 2 illustrates survival over time (see Appendix E1 and Figure 3 for effect of age on late mortality as a continuous variable).

AV Reoperations

In total, 15 patients had reoperations on the AV from 2 days to 23 years after RAV. The second patient in this series had a Bentall procedure on the second postoperative day because of technical error; 1 patient had AV repair 1 year after RAV for AI due to unexplained cusp perforation (performed by Dr H. J. Schäfers, Germany); 1 patient needed coronary artery bypass and the AV was replaced for moderate AI 9 years after RAV (in Athens, Greece); 1 patient had AV replacement for AI due to cusp detachment from a commissure 9 years after RAV; 1 patient had a Bentall for AI 11 years after RAV (outside hospital); 1 patient had RAV after a failed Ross procedure and developed AI due to pulmonary cusps degeneration 12 years later; 1 patient had a transcatheter AV implantation for AI 20 years after RAV; 3 patients had AV replacement for mixed AV lesions due to BAV disease at 6, 9, and 10 years after RAV; 1 patient had AV replacement for BAV stenosis 6 years after RAV; and 4 patients had Bentall procedure for infective endocarditis at 1, 3, 19, and 23 years after RAV. In addition to AV reoperation, 2 patients had mitral valve surgery (1 repair and 1 replacement) and 1 pulmonary valve replacement (in a Ross patient), and 1 coronary artery bypass. One patient died at reoperation. The cumulative proportion of AV reoperations at 20 years was 6.0% (95% CI, 2.8%-12.9%) (Figure 1 and Table 4). The number of reoperations on the AV was too small for meaningful multivariable analysis. The only variable associated with reoperation on the AV by univariable analysis was BAV (HR, 6.20; 95% CI, 2.07-18.55; $P = .001$).

Other Reoperations

A total of 20 patients had 21 cardiovascular interventions: 6 mitral valve surgeries (5 repair and 1 replacement), 4 thoracoabdominal aneurysm repair, 1 arch replacement with elephant trunk, 4 endovascular stent of the descending thoracic aorta, 1 coronary artery bypass (in a patient with a stent in the descending thoracic aorta), and 5 abdominal aortic aneurysm (4 open and 1 endovascular). One patient died after thoracoabdominal aneurysm repair.

AV Function

Moderate or severe AI developed in 28 patients from 2 days up to 27 years after RAV: 10 patients were reoperated on, 5 died (noncardiovascular deaths), and 12 continue to be followed. Figure 4 and Table 4 shows the cumulative risk of developing moderate and severe AI, which at 20 years was

TABLE 4. Cumulative proportions of adverse events over time shown as percentages and 95% confidence intervals inside the brackets

Variable/time	10 y	15 y	20 y
Death from any cause	9.2 [6.5-12.9]	16.0 [11.9-21.5]	24.8 [18.1-34.1]
Event-free survival*	88.7 [85.3-92.2]	80.1 [75.1-85.4]	69.1 [60.9-78.5]
Aortic valve reoperation	2.1 [1.0-4.5]	4.0 [2.2-7.3]	6.0 [2.8-12.9]
Cumulative proportion with death or aortic valve reoperation as a competing risk			
Thromboembolism	5.1 [3.3-8.0]	5.9 [3.7-9.3]	8.8 [5.0-15.5]
Endocarditis	0.5 [0.1-1.8]	0.5 [0.1-1.8]	2.5 [0.5-12.3]
Pacemaker implantation	5.0 [3.2-7.7]	6.0 [3.9-9.3]	6.0 [3.9-9.3]
Distal aortic dissection	2.1 [0.9-4.7]	6.1 [3.5-10.6]	13.8 [7.6-25.1]
Estimates of moderate/severe AI using generalized estimating equations			
Moderate/severe AI	5.3 [3.7-7.4]	7.3 [4.7-11.2]	10.2 [5.7-17.4]

AI, Aortic insufficiency. *Alive and free from reoperation.

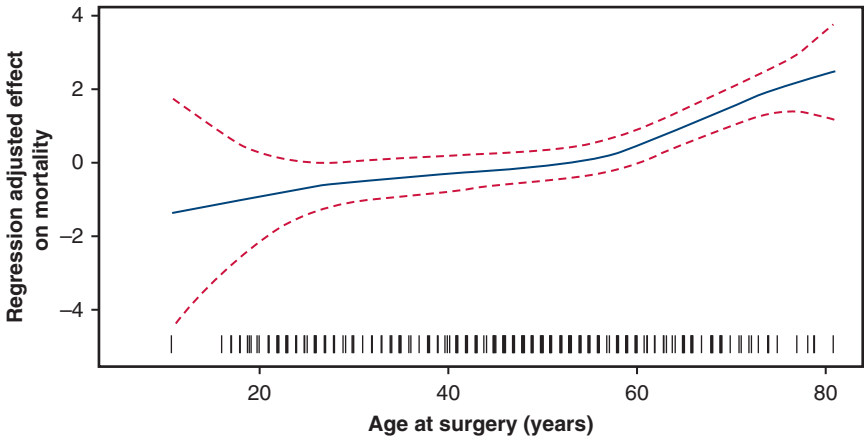


FIGURE 3. Effect of age on patients' mortality over time. The regression-adjusted effect of age on mortality suggests there might be a change point between 55 and 60 years of age.

10.2% (95% CI, 5.7%-17.4%). Time since surgery, preoperative aortic dissection, preoperative moderate or severe AI, and BAV were associated with increased risk of postoperative AI by univariable analysis, but only time since surgery by 1-year increments was associated with the development of postoperative AI by multivariable analysis (HR, 1.06; 95% CI, 1.02-1.10; $P = .006$). Only 1 patient with tricuspid AV is developing aortic stenosis (mean systolic gradient of 20 mm Hg at 19 years after surgery). In patients with BAV, the peak systolic gradients did not increase significantly (12.9 to 15 mm Hg, $P = .9$) during a mean follow-up of 8 ± 5 years, but 5 patients developed peak systolic gradients >40 mm Hg, mean gradients of >20 mm Hg, and 1 needed reoperation for severe aortic stenosis (AV area of 0.75 cm^2) 6 years after RAV.

New Aortic Dissections

In total, 22 patients developed new distal aortic dissections (19 in patients with Marfan or Loeys–Dietz syndromes) several years after RAV. Figure 5 and Table 4

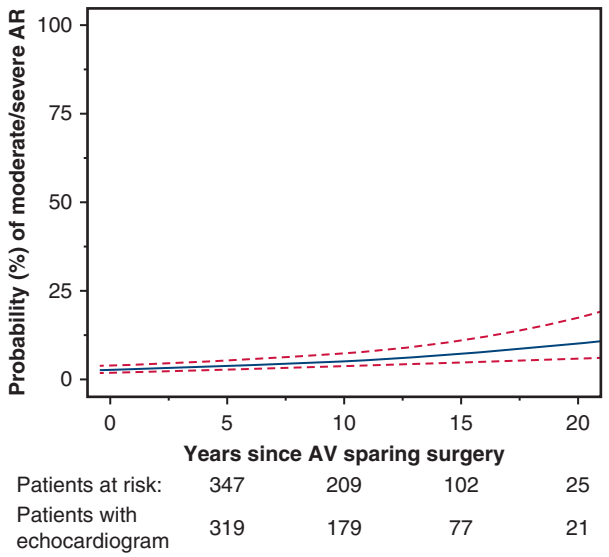


FIGURE 4. Development of moderate or severe aortic insufficiency after reimplantation of the aortic valve. Estimates of aortic insufficiency over time using generalized estimating equations: at 20 years 10.2% (95% confidence interval, 5.7%-17.4%) developed moderate or severe aortic insufficiency. *AR*, Aortic regurgitation; *AV*, aortic valve.

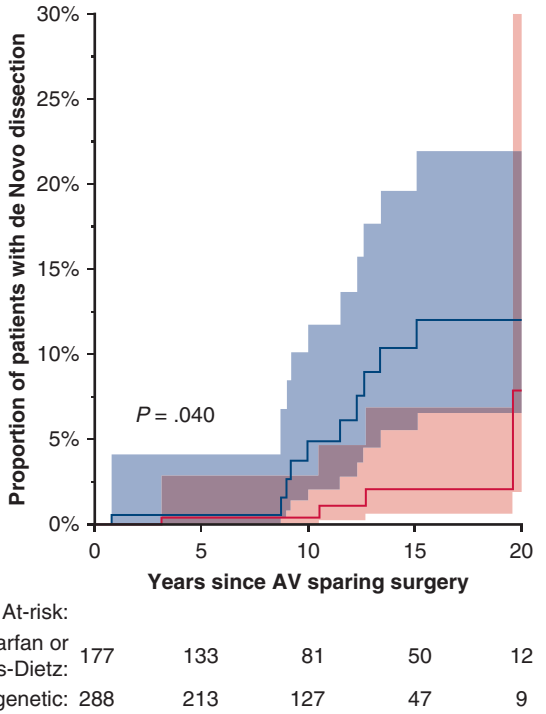


FIGURE 5. Cumulative probability of distal aortic dissection after reimplantation of the aortic valve. Patients with associated genetic syndromes were at a greater risk of developing this complication. For all patients, the cumulative proportion at 20 years was 13.8+% (95% confidence interval, –7.6% to 25.1%). *AV*, Aortic valve.

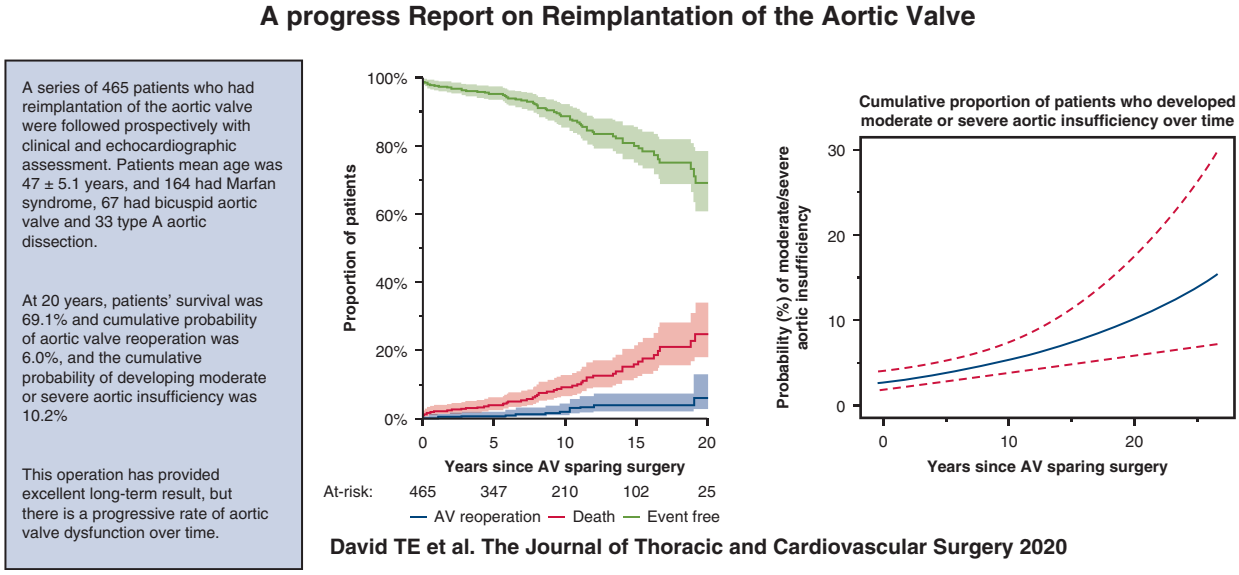


FIGURE 6. A series of 465 patients had reimplantation of the aortic valve, and the cumulative probability of reoperation on the aortic valve was 6% at 20 years. *AV,* Aortic valve.

show the cumulative probability of new aortic dissections over time.

Other Adverse Events

Four patients developed infective endocarditis of the AV (3 aortic root abscess and 1 graft infection 1-23 years after RAV) and all required reoperation with a Bentall procedure. One patient died. The cumulative risk of infective endocarditis in the AV at 20 years was 2.5% (95% CI, 0.5%-12.3%). Three other patients developed endocarditis of the mitral valve and 2 were medically treated and 1 had mitral valve repair. All 3 survived.

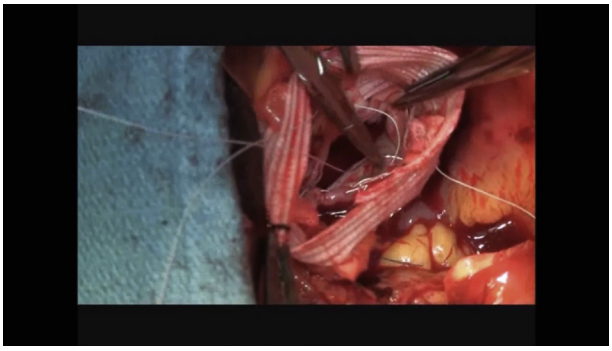
Eleven patients suffered a stroke (4 died) and 15 had 1 or more transient ischemic attacks. The cumulative proportion of thromboembolism at 20 years was 8.8% (95% CI, 5.0%-15.5%).

Nine patients required implantation of permanent transvenous pacemaker while in hospital, and 13 patients had during the follow-up period. The cumulative proportion of patients requiring pacemaker was 2.2% (95% CI, 1.2%-4.0%) at 1 year and 6.0% (95% CI, 3.9%-9.3%) at 20 years.

DISCUSSION

This study indicates that RAV is a durable operation and it is associated with relatively low adverse events during the first 2 decades of follow-up. AV dysfunction appears to be progressive but at a slow rate. After a mean follow-up of 10 years, only 28 patients developed moderate or severe AI. The cumulative proportion of patients with moderate or severe AI was only 10.2% at 20 years, whereas the probability of reoperation in the AV was only 6.0% (Figure 6). It is important to notice that more than one-half of our patients needed cusp repair either by plication of its central portion along the nodule of Arantius or by weaving a double layer of a fine expanded polytetrafluoroethylene suture along its free margins from commissure to commissure in patients with large stress fenestrations. This was not done entirely because of elongated or prolapsing cusp but also because of mismatch between the size of graft chosen from the RAV and the length of the free margin of the cusps. Thus, if a smaller-than-ideal size of graft is used, 1 or more cusps will prolapse and shortening along the nodule of Arantius solves this problem. Conversely, if a graft larger than ideal is used, the cusp my not reach the geometric center of the reconstructed root and plication of the graft along the sinotubular junction is needed to allow the cusp to move more centrally. Cusp repair or creation of neoaortic sinuses had no adverse effect on AV function over time. Cusp repair has allowed the expansion of RAV to young patients who otherwise would have a Bentall with a mechanical valve.

Are our results reproducible? In our cardiac unit, there has been no difference in outcomes among 3 surgeons who perform this operation using similar techniques. Mentoring has been very important in maintaining consistent outcomes during the learning curve of surgeons performing RAV. However, once the technical hurdles are overcome, late outcomes become an issue of patient selection, which hinges on the quality of the aortic cusps in patients with tricuspid AV. We have been relatively conservative in selecting patients for RAV, and this operation is not performed if the cusps are sclerotic, shortened, or calcified. Overstretched and flattened cusps sometimes seen in patients



VIDEO 1. Reimplantion of the aortic valve in a young patient with Marfan syndrome and aortic cusps with stress fenestrations. Video available at: https://www.jtcvs.org/article/S0022-5223(20)32560-5/fulltext.

with excessively large aortic root aneurysms are not preserved either. The size of the aneurysm and the degree of AI is less important than the quality of aortic cusps to select patients for RAV. The patient in Video 1 was a teenager with associated genetic syndrome and all 3 cusps had large stress fenestrations and we decided to preserve the AV. We tend to be more aggressive in preserving the AV in younger patients than we are in older, particularly older than 70 years.

We introduced RAV in 1989 to treat aortic root aneurysm in patients with tricuspid AV with near normal cusps.[1] We did not use it in BAV until the year 2000, and initially only in patients with commissures oriented at approximately 180°. Patients with Sievers' type 0 BAV will probably have as good long-term results as patients with tricuspid AV. However, Sievers' type 1 is a very heterogeneous subgroup, and there is no agreement on how to reimplant this type of BAV. The group from Belgium believes that realignment of the 2 commissures to 180° is important for durability of the repair.[8,9] Other investigators believe that the geometric configuration of the cusps should be maintained during reimplantation of the BAV.[10,11] Longer follow-up with objective assessment of valve function is needed to determine the usefulness of reimplantation of the AV in Sievers' type 1 BAV and how to align the commissures inside the graft. Our experience with BAV is limited by the sample size and by the duration of follow-up. Mokashi and colleagues[12] from the Cleveland Clinic reported on a series of 92 patients and the freedom from reoperation after RAV for BAV of 77% at 8 years, whereas it was 98% for tricuspid AV. de Kerchove and colleagues[13] suggested that RAV is a more appropriate approach to treat patients with BAV than AV valve repair because annuloaortic ectasia is a frequently associated lesion. Those investigators recently published the outcomes of RAV in 440 patients and the freedom from reoperation at 10 years was approximately 90% and similar for both BAV and tricuspid AV.[14] The greater rate of reoperation reported by this experienced group of aortic surgeons from Belgium is likely due to more liberal patient selection. The proportion of patients with BAV was much greater than in our series, and they included patients who needed patch repair of the AV cusps.[14] Among 19 patients who required reoperation, 3 had aortic stenosis.[14] Therefore, it may be important to include peak and mean systolic gradients over time in studies on longitudinal outcomes after RAV in patients with BAV.

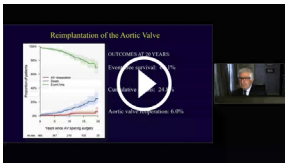
As with any patient with heart valve disease, patients undergoing RAV require lifelong surveillance not only for AV failure but also for other cardiac and vascular complications such aortic dissections, other aneurysms, thromboembolism, anticoagulation-related hemorrhage, and endocarditis, as described in this study. Distal aortic dissection is a serious complication after RAV, particularly in patients with associated genetic syndromes. The recognition of this problem is not new.[15,16] An observational study by den Hartog and colleagues[16] on 600 patients with Marfan syndrome from a Dutch registry examined the issue of distal aortic dissections. They excluded patients who had previous aortic dissections but included 194 patients who had prophylactic aortic root surgery, either before or during the median observation time of 6 years.[16] Distal aortic dissections occurred in 54 patients for an annualized rate of 1.5%. Multivariable analysis identified an association of aortic root surgery and a descending thoracic aorta diameter >27 mm with late type B aortic dissection.[16] The authors speculated that replacement of the ascending aorta with a noncompliant Dacron graft may result in greater pulsatile forces on the aortic arch and proximal descending thoracic aorta, increasing the risk of dissection.[16] Studies using time-resolved 3-dimensional magnetic resonance phase contrast imaging (4-dimensional flow magnetic resonance imaging) reveal that RAV into a prosthesis with aortic sinuses result in blood flows that resemble that of a normal aortic root, particularly when compared with RAV into a straight graft.[17,18] However, a more recent study indicates grossly abnormal blood flow in the ascending aorta after RAV regardless of the type of prosthesis used.[19] This type of research is extremely important to lead us to the best surgical approach to treat patients with aortic root aneurysms. At present, clinical experience far exceeds the scientific basis of most operations we do and RAV into a straight tubular Dacron is no exception. It remains to be proven that a Dacron graft with aortic sinuses will enhance the durability of the AV or reduce the risk of distal aortic dissections.

CONCLUSIONS

RAV has now been performed for 3 decades in our cardiac unit, and the long-term results have been excellent. Surgical expertise and patient selection play an important role in the long-term outcomes. AV dysfunction occurs slowly over the years, and these patients may also develop other vascular complications. Continued medical surveillance for late valvular and vascular complications is essential.

Webcast

You can watch a Webcast of this AATS meeting presentation by going to: https://aats.blob.core.windows.net/media/20AM/Presentations/Reimplantation%20of%20the%20Aortic%20Valve%20i.mp4.



Conflict of Interest Statement

The authors reported no conflicts of interest.

The *Journal* policy requires editors and reviewers to disclose conflicts of interest and to decline handling or reviewing manuscripts for which they may have a conflict of interest. The editors and reviewers of this article have no conflicts of interest.

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Key Words: aortic valve–sparing operation, reimplantation of the aortic valve, David operation, aortic root aneurysm, aortic insufficiency

Discussion

Presenter: Dr Tirone E. David

Dr Ismail El-Hamamsy (*New York, NY*). Thank you. It is my privilege to discuss this paper by Dr David and the Toronto group. This series is notable not only for the excellent short- and long-term results, but importantly for the quality and the completeness of patient follow-up, both clinical and echocardiographic, despite the 30-year span of the study. This serves as an example to all surgeons, young or established, illustrating the critical role of longitudinal assessment of surgical results to advance science and improve our outcomes.

This is all the more significant when the target population is a young one, such as for reconstructive root surgery. It will never be enough to talk about 30-day or 1-year results. Long-term outcomes represent the truly relevant questions for these patients, and systematic follow-up is the only means to attain that, as Dr David continues to demonstrate.

Furthermore, your study clearly shows that achieving excellent surgical outcomes is a combination of 2 things: meticulous surgical technique and careful patient selection.

Over a 30-year period, 465 patients underwent reimplantation procedures by 3 surgeons at the Toronto General Hospital. While these were carefully selected, nevertheless 33 patients were acute type A dissections, 27 were redo operations, and 177 patients had a connective tissue disorder.

In addition, 63% of the cohort had more than mild aortic insufficiency preoperatively. With that in mind, your results provide further confirmation that aortic valve reimplantation is an excellent operation. At the same time, your data highlight 2 important points. The first is the continued risk of acute aortic dissections in the downstream aorta, especially in patients with connective tissue disorders.

Second, your reported rate of stenosis in patients with bicuspid aortic valves undergoing reimplantation: of the 67 patients with bicuspid aortic valves, 5 developed stenosis. While the numbers are too small to draw any definitive conclusions, it certainly gives pause and sheds some light as to potential modes of failure.

I have 3 questions. My first is: Your data clearly confirm that valve-sparing reimplantation is associated with excellent long-term clinical outcomes in selected patients. Based on these results, would you agree or disagree that it is justified to be a bit more liberal in the patient selection process to avoid prosthetic valve complications?

In other words, do you think that reoperation is the main metric to measure the success or failure of choosing reimplantation, or should we accept a slightly greater rate of reoperation if survival and quality of life can be close to normalized?

Dr Tirone E. David (*Toronto, Canada*). I don't know the answer to this question. However, every time you develop something new, you better be very careful what you say and what you publish. I've been extremely careful—and to be quite honest, until some 10 years ago, I was extremely selective. I would not do this operation in many patients that I watched other surgeons doing without reservation.

I had been highly conservative, and perhaps that's why the results are the way they are. We have been more liberal lately. We are including patients with minor calcification in bicuspid aortic valves, and more defective tricuspid aortic valves. I can tell you that one technique that surprised me (and on which we are planning to publish a paper) is Gore-Tex in the free margin, particularly in patients with Loeys–Dietz syndrome or Marfan—provides great results at 15 and 20 years.

In other words, in young people (17, 18 years old) with a defective tricuspid aortic valve, it's a tragedy to put in a mechanical valve in that age group. So, we have saved many of them and, to my surprise, 15 years later, those valves are working as well as those that are defect-free. So that's the only area where I extend the indication.

But you're probably right, now as we have a reoperation rate of 6% at 20 years, which is probably lower than with mechanical valves, we should be more liberal in the use of this operation and include patients with diseased cusps.

The input from Laurent would be important because Gebrine El Khouy has been more liberal with this operation and I would ask Laurent to make a comment in this regard.

Dr Laurent De Kerchove (*Brussels, Belgium*). The Gore-Tex technique maybe a better technique than what we usually thought. We actually think that it may favor calcification in bicuspid valve and we stopped using it in this indication. But in tricuspid, we have not the same impression, and we showed in our presentation today that it reduced the occurrence of aortic insufficiency, and it's probably a good technique to explore more for the tricuspid valve.

Dr David. But maybe it's important to mention something about technique. Gebrine changed the way he learned with us. We weave the Gore-Tex suture along the free margin by passing in and out the leaflet. The Gore-Tex becomes part of the body of the cusp. Gebrine runs over and over. Isn't this the reason for the calcification? If you expose a Gore-Tex to the trauma of the cardiac cycle, in other words, every time the aortic valve opens and closes, it will be banging against the Gore-Tex. I use 7-0 Gore-Tex to reinforce these cusps.

Dr El-Hamamsy. So are you suggesting that the Gore-Tex would be a better tool to correct leaflet prolapse than just central plications?

Dr David. Overstretched leaflets may contain large stress fenestration; they are not congenital. I believe these cusps are better repaired with Gore-Tex than central plications

Dr El-Hamamsy. Looking at the aortic dissection figure, as you mentioned, the inflection point occurs about 8 to 10 years after surgery. If any of these patients had imaging leading to the dissection, were these the current normal aortic diameters, or where they dilated at the time of surgery?

Dr David. I'm sorry to say we don't have this information; we tried to collect, because there are other papers showing similar outcomes after Bentall, and they correlate well with size of the descending thoracic aorta. Twenty-seven millimeters was the cut-off for patients with Marfan syndrome. Patients with a descending thoracic of 27 or larger had a greater risk of dissection.

We don't have sequential magnetic resonance imaging and computed tomography scans to give this answer. We have been collecting this information since Maral

Ouzounian joined in the past 5 years. But it's going to take another 5 or 10 years to get the answer.

Dr El-Hamamsy. Finally, the notion that bicuspid aortic valve preservation can result in stenosis in the long-term obviously gives some pause. In a separate series, the Homburg group also shows the cumulative incidence of about 8% at 15 years, not unlike your results. Do you want to comment on possible anatomical or technical factors that may predict or prevent the occurrence of stenosis, and do you think that this is enough reason to be less liberal with the use of reimplantation in this setting?

Dr David. Just like our results in tricuspid are unique, so are Hans-Joachim Schäfers' long-term results in bicuspid. He must know something that the rest of us don't. I don't know why in bicuspid aortic valve he has so few failures. No stenosis. Is it patient selection, or is he doing something that we may not have grasped yet? I can tell you that in reimplanting a bicuspid aortic valve, the results are very different, and largely dependent on the phenotype. In my hands, very small number of cases; I've done maybe 40 of the 67 reported. If the cusps were oriented at 180°, I have no failures at 15 years. The moment you start taking bicuspid aortic valve with tricuspid phenotype, in other words, commissures at almost 120° from each other, the results are not as good. But this reflects from personal experience. Again, I think Gebrine has the largest experience on reimplantation of bicuspid aortic valve, and Laurent may have a comment to complement what I said.

Dr De Kerchove. Anyone who pushes the limits in bicuspid valve repair will experience long-term stenosis. The Homburg group achieved 15-, 20-year follow-up, and they reported 10% of stenosis after 15 years follow-up and that's what we observed, too.

In the patients we operated on for bicuspid valve at the age of 40 years due to regurgitation, we saved the valve from being replaced, but approximately 15% of those valves, after 15 to 20 years, will become stenotic and that is part of the natural history of the bicuspid valve. With a strict patient selection, exactly as Tirone says, repairing only symmetric valve and discarding the very asymmetric ones, we may reduce this rate of long-term stenosis.

Also, to reduce risk of stenosis, as explained earlier in the discussion, we have stopped using Gore-Tex in the bicuspid valve. And the third important aspect is that when you do a repair, you have to take care that the fused cusp repaired with central plication is still moving. If it's not moving, it will create a gradient that will continue to increase following the operation.

Finally, avoid patch repair, and avoid repairing bicuspid valves that already have calcification may also of course reduce the risk of late stenosis.

Dr Ruggero De Paulis (*Rome, Italy*). The last paper on this subject was published together, by the group from Brussels and Schäfers in Homburg. They just demonstrated that in the asymmetric group, the result was exactly as Tirone David was saying now. I think, with respect to the first initial years, we are learning much more how to treat the bicuspid valve and how to select it; this will probably change over time. For instance, I started to treat bicuspid valves more or less about 14 years ago, and I can tell you that in the last 5 or 6 years, the technique has already changed. So today, we are much more confident even in the long-term results.

Another point: we certainly do not have a huge number of cases, but still around 50 cases and we don't have yet a reoperation for stenotic bicuspid valve so far, but of course we have to consider that the long-term follow-up is only around 10 years.

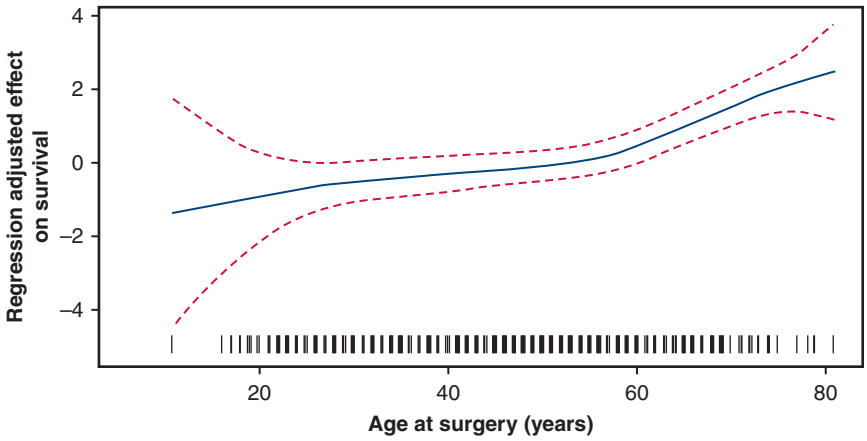
Dr Vaughn A. Starnes (*Los Angeles, Calif*). Tirone, such a great experience with the patients with Marfan syndrome. Are there some patients that you don't do—some cusp size, annular size, in that Marfan group?

Dr David. Yes, of course. On the basis of age, Laurent made a good point: if the patient is 20, 30, 40 years old, the alternative to valve-sparing would be a Bentall with a mechanical valve. We don't do very well with mechanical valves in Toronto. Our population is very heterogeneous, and anticoagulation in our patients is not simple.

If the patient is highly educated yes, we don't repair and use a mechanical valve. But these are the cases in the past decade we are now repairing more and more. That's why I mentioned Gore-Tex. You can take a cusp that is literally flat and create convex-concave again by weaving a double layer of Gore-Tex suture and free margin is shortened at the same time. In those patients, if they are younger than 40 years, we repair. If they are over 40 or 50 years, we tend to replace them. We simply don't have a good alternative to mechanical valves in young patients.

APPENDIX E1

Patients' age was examined as a continuous variable and to address potential nonlinear effects of age on mortality, an exploratory analysis was performed to quantify the association of age using penalized splines with 4 degrees of freedom in current covariate adjusted proportional hazard regression model. The results showed that the overall association of age with mortality was statistically significant (overall $P < .001$), but the nonlinear component of this association was not ($P = .12$). Figure 3 shows the regression-adjusted effect of age on mortality and suggests there might be a change point between 55 and 60 years of age at surgery. Nonetheless, the evidence was not strong.



We also performed a similar analysis for the proportional hazard model for reoperation. The results of the exploratory analysis were consistent with the current results, and the data do not provide strong evidence of a nonlinear association of age at surgery with reoperation ($P = .18$).