Long-Term Outcomes of the Ross Procedure Versus Mechanical Aortic Valve Replacement

Propensity-Matched Cohort Study

Editorial, see p 586

BACKGROUND: The ideal aortic valve substitute in young and middle-aged adults remains unknown. We sought to compare the long-term outcomes of patients undergoing the Ross procedure and those receiving a mechanical aortic valve replacement (AVR).

METHODS: From 1990 to 2014, 258 patients underwent a Ross procedure and 1444 had a mechanical AVR at a single institution. Patients were matched into 208 pairs through the use of a propensity score. Mean age was 37.2±10.2 years, and 63% were male. Mean follow-up was 14.2±6.5 years.

RESULTS: Overall survival was equivalent (Ross versus AVR: hazard ratio, 0.91, 95% confidence interval, 0.38–2.16; *P*=0.83), although freedom from cardiac- and valve-related mortality was improved in the Ross group (Ross versus AVR: hazard ratio, 0.22; 95% confidence interval, 0.034–0.86; *P*=0.03). Freedom from reintervention was equivalent after both procedures (Ross versus AVR: hazard ratio, 1.86; 95% confidence interval, 0.76–4.94; *P*=0.18). Long-term freedom from stroke or major bleeding was superior after the Ross procedure (Ross versus AVR: hazard ratio, 0.09; 95% confidence interval, 0.02–0.31; *P*<0.001).

CONCLUSIONS: Long-term survival and freedom from reintervention were comparable between the Ross procedure and mechanical AVR. However, the Ross procedure was associated with improved freedom from cardiac- and valve-related mortality and a significant reduction in the incidence of stroke and major bleeding. In specialized centers, the Ross procedure represents an excellent option and should be considered for young and middle-aged adults undergoing AVR.

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Clinical Perspective

What Is New?

- There is a paucity of long-term (≥20 years) data comparing outcomes between the Ross procedure and mechanical aortic valve replacement (AVR); we therefore conducted a propensity-matched cohort study with the objective of comparing long-term survival and adverse valve-related events between the 2 approaches.
- We found that the Ross procedure was associated with improved freedom from cardiac- and valve-related mortality compared with mechanical AVR.
- Furthermore, patients receiving mechanical AVR had significantly worse freedom from stroke and major hemorrhage. Surprisingly, the risk of valve reintervention was not different between the Ross and mechanical AVR groups.

What Are the Clinical Implications?

- The clinical implication of this study is that young and middle-aged adults requiring AVR may benefit from a Ross procedure.
- The long-term freedom from stroke and major hemorrhage should be considered in discussions of valve replacement options.
- Findings from this study suggest that in specialized centers, the Ross procedure represents an excellent option and should be considered for young and middle-aged adults undergoing AVR.

Young and middle-aged adults with diseased aortic valves constitute a challenging population. Because of their longer anticipated life expectancy, these patients present a higher cumulative lifetime risk of prosthesis-related complications. The ideal aortic valve substitute in this patient population should allow improved survival, avoidance of reoperation and prosthesis-related complications, and maintenance of an active lifestyle with a good quality of life.

As a result of their proven durability and ease of implantation, mechanical prostheses have long been the most frequently used option for aortic valve replacement (AVR) in young and middle-aged adults. However, recent reports suggest an excess in long-term mortality in young patients who undergo mechanical AVR compared with the age- and sex-matched general population.[1,2] In addition, for female patients of childbearing age, mechanical prostheses are associated with an increased risk of thromboembolic events and warfarin-associated fetal malformations.[3,4]

The Ross procedure (pulmonary autograft replacement) alleviates the need for lifelong anticoagulation. It allows the replacement of the diseased aortic valve with a living substitute,[5] thus allowing adaptive remodeling and conferring a hemodynamic profile similar to that of the native aortic valve. Several recent studies have shown that the Ross procedure may confer long-term survival equivalent to that of the age- and sex-matched general population.[6–10] Despite these excellent long-term outcomes, the Ross procedure has been the object of much criticism because of the complexity of surgical implantation, the exposure to a broad spectrum of complex reoperations, and the notion of transforming a single-valve disease into a double-valve disease.[11,12] As a result, the routine use of this procedure has not gained widespread adoption and is limited to a few centers worldwide.

There is a paucity of data comparing outcomes between the Ross procedure and mechanical AVR in young and middle-aged adults,[13–16] and no longitudinal study comparing long-term (≥20 years) outcomes between these 2 techniques has been published. Furthermore, a randomized trial is unlikely to be feasible because most surgeons and patients have a clear preference for a particular approach in this population. We therefore conducted a propensity-matched cohort study with the objective of comparing long-term survival and adverse valve-related events among patients undergoing the Ross procedure and those receiving mechanical AVR.

METHODS

Patient Population

Between February 1990 and August 2014, 258 consecutive patients underwent a Ross procedure and 1444 underwent mechanical AVR at the Toronto General Hospital, Peter Munk Cardiac Center. Patients with acute aortic dissection or active endocarditis or requiring emergency surgery were excluded from the present study. To mitigate the effects of measurable baseline confounders, patients were matched into 208 pairs through propensity score matching. Baseline characteristics of the propensity-matched cohort are given in Table 1. Mean age was 37.2±10.2 years (range, 16–63 years), and 63% were male. The indication for surgery was aortic stenosis in 189 patients (45%), aortic insufficiency in 152 (37%), and mixed pathology in 75 (18%). The vast majority of the Ross procedures were performed by a single surgeon (T.E.D.), who also performed nearly half of the mechanical AVRs.

Operative Details

Intraoperative details are presented in Table 1. In the mechanical AVR group, 180 patients (87%) received a St. Jude mechanical prosthesis (St. Jude Medical, Saint Paul, MN), and 28 patients (13%) received a CarboMedics mechanical prosthesis (LivaNova PLC, Saluggia, Italy). All patients in the mechanical AVR group were started on lifelong oral anticoagulation with warfarin, with a target international normalized ratio of 2 to 3.

The operative techniques used in the Ross patients have been described elsewhere.[7,17,18] Briefly, the pulmonary autograft was secured in the aortic position with a modified subcoronary implantation or aortic root inclusion technique in

Table 1. Baseline Characteristics of the Matched Cohort

Variables	Ross Procedure (n=208)	Mechanical AVR (n=208)	*P* Value
Age at surgery, mean±SD, y	37.3±9.5	37.1±10.9	0.89
Male sex, n (%)	133 (63.9)	130 (62.5)	0.84
Year of surgery, n (%)			0.01
1990–1995	45 (22.0)	76 (36.5)	
1996–2000	73 (35.1)	67 (32.2)	
2001–2005	45 (21.6)	34 (16.4)	
2006–2010	28 (13.5)	22 (10.6)	
2011–2014	17 (8.2)	9 (4.3)	
Surgeon, n (%)			<0.001
Surgeon A	2 (1)	42 (20)	
Surgeon B	201 (96)	102 (49)	
Other surgeon	5 (2)	64 (31)	
Previous cardiac interventions, n (%)			
Any previous cardiac surgery	41 (19.7)	45 (21.6)	0.72
Previous aortic valve surgery	31 (14.9)	31 (14.9)	1.00
Previous nonsurgical catheter interventions	12 (5.8)	13 (6.2)	1.00
Cardiovascular risk factors, n (%)			
Hypertension	41 (19.7)	42 (20.2)	1.00
Hyperlipidemia	27 (13.0)	20 (9.6)	0.35
Diabetes mellitus	3 (1.4)	5 (2.4)	0.73
Current or previous smoker	102 (49.0)	80 (38.7)	0.04
Associated conditions, n (%)			
Healed endocarditis	9 (4.3)	8 (3.9)	0.80
Chronic obstructive pulmonary disease	4 (1.9)	1 (0.5)	0.37
Previous stroke or transient ischemic attack	7 (3.4)	10 (4.8)	0.62
Myocardial infarction within 30 d	5 (2.4)	2 (1.0)	0.45
Atrial fibrillation or flutter	2 (1.0)	7 (3.4)	0.14
Left ventricular ejection fraction <40%	16 (7.7)	25 (12.0)	0.19
Clinical presentation, n (%)			
Angina pectoris	45 (21.6)	36 (17.3)	0.32
Congestive heart failure	36 (17.3)	49 (23.6)	0.14
Syncopal episodes	16 (7.7)	23 (11.1)	0.31
NYHA functional class, n (%)			<0.001
I	38 (18.3)	51 (24.5)	
II	132 (63.5)	90 (43.3)	
III	32 (15.4)	47 (22.6)	
IV	6 (2.9)	19 (9.1)	
Aortic valve lesion, n (%)			<0.001
Stenosis	119 (57.2)	70 (33.7)	
Insufficiency	54 (26.0)	98 (47.1)	
Mixed lesion	35 (16.8)	40 (19.2)	

(*Continued*)

Table 1. Continued

Variables	Ross Procedure (n=208)	Mechanical AVR (n=208)	*P* Value
Aortic valve pathology, n (%)			
Bicuspid	151 (72.6)	101 (48.6)	<0.001
Other congenital	24 (11.5)	15 (7.2)	0.21
Tricuspid calcific	4 (1.9)	13 (6.3)	0.04
Rheumatic	4 (1.9)	26 (12.5)	<0.001
Operative data			
Autograft implantation technique, n (%)			
Inclusion or modified subcoronary	104 (50.0)	…	
Root replacement	104 (50.0)	…	
Concomitant procedures, n (%)			
Coronary artery bypass grafting	6 (2.9)	6 (2.9)	1.00
Mitral valve surgery	5 (2.4)	17 (8.2)	0.01
Tricuspid valve repair	0 (0.0)	3 (1.4)	0.25
Ascending aortic replacement	69 (33.2)	76 (36.5)	0.54
Cross-clamp time, median (IQR), min	125 (116–137)	70 (54–99)	<0.001
CPB time, median (IQR), min	144 (133–156)	92 (73–123)	<0.001

AVR indicates aortic valve replacement; CPB, cardiopulmonary bypass; IQR, interquartile range; and NYHA, New York Heart Association.

104 patients (50%) and as a free-standing neoaortic root in 104 patients (50%). The choice between an inclusion technique or a root replacement was dictated largely by the pathology of the aortic root, sizes of the native aortic and pulmonary roots, and anatomy of the coronary arteries. In an attempt to prevent late malfunction of the pulmonary autograft, surgical reduction of the aortic annulus and/or sinotubular junction was performed before implantation of the pulmonary autograft in the aortic position if the aortic root was larger than the pulmonary root by >2 to 3 mm, as previously published.[19]

Data Sources

This observational, single-center, cohort study was approved by the Review Ethics Board of University Health Network (Toronto, ON, Canada), and a waiver of consent was obtained. Perioperative data were entered prospectively into an institutional clinical database. Patients were contacted by phone or electronically to determine morbid outcomes and to confirm vital status. Echocardiogram reports were reviewed, and patients' cardiologists were contacted to determine valve-related complications. The follow-up period was closed on September 1, 2014. Clinical follow-up (or terminal event) was available for 98.3% of patients with a mean follow-up duration of 14.2±6.6 years postoperatively, for a total of 5906 patient-years. Mean follow-up was 13.6±5.8 years in the Ross group and 14.8±7.2 years in the mechanical AVR group (*P*=0.07). Echocardiographic follow-up was available for 90% of patients with a mean follow-up duration of 11.0±9.5 years in the Ross group and 12.5±10.2 years in the mechanical AVR group (*P*=0.14).

Study Outcomes

All outcomes of interest were reported according to the American Association for Thoracic Surgery "Guidelines for Reporting Mortality and Morbidity After Cardiac Valve Interventions."[20] The primary outcome of this study was death resulting from any cause and was divided into early mortality (occurring within 30 days of surgery or during the index hospitalization) and late mortality. The cause of death was determined by review of the hospital chart, death certificates, or information from the physician who was caring for the patient at the time of death. Mortality was classified as valve related, cardiac related, or noncardiac. All sudden or unknown causes of death were considered valve related.

Secondary outcomes included valve reintervention, thromboembolic events (stroke and transient ischemic attack), endocarditis, valve thrombosis, and significant hemorrhage (defined as major bleeding leading to death or stroke or requiring hospitalization and/or transfusion). Valve deterioration was defined as a composite end point that included structural and nonstructural valve deterioration and was determined by reoperation and periodic echocardiographic surveillance according to the valve-reporting guidelines.[20] Structural valve deterioration included changes intrinsic to the valve such as wear, calcification, leaflet tear, leaflet retraction of a repaired valve, and suture line disruption of a prosthetic valve.[20] Nonstructural dysfunction included problems that did not directly involve valve components yet resulted in dysfunction of an operated valve, for example, entrapment by pannus, tissue, or suture; paravalvular leak; inappropriate sizing or positioning; or residual leak or obstruction after valve implantation or repair.[20] In addition, nonstructural dysfunction included the development of

aortic or pulmonic regurgitation as a result of technical errors, dilatation of the sinotubular junction, or dilatation of the valve annulus.[20] Valve deterioration included any pulmonary or aortic insufficiency of a moderate or severe degree and/or a mean systolic gradient ≥20 mm Hg, respectively, of any operated valve (mechanical aortic valve, pulmonary autograft, or pulmonary homograft). When applicable, outcomes of interest in the Ross group were reported separately for the aortic and pulmonary positions.

Statistical Analysis

Propensity score matching was used to select comparable cohorts of patients who underwent the Ross procedure versus mechanical AVR.[21] The propensity score was estimated with multivariate logistic regression. In the model, the choice of operation (Ross procedure or mechanical AVR) was the dependent variable. The independent variables consisted of demographic data, admission information, preoperative clinical characteristics, intraoperative data, and disease characteristics. The complete list of covariates used to generate the propensity score is given in the Methods section in the online-only Data Supplement.

On estimation of the propensity score, patients in the Ross group (cases) were matched to those with mechanical AVR (controls) in a 1-to-1 fashion. The optimal matching algorithm with a caliper size of 3% of the estimated propensity score was used to construct a matched-paired sample. Of note, 1-to-n matching was considered but deemed infeasible because of insufficient overlap between groups in the tail regions of the propensity score distribution. The matched-paired sample consisted of 208 pairs of patients. The average±SD distance in the estimated propensity score was 0.1±1.6%.

The characteristics of the matched-paired sample were summarized in terms of mean±SD for normally distributed continuous variables, median (interquartile range) for nonnormally distributed continuous variables, and frequency (proportion) for dichotomous and polytomous variables. Postmatching baseline differences were assessed with 2-sample *t* tests for continuous variables and the Pearson χ^2 or Fisher exact test for dichotomous and polytomous variables as appropriate.

Freedom from long-term adverse events (ie, all-cause mortality, cardiac- and valve-related mortality, valve reintervention, valve deterioration, cerebral thromboembolism, and major bleeding) was estimated with the Kaplan-Meier method. Patients who had reoperations or other adverse events continued to be followed up and were entered into the survival analysis with an intention-to-treat approach. The differences in freedom from these adverse events between the 2 cohorts were assessed with likelihood ratio tests stratified by matched pair. Given the differences in New York Heart Association class in the propensity-matched group, we also examined differences in freedom from each of the adverse outcomes of interest for the subgroup of patients of functional capacity New York Heart Association class I or II.

RESULTS

Perioperative Outcomes

Rates of early mortality were similar between the 2 matched groups with 1 early death in each group (Ross, 0.5%; AVR, 0.5%; *P*=1.00). The frequency of all early complications was similar between the 2 groups, including stroke (*P*=0.25), transient ischemic attack (*P*=0.50), myocardial infarction (*P*=0.45), atrial fibrillation (*P*=0.66), renal failure (*P*=1.00), and reoperations (*P*=0.69; Table I in the online-only Data Supplement).

Survival

In the cohort of 208 matched pairs, a total of 35 patients died, with 12 late deaths in the Ross group and 21 late deaths in the AVR group. There was no difference in the long-term freedom from death between the groups (Ross versus AVR: hazard ratio, 0.91; 95% confidence interval [CI], 0.38–2.16; *P*=0.83; Figure, A).

Cause of Death

In the Ross group, late mortality was valve related in 3 patients (25%; sudden/unexplained death, n=2; endocarditis, n=1) and noncardiac in 9 patients (75%). In the AVR group, late mortality was valve related in 12 patients (57%; sudden/unexplained death, n=6; stroke/major bleeding, n=3; death at valve reintervention, n=2; congestive heart failure secondary to aortic valve disease, n=1), cardiac in 4 patients (19%), and noncardiac in 5 patients (24%). Details of noncardiac causes of death are reported in the Results section in the online-only Data Supplement. Freedom from cardiac- and valve-related mortality is presented in Table 2 and was better after the Ross procedure (Ross versus AVR, 97.3% versus 88.7% at 20 years). Patients undergoing the Ross procedure had improved long-term freedom from cardiac- and valve-related mortality (Ross versus AVR: hazard ratio, 0.22; 95% CI, 0.034–0.86; *P*=0.03; Figure, B).

Valve Reintervention

Freedom from operated valve reintervention (aortic valve in the mechanical AVR group and aortic or pulmonary valve in the Ross group) is presented in Table 2 and was excellent in both groups (Ross versus AVR, 87.3% versus 94.0% at 20 years). For the Ross group, freedom from aortic valve reintervention and freedom from pulmonary valve reintervention (either surgical or percutaneous) are presented separately in Table II in the online-only Data Supplement. There was no difference in long-term freedom from valve reintervention between the groups (Ross versus AVR: hazard ratio, 1.86; 95% CI, 0.76–4.94; *P*=0.18; Figure, C). Of note, there were no operative mortalities among the 17 patients in the Ross group who required valve reintervention. Among the 10 patients in the mechanical AVR group who required valve reintervention, 2 died at reoperation. Details of valve reintervention are presented in the Results section in the online-only Data Supplement.

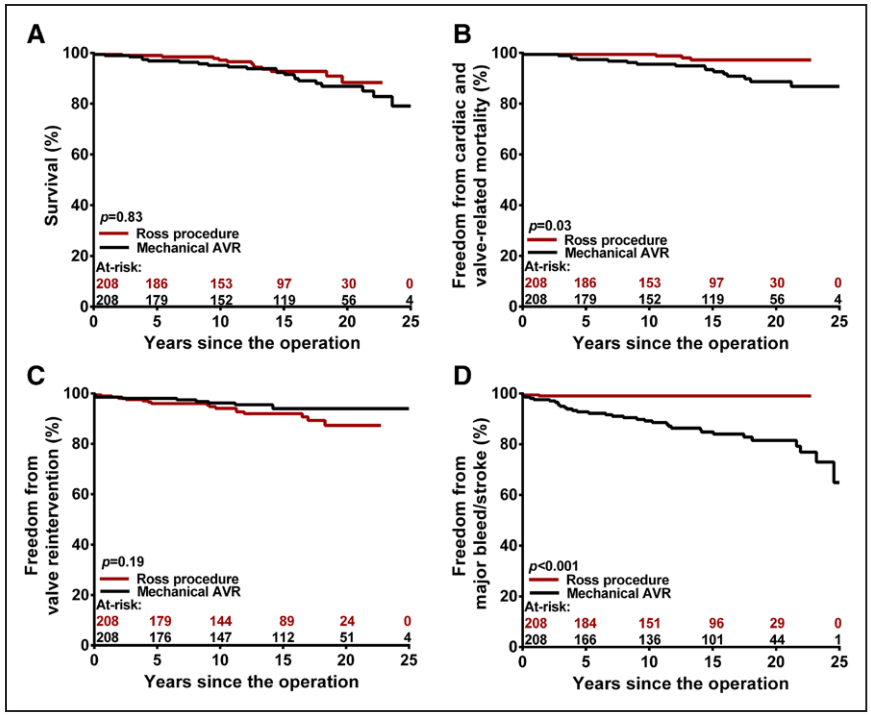

Figure. Long-term outcomes after the Ross procedure vs mechanical aortic valve replacement (AVR).
A, Survival after the Ross procedure vs mechanical AVR. **B**, Freedom from cardiac- and valve-related mortality after the Ross procedure vs mechanical AVR. **C**, Freedom from valve reintervention after the Ross procedure vs mechanical AVR. In the Ross group, this includes percutaneous or surgical reintervention on the pulmonary autograft and/or pulmonary homograft. **D**, Freedom from stroke or major bleeding after the Ross procedure vs mechanical AVR. The differences in freedom from these adverse events between the 2 cohorts were assessed with likelihood ratio tests stratified by matched pair.

Valve Deterioration

Freedom from valve deterioration is presented in Table 2 and was not different between the groups (Ross versus AVR, 77.0% versus 88.6% at 20 years). There was no difference in long-term freedom from valve deterioration between the groups (Ross versus AVR: hazard ratio, 1.13; 95% CI, 0.57–2.23; *P*=0.73). For the Ross group, freedom from pulmonary autograft deterioration and freedom from pulmonary homograft deterioration at various time points are presented separately in Table II in the online-only Data Supplement. Details of valve deterioration are presented in the Results section in the online-only Data Supplement.

Thromboembolic and Hemorrhagic Complications

Freedom from cerebral thromboembolism and major bleeding at various time points is presented in Table 2. Freedom from stroke or major bleeding was superior after the Ross procedure (Ross versus AVR: hazard ratio, 0.09; 95% CI, 0.02–0.31; *P*<0.001; Figure, D). Details of thromboembolic and hemorrhagic complications are presented in the Results section in the online-only Data Supplement.

Infective Endocarditis and Valve Thrombosis

The incidence of operated valve endocarditis at follow-up was equivalent between the 2 groups (Ross, n=7 [3.3%]; mechanical AVR, n=9 [4.3%]; *P*=0.80). Similarly, the incidence of operated valve thrombosis at follow-up was not different between the 2 groups (Ross, n=0; mechanical AVR, n=2 [1%]; *P*=0.50). Details of these events are presented in the Results section in the online-only Data Supplement.

Subgroup Analysis

When we restricted the propensity-matched cohort to patients of functional New York Heart Association class I or II, the results were not substantially different for each of the outcomes of interest, although there was an expected loss of statistical significance because of a reduction in power. The differences between the Ross and mechanical AVR groups for each outcome of interest are presented in the Results section in the online-only Data Supplement.

DISCUSSION

The most important novel finding of this study is that the Ross procedure was associated with improved freedom from cardiac- and valve-related mortality compared with patients receiving a mechanical AVR. Furthermore, freedom from stroke and major bleeding was significantly improved after the Ross procedure. To the best of our knowledge, this is the first large series comparing >20-year outcomes after the Ross procedure and mechanical AVR in patients undergoing AVR.

Long-Term Survival

Comparative studies between the Ross procedure and mechanical AVR in young and middle-aged adults are scarce

Table 2. Freedom From Adverse Events at Various Time Intervals

End Point	Years	Ross Procedure Freedom From Event (95% CI)	Mechanical AVR Freedom From Event (95% CI)	*P* Value
Cardiac- and valve-related mortality	5	99.5 (96.6–99.9)	97.4 (93.8–98.9)	0.03
	10	99.5 (96.6–99.9)	95.6 (91.4–97.8)	
	15	97.3 (92.8–99.0)	93.4 (88.4–96.3)	
	20	97.3 (92.8–99.0)	88.7 (81.8–93.1)	
Operated valve reintervention*	5	96.0 (92.1–98.0)	98.0 (94.8–99.2)	0.18
	10	94.1 (89.5–96.7)	96.2 (92.1–98.2)	
	15	92.0 (86.7–95.2)	94.0 (89.0–96.7)	
	20	87.3 (79.0–92.5)	94.0 (89.0–96.7)	
Valve deterioration†	5	95.5 (91.5–97.6)	95.3 (91.2–97.5)	0.73
	10	93.6 (89.0–96.3)	92.9 (88.1–95.8)	
	15	89.9 (84.1–93.7)	90.2 (84.6–93.8)	
	20	77.0 (65.4–85.1)	88.6 (81.9–92.9)	
Stroke	5	99.0 (96.2–99.8)	97.5 (94.0–98.9)	0.03
	10	99.0 (96.2–99.8)	95.6 (91.4–97.8)	
	15	99.0 (96.2–99.8)	94.2 (89.3–96.8)	
	20	99.0 (96.2–99.8)	94.2 (89.3–96.8)	
Transient ischemic attack	5	100	96.5 (92.8–98.3)	0.02
	10	99.4 (96.1–99.9)	93.6 (89.0–96.3)	
	15	99.4 (96.1–99.9)	92.8 (87.9–95.8)	
	20	98.1 (91.8–99.6)	91.8 (86.4–95.2)	
Major bleeding	5	100	95.3 (91.1–97.5)	<0.001
	10	100	93.5 (88.8–96.3)	
	15	100	89.9 (84.1–93.6)	
	20	100	86.5 (79.3–91.3)	

AVR indicates aortic valve replacement; and CI, confidence interval.

*In the Ross group, this includes any percutaneous or surgical reintervention on the pulmonary autograft and/or pulmonary homograft.

†Valve deterioration was defined as pulmonary or aortic insufficiency of a moderate or severe degree and/or a mean systolic gradient ≥20 mm Hg, respectively. This includes both structural valve deterioration and nonstructural valve dysfunction. In the Ross group, this includes deterioration of the pulmonary autograft and/or pulmonary homograft.

and limited by either small sample size or limited duration of follow-up. In a propensity-matched cohort study with a mean follow-up of 5.7 years, Mokhles et al[15] reported equivalent survival between the Ross procedure and mechanical AVR. Our data suggest that although overall survival is equivalent up to 20 years after surgery, patients undergoing mechanical AVR experience an excess of cardiac- and valve-related mortality, most of which occurs after 15 years. This excess mortality occurred secondary to thrombohemorrhagic events, death at reintervention, and heart failure and may reflect the beneficial effects of improved hemodynamics on left ventricular health and the avoidance of anticoagulation in the Ross group.

Reintervention

The excellent durability and low rates of reoperation are the main arguments justifying the preferential use of mechanical AVRs in young adults. Freedom from valve-related reintervention after mechanical AVR has been reported to be between 93% and 99% at 10 years.[1,2,22–26] In contrast, the risk of reintervention after the Ross pro-

cedure is considered by many to be its Achilles heel. The Rotterdam group reported a freedom from reoperation on the autograft and homograft of 57% and 93%, respectively, at 13 years, leading them and others to abandon the use of the Ross operation in adults.[27] Advocates for the Ross procedure have suggested that the risk of reintervention may be mitigated by attention to surgical details and minute technical refinements. Supporting this position, several contemporary series have reported a rate of reintervention (for the pulmonary autograft and/or pulmonary homograft) ranging between 0.5% and 1.5% per patient-year, yielding a freedom from reintervention of 85% to 95% at 10 years.[6,8,18,28,29] In this series, the freedom from any surgical or percutaneous valve reintervention after the Ross procedure was 87% at 20 years and was better than our previously published results,[7] reflecting the more contemporary cohort in the present study.

Surprisingly, the risk of valve reintervention was not significantly different between the Ross and mechanical AVR groups. This was observed despite the fact that patients in the mechanical AVR group had a very low rate of reoperation (6% at 20 years), which compares favorably with previously published series.[1,2,22–26] Consistent with previous reports, the most common indication for reintervention in the Ross group was structural deterioration of the pulmonary autograft, whereas in the mechanical AVR group, the main indications for reintervention were endocarditis, thrombosis, and nonstructural valve dysfunction. Therefore, contrary to widely accepted notions, these data suggest that despite the potential for failure of 2 valves with the Ross procedure, this operation can achieve long-term durability that is not significantly different from that of mechanical AVR after 20 years. Furthermore, no operative mortality was observed among the 17 patients in the Ross group who required reintervention. Thus, our findings also refute the argument that the Ross procedure exposes patients to a wide range of complex reoperations associated with substantial mortality.

Cerebral Thromboembolism and Major Bleeding

Major bleeding and thromboembolic events after mechanical AVR occur at a linearized rate of 1% to 2% and 1% per year, respectively.[2,25,30,31] Recent reports suggest that these risks may be significantly mitigated by self-monitoring of oral anticoagulation.[32] Similarly, preliminary data from the PROACT study (Prospective Randomized On-X Valve Anticoagulation Clinical Trial) suggest that the incidence of major bleeding may be reduced with a lower target international normalized ratio of between 1.5 and 2.0 without any increase risk of thromboembolism in patients receiving the On-X valve.[33] Nonetheless, rates of major bleeding (1.48%/patient-year) and ischemic stroke (0.74%/patient-year) in this carefully selected and prospectively followed up trial population were substantial.[33] We observed that after mechanical AVR, nearly 20% of patients will experience a stroke or major bleeding at 20 years, a rate that compares favorably with the published literature. In contrast, the risk of major bleeding or stroke was essentially nonexistent after the Ross procedure, the significance of which should be considered in discussions of valve replacement options with young and middle-aged patients (Table II in the online-only Data Supplement).

Patient Selection for the Ross Procedure

Young adults with aortic stenosis and a normal-sized aortic annulus are the best candidates for the Ross procedure. Furthermore, the Ross procedure may be of particular benefit to patients who are physically active, women of childbearing age, and young patients with contraindications to anticoagulation. We do not recommend the Ross procedure for patients with aortic insufficiency and a dilated aortic annulus. The majority of our patients had a stenotic bicuspid aortic valve, and about one-third also had their ascending aorta replaced. We have very limited experience with the Ross procedure in the setting of rheumatic disease, which often presents with multivalvular involvement.

Limitations

The main limitations of this study are its observational design and the fact that treatment allocation was nonrandomized. Although propensity score matching mitigates the impact of a potential selection bias, it does not entirely alleviate it and does not consider potential unmeasured confounders. Despite the fact that the year of surgery was considered in the propensity score, the mean duration of follow-up was slightly longer in the mechanical AVR group. Furthermore, despite matching, patients undergoing mechanical AVR were more symptomatic and had higher rates of rheumatic disease and concomitant mitral valve pathology, which may account for some of the long-term differences we observed. This was a single-center study performed at a tertiary academic hospital, and the vast majority of the procedures were performed by a single surgeon, thus limiting the generalizability of our findings. Another limitation is the fact that no data were collected on the quality of international normalized ratio monitoring in patients who were receiving oral anticoagulation. The impact of the 2 surgical approaches on postoperative quality of life was also not measured. Finally, because of the low incidence of adverse events at follow-up, it is possible that the present study was not sufficiently powered to detect subtle differences in long-term outcomes.

Despite these limitations, this study represents the longest available comparative longitudinal study examining long-term outcomes of the Ross procedure versus

mechanical AVR. The relatively large sample size and the excellent availability of comprehensive long-term follow-up make the results relevant and provide important comparative data to the current body of literature.

Conclusions

In this propensity-matched cohort study, early outcomes, long-term survival, and freedom from reintervention were comparable between the Ross procedure and mechanical AVR. However, the Ross procedure was associated with improved freedom from cardiac- and valve-related mortality and a significant reduction in the incidence of stroke and major bleeding at follow-up. Together, these data suggest that in specialized centers, the Ross procedure represents an excellent option and should be considered for young and middle-aged adults undergoing AVR.

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None.

AFFILIATIONS

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FOOTNOTES

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