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Long-Term Clinical and Echocardiographic Outcomes Following the Ross Procedure

A Post Hoc Analysis of a Randomized Clinical Trial

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IMPORTANCE The Ross procedure as treatment for adults with aortic valve disease (AVD) has been the subject of renewed interest.

OBJECTIVE To evaluate the long-term clinical and echocardiographic outcomes following the Ross procedure for the treatment of adults with AVD.

DESIGN, SETTING, AND PARTICIPANTS This post hoc analysis of a randomized clinical trial included adult patients (age <69 years) who underwent a Ross procedure for the treatment of AVD, including those with active endocarditis, rheumatic AVD, decreased ejection fraction, and previous cardiac surgery. The trial, conducted from September 1, 1994, to May 31, 2001, compared homograft root replacement with the Ross procedure at a single center. Data after 2010 were collected retrospectively in November and December 2022.

EXPOSURE Ross procedure.

MAIN OUTCOMES AND MEASURES The primary end point was long-term survival among patients who underwent the Ross procedure compared with that in the age-, country of origin– and sex-matched general population. Secondary end points were freedom from any reintervention, autograft reintervention, or homograft reintervention and time-related valve function, autograft diameter, and functional status.

RESULTS This study included 108 adults (92 [85%] male) with a median age of 38 years (range, 19-66 years). Median duration of clinical follow-up was 24.1 years (IQR, 22.6-26.1 years; 2488 patient-years), with 98% follow-up completeness. Of these patients, 9 (8%) had active endocarditis and 45 (42%) underwent reoperations. The main hemodynamic lesion was stenosis in 30 (28%) and regurgitation in 49 (45%). There was 1 perioperative death (0.9%). Twenty-five year survival was 83.0% (95% CI, 75.5%-91.2%), representing a relative survival of 99.1% (95% CI, 91.8%-100%) compared with the general population (83.7%). At 25 years, freedom from any reintervention was 71.1% (95% CI, 61.6%-82.0%); from autograft reintervention, 80.3% (95% CI, 71.9%-89.6%); and from homograft reintervention, 86.3% (95% CI, 79.0%-94.3%). Thirty-day mortality after the first Ross-related reintervention was 0% and after all Ross-related reinterventions was 3.8% (n = 1); 10-year survival after reoperation was 96.2% (95% CI, 89.0%-100%).

CONCLUSIONS AND RELEVANCE This study found that the Ross procedure provided excellent survival into the third decade postoperatively that was comparable to that in the general population. Long-term freedom from reintervention demonstrated that the Ross procedure may be a durable substitute into late adulthood, showing a delayed but progressive functional decline.

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Invited Commentary page 14

Supplemental content

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Heart valve disease is a prevalent condition affecting an estimated 74 million patients globally.[1] Absolute numbers of deaths due to aortic valve disease (AVD) tripled between 1979 and 2009,[2] making AVD responsible for the highest proportion of deaths within the spectrum of valvular heart disorders. For many years, prosthetic aortic valve replacement (AVR) has been the standard of care for the surgical treatment of patients with AVD despite the fact that both biological[3-6] and mechanical prostheses[3,5,7,8] have intrinsic characteristics that represent major drawbacks to patients. Additionally, survival after prosthetic AVR in adults younger than 65 years is significantly lower compared with that in the general population.[4,7,9] Interest in valve repair has grown, but most patients with AVD require replacement of their valve. Recently, a renewed interest has gathered around the Ross procedure (pulmonary autograft) for the treatment of AVD in adults.[3,10-12]

The pulmonary autograft is the only living aortic valve substitute currently available and was first performed in 1967.[13] Its long-term outcomes have recently been delineated,[14-17] and studies have revealed that after the Ross procedure, unlike other valve substitute procedures, patients experienced survival that was equivalent to that of an age-, sex- and country of origin–matched general population.[3,14,18,19] These findings suggest that a living valve substitute in the aortic valve position is associated with clinically relevant superior outcomes. Valve-related events, such as bleeding and endocarditis, rarely occur after the Ross procedure, but late dilatation of the autograft root accompanied by autograft regurgitation remains a concern,[3] leading to limited application.[20,21]

In the search for an ideal aortic valve substitute, insights into long-term survival and clinical outcome remain of utmost importance to guide decision-making. We report the long-term results following the Ross procedure over a period of 29 years.

Key Points

Question In adults who have undergone the Ross procedure using a freestanding root technique, what are the clinical outcomes beyond the second decade?

Finding In this post hoc analysis of a randomized clinical trial of 108 adults who underwent the Ross procedure, survival into the third postoperative decade was 83%, comparable to that in the matched general population.

Meaning These findings suggest that the Ross procedure is associated with excellent clinical outcomes into the third postoperative decade.

Methods

We performed a post hoc analysis of a randomized clinical trial comparing homograft root replacement with the Ross procedure (ISRCTN03530985).[12] Approval for this study was obtained from the local ethics committee at Harefield Hospital. Written informed consent was obtained in the trial. Verbal informed consent was obtained during telephone calls with all living patients for this study.

Study Population

In the randomized clinical trial, conducted from September 1, 1994, to May 31, 2001, 216 adults (age <69 years) were randomly assigned to undergo a Ross procedure or homograft aortic root replacement at the Royal Brompton & Harefield NHS Foundation Trust, London, UK. Randomization and masking details are provided elsewhere.[12] In the current study, the principal focus was to analyze long-term outcomes after the Ross procedure. We have therefore refrained from presenting outcomes in the homograft cohort. Patients with AVD, aortic root or ascending aortic dilatation, bicuspid aortic valves, active endocarditis, rheumatic heart valve disease, decreased ejection fraction, or previous cardiac surgery and patients requiring emergent surgery were included. Patients with Marfan syndrome, rheumatoid arthritis, and Reiter syndrome were excluded.

Surgical Technique

One surgeon (M.H.Y.) undertook all Ross procedures using the same technique during the inclusion period. All patients underwent total aortic root replacement using a freestanding root technique. During autograft harvesting, the pulmonary root was harvested in a scalloped fashion, leaving 1 to 2 mm below the attachment of the cusps (nadir), representing the lowest point of the valve insertion. In patients with aortic-to-pulmonary annulus mismatch, intertrigonal compression plication was performed using a 2-0 monofilament suture. Close interrupted sutures were used for the proximal aortic anastomosis. The left-facing autograft sinus was positioned in the left coronary sinus, and the autograft was placed in an intra-annular position to provide external fibrous support to the muscular pulmonary root. The coronary ostia were anastomosed to their respective sinuses. The distal anastomosis was completed 2 to 3 mm above the level of the commissures to mitigate the hazard of autograft dilatation. No foreign material was used to support the proximal or distal anastomoses. A pulmonary homograft was placed in the pulmonary position, and the largest available size was always used. Strict blood pressure control (systolic blood pressure <110 mm Hg) was maintained perioperatively and for the first 6 months to allow adaptive remodeling of the pulmonary autograft.

Primary and Secondary Outcomes

The primary outcome was long-term survival, which was compared with that in an age-, sex-, and country of origin–matched general UK population. Secondary outcomes were freedom from any valve-related reintervention, autograft reintervention, or homograft reintervention and longitudinal evolution of autograft and homograft regurgitation and of autograft dimensional and functional status at last follow-up using the New York Heart Association (NYHA) classification.[22]

Data Collection and Definitions

All data up to 2010 were collected prospectively as a part of the randomized clinical trial.[12] Clinical and

echocardiographic outcome data after 2010 were collected retrospectively at the Harefield hospital in November and December 2022. Patient and procedural characteristics were collected earlier.[12] Patients that had moved were contacted by telephone or through their general practitioner in October 2022. For all patients, vital status was determined in November and December 2022 through the Harefield medical records and linked to the national UK death register; all living patients received an additional telephone call (G.M., G.C.). If no clinical outcomes were documented at the Harefield hospital in case of patients having moved abroad, outcomes were only obtained by reaching out to patients through telephone. Follow-up completeness was calculated using the Clark C method.[23]

During data collection, the original prospective database was updated, and all echocardiographic imaging studies and relevant valve-related events were collected retrospectively. Valve-related events were defined according to the 2008 guidelines by Akins and colleagues.[24] Autograft dilatation with or without regurgitation was defined as structural valve deterioration (SVD). Early outcome events were defined as events occurring within 30 days postoperatively and were reported previously.[12] Late outcome events were defined as events occurring after 30 days postoperatively.

Imaging Follow-Up

All serial transthoracic echocardiographic imaging studies after surgery were performed at Harefield Hospital. Valve function of the pulmonary autograft in the aortic position and the pulmonary homograft in the pulmonary position was evaluated by echocardiographic follow-up studies. Echocardiographic parameters longitudinally studied included autograft root diameter, autograft regurgitation grade (1-4), pulmonary homograft regurgitation (PR) grade (1-4), left-ventricular ejection fraction, left-ventricular end-diastolic diameter, and left-ventricular end-systolic diameter.

Echocardiographic follow-up was only performed for patients who were still being seen at Harefield Hospital. The latest echocardiographic study was used to calculate echocardiographic follow-up completeness.

Statistical Analysis

Continuous data are presented as means and SDs (gaussian) or medians with IQRs (nongaussian). Categorical data are presented as proportions. The Shapiro-Wilk test was used to analyze whether the data were normally distributed. Long-term survival and freedom from intervention after surgery were estimated and presented according to the Kaplan-Meier method. Patient survival was compared with survival in the general population by a novel, patient-level matching strategy.[25] Patients were matched on an individual level using country of origin, patient sex, individual patient age (updating annually), calendar year at time of follow-up (updating annually), and time of censoring, if applicable. Reinterventions on the autograft and homograft were considered competing risks with death, and Fine-Gray competing risk models were constructed to gain inferences on the cumulative incidence of reintervention. Univariable Cox proportional hazards regression models were used to investigate factors associated with mortality and reintervention. Two-sided $P \leq .05$ was considered statistically significant. All statistical analyses were performed in RStudio, version 2022.07.2 (R Project for Statistical Computing).

To capture valve function over time, one should account for the dependency between multiple measurements taken from each individual over time as well as the independence of measurements taken among patients. Linear mixed-effects models (diameters/gradients) and continuation ratio mixed-effects models (regurgitation grades) were constructed as they allow for such correlations between repeated measurements and for unbalanced data.[26,27] The backward formulation of the continuation model was used for the regurgitation grades, estimating the odds of more severe disease compared with less severe disease. Random intercept and random slope terms were included at the level of the patient. Natural cubic splines were placed at 2 time points, allowing flexible longitudinal outcomes modeling over 2 or 3 different time intervals. Interaction terms were only explored in the evolution of autograft root diameter. Correlation between covariates was tested through the Spearman or Pearson method, as appropriate. In the case of high correlations between covariates (r or ρ >0.70), the variable that was most clinically relevant was retained. Autograft root diameter was also modeled according to this method. Effect plots were generated to visualize evolution of autograft function, homograft function, and autograft diameter.

Results

Patients and Follow-Up

This study included 108 adult patients (16 [15%] female; 92 [85%] male; median age, 38 years [range, 19-66 years]) who underwent a Ross procedure using a freestanding root technique (**Table 1**). The country of origin was the UK for 95 patients (88%), Italy for 6 (6%), Greece for 5 (5%), Egypt for 1 (0.9%), and Turkey for 1 (0.9%). The main hemodynamic lesion was aortic stenosis in 30 patients (28%) and aortic regurgitation (AR) in 49 (45%), while 29 patients (27%) had mixed aortic stenosis and AR and 2 (2%) had a thoracic aortic dilatation. Nine patients had active endocarditis (8%), and 45 (42%) underwent reoperations.

Median clinical follow-up duration was 24.1 years (IQR, 22.6-26.1 years; 2488 patient-years), with 98% follow-up completeness. Three patients dropped out of the study (ie, were lost to clinical follow-up), translating to 40 unobserved patient-years. Median echocardiographic follow-up duration was 21.7 years (IQR, 6.0-24.3 years; 1791 patient-years), with 71% follow-up completion. Of 91 surviving patients, 48 had an available echocardiograph between January 1, 2021, and December 31, 2022. Surgical details are listed in eTable 1 in Supplement 1.

Long-Term Survival

There was 1 perioperative death (0.9%). During follow-up, 16 of 107 patients died after discharge from the hospital. Causes

Table 1. Baseline Patient Characteristics for All Patients That Underwent a Ross Procedure

Characteristic	Patients (N = 108)[a]
Age, median (range), y	38 (19-66)
Age, y	
18-34	47 (44)
35-49	39 (36)
50-59	13 (12)
≥60	9 (8)
Sex	
Female	16 (15)
Male	92 (85)
Country of origin	
UK	95 (88)
Italy	6 (6)
Greece	5 (5)
Egypt	1 (0.9)
Turkey	1 (0.9)
Body surface area, mean (SD), m^2	1.9 (0.2)
Smoking status	
Smoker	18 (17)
Ex-smoker	18 (17)
Never	72 (67)
Comorbidities	
Hypertension	21 (19)
Dyslipidemia	3 (3)
Diabetes	1 (1)
Kidney failure[b]	6 (6)
Preoperative AR grade	
0	8 (1)
1	1 (1)
2	21 (19)
3	34 (31)
4	44 (41)
Surgical indication	
Primary isolated AS	30 (28)
Primary isolated AR	49 (45)
Mixed AS and AR	29 (27)
Thoracic aortic dilatation	2 (2)
Etiology	
Degenerative	48 (44)
Congenital	53 (49)
Rheumatic	7 (6)
Endocarditis	
None	89 (82)
Active	9 (8)
Treated	10 (9)
Previous intervention[c]	45 (42)
Homograft AVR	24 (22)
Mechanical or bioprosthetic AVR	13 (12)
Aortic valve repair	12 (11)
Coarctation repair	9 (8)
New York Heart Association classification	
I	33 (31)
II	49 (45)
III	21 (19)
IV	5 (5)
Heart rhythm	
Sinus rhythm	103 (95)
Atrial fibrillation	1 (1)
Pacemaker	4 (4)
Type of surgery	
Emergent	5 (5)
Urgent	5 (5)
Elective	98 (91)

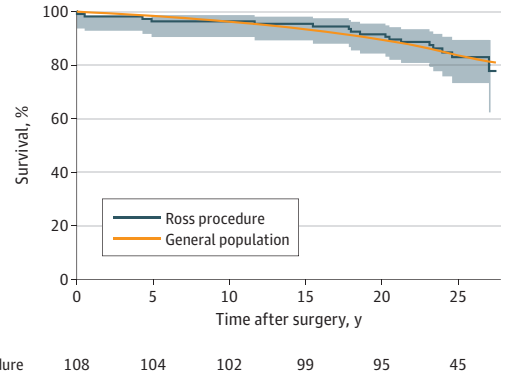
Abbreviations: AR, aortic regurgitation; AS, aortic stenosis; AVR, aortic valve replacement.

[a] Data are presented as number (percentage) of patients unless otherwise indicated.

[b] Defined as estimated creatinine clearance of less than 50 mL/min/1.73 m^2 (to convert to mL/s/m^2, multiply by 0.0167).

[c] Refers to the last surgery before enrollment; some patients had more than 1 procedure at the last intervention.

Figure 1. Long-Term Survival After the Ross Procedure Compared With the Age-, Country of Origin–, and Sex-Matched General Population

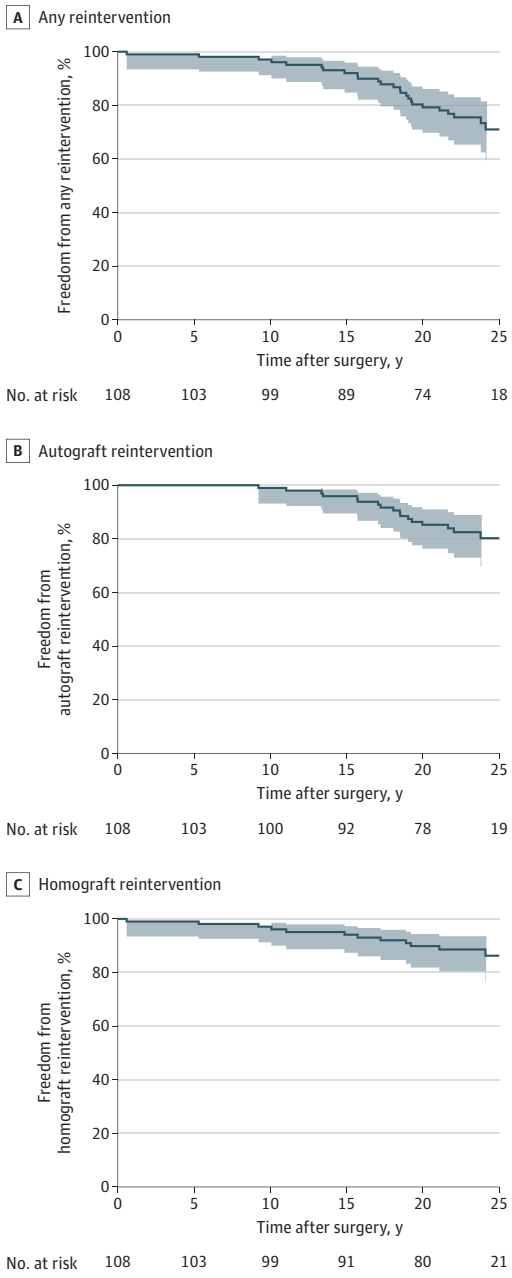


of death were cardiac (11 [69%]), including 2 sudden deaths and 3 heart failure–related deaths; noncardiac (3 [19%]); and unknown (2 [13%]). Survival at 25 years was 83.0% (95% CI, 75.5%-91.2%), representing a relative survival of 99.1% (95% CI, 91.8%-100%) compared with the age-, country of origin- and sex-matched general population (survival in general population, 83.7%). Survival estimates compared with the age-, sex- and country of origin-matched general population are depicted in **Figure 1**.

Reinterventions

Seventeen patients (15.7%) underwent 18 aortic valve reinterventions. During follow-up, 3 patients (17.6%) underwent a valve-sparing root replacement; 10 (58.8%), a bioprosthetic

Figure 2. Freedom From Any Reintervention, Autograft Reintervention, and Homograft Reintervention After the Ross Procedure



AVR; and 5 (29.4%), a mechanical AVR. The indication for autograft reintervention was AR with or without root dilatation in all 17 cases. Seven patients (41.2%) required reintervention for autograft dilatation with moderate-to-severe or severe AR. Fourteen patients (13.0%) underwent 18 reinterventions on their pulmonary homograft (17 surgical, 1 transcatheter), 7 of which were due to severe pulmonary stenosis, 5 to endocarditis, 2 to severe PR; 4 causes were undocumented. One additional patient was awaiting a homograft reintervention (due to severe stenosis) at the end of follow-up. At 25 years, actuarial freedom from any Ross-related reintervention was 71.1% (95% CI, 61.6%-82.0%); from autograft reintervention, 80.3% (95% CI, 71.9%-89.6%); and from homograft reintervention, 86.3% (95% CI, 79.0%-94.3%). At first Ross-related reintervention, 30-day mortality was 0%. One patient died after bioprosthetic AVR that was preceded by a valve-sparing root replacement earlier. Thirty-day mortality after first or second Ross-related reintervention was 3.8% (n = 1, after bioprosthetic AVR), and 10-year survival after reoperation was 96.2% (95% CI, 89.0%-100%). Five patients underwent mitral valve surgery, of which 2 were during Ross-related reinterventions, and 1 patient underwent coronary bypass surgery. Freedom from reintervention is depicted in **Figure 2**. Cumulative incidence of any reintervention, autograft reintervention, and homograft reintervention with death as a competing risk is shown in eFigure 1 in Supplement 1.

Univariable Cox proportional hazards regression models revealed that older age was associated with a lower hazard for any reintervention (hazard ratio [HR], 0.96; 95% CI, 0.92-0.99; P = .02) and for homograft reintervention (HR, 0.93; 95% CI, 0.88-0.99; P = .02). Results of univariable Cox proportional hazards regression is shown in **Table 2**. Preoperative severe AR was not associated with greater hazards of autograft reintervention (HR, 1.09; 95% CI, 0.41-2.86; P = .86). Freedom from autograft reintervention for patients with severe preoperative AR vs those without severe preoperative AR is shown in eFigure 2 in Supplement 1.

Valve-Related Events and Functional Status

During a median follow-up of 24.1 years (IQR, 22.6-26.1 years; 2488 patient-years), there was 1 case of autograft endocarditis (0.04% per year) and 9 cases of homograft endocarditis (0.36% per year). No cases of late bleeding, thromboembolism, valve thrombosis, and cerebrovascular events were reported. At a median last follow-up of 24.6 years (IQR, 23.2-26.2 years) among 93 patients, 80 (86%) had NYHA class I or II classification.

Longitudinal Echocardiographic Analyses

Autograft Function and Root Dimensions

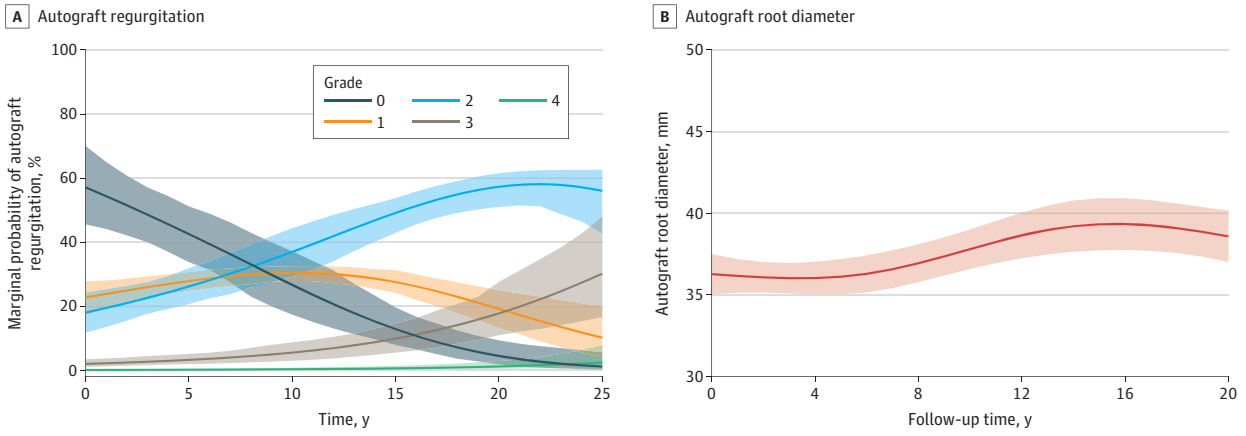
Marginal probabilities of autograft regurgitation over time are depicted in **Figure 3**. Continuation ratio mixed-effects models of AR over time revealed that the probability of developing higher grades of AR increased over time (eTable 2 in Supplement 1). In multivariable analysis including age at surgery, hypertension, sex, preoperative severe AR, and previous interventions, there were no factors independently associated with an increased probability of developing higher-grade AR (eTable 2 in Supplement 1). Marginal probabilities of postoperative AR stratified by patients with and without severe preoperative AR are shown in eFigure 3 in Supplement 1.

Autograft root dilatation was observed after the Ross procedure, which is depicted in the plot of autograft root diameter over time in Figure 3. Autograft dilatation occurred in some but not all patients and was more pronounced in the first 11 years compared with the last 11 years of follow-up. Results of multivariable analysis are presented in eTable 2 in Supplement 1.

Table 2. Univariable Cox Proportional Hazards Regression Model for Factors Associated With Any Reintervention, Autograft Reintervention, and Homograft Reintervention

	Any reintervention (n = 26)		Autograft reintervention (n = 17)		Homograft reintervention (n = 13)	
Univariable model	Hazard ratio (95% CI)	*P* value	Hazard ratio (95% CI)	*P* value	Hazard ratio (95% CI)	*P* value
Age at operation, y	0.96 (0.92-0.99)	.02	0.97 (0.93-1.01)	.13	0.93 (0.88-0.99)	.02
Male	1.06 (0.37-3.08)	.92	0.89 (0.26-3.10)	.86	2.32 (0.30-17.87)	.42
Preoperative severe aortic regurgitation	0.98 (0.45-2.17)	.97	1.09 (0.41-2.86)	.86	0.68 (0.21-2.21)	.52
Hypertension at operation	1.10 (0.44-2.75)	.83	1.13 (0.37-3.46)	.84	1.12 (0.31-4.06)	.87
Previous intervention	0.95 (0.43-2.10)	.90	0.80 (0.30-2.15)	.65	1.33 (0.44-3.97)	.61

Figure 3. Marginal Probabilities of Autograft Regurgitation and Evolution of Autograft Root Diameter Over Time After the Ross Procedure



Homograft Function and Other Longitudinal Parameters

Marginal probabilities of PR over time are depicted in eFigure 4 in Supplement 1. Continuation ratio mixed-effects models of PR over time revealed that the odds of developing higher grades of PR increased over time, which mainly occurred in the first years after the operation. In multivariable analysis, no factors were associated with an increased odds of developing higher-grade PR (eTable 2 in Supplement 1). Plots of the longitudinal evolution of left-ventricular ejection fraction, left-ventricular end-systolic diameter, and left-ventricular end-diastolic diameter are depicted in eFigure 5 in Supplement 1.

Discussion

The Ross procedure is the only available living aortic valve substitute, preserves mobility of the neo-aortic root, and is the only option for adults, providing a life expectancy that resembles life expectancy in the general population. In this study, a delayed but progressive functional decline of the neo-aortic root that may require a reintervention in the long term was observed. Moreover, the study showed that reoperative mortality after the Ross procedure was low, suggesting the importance of not delaying intervention when necessary.

Hemodynamics and Etiology

Over the years, several arguments have been put forward discouraging the use of the Ross procedure under specific conditions. It has been suggested that the potential benefits of the Ross procedure may not be fully realized in patients who have preoperative AR and dilation of the aortic annulus and is mainly indicated for patients with aortic valve stenosis.[14,15,28-30] In this study, no increased hazard for autograft deterioration was observed in patients presenting with preoperative AR compared with those without preoperative AR, which could have been due to a tailored surgical technique in patients who presented with a mismatch between the aortic and pulmonary annuli. Patient-tailored modifications that avoid aortic-to-pulmonary annular mismatch, while taking into account root physiology, are able to tailor the Ross procedure to patients with AR and a dilated annulus; in this study, this consisted of intertrigonal compression plication of the annulus. Other reports have also demonstrated excellent longevity of the autograft in selected patients with AR.[18,31]

Survival

While all prosthetic valve substitutes are associated with substantial excess mortality from causes not directly related to valve-related complications,[4,6,7,9,32] excess mortality after the Ross procedure in children[16,33] and adults[16] is negligible, which is likely a reflection of the cumulative benefits of a living aortic valve substitute over a lifetime. We found relative survival of 99.1% (95% CI, 91.8%-100%) at 25 years when 42% of patients were still being followed up. This important finding is in line with previous reports on the Ross procedure in young adults.[3,10,14] Of note, these results up to 29 years suggest that a living aortic valve remains beneficial in terms of survival in the long term.

David et al[15] published their long-term results of 212 consecutive Ross procedures in 2018, with a median follow-up of 18 years. Twenty-year survival was 89.2% in their population, which is comparable to that in the current study (91.5%). In both cohorts, survival was equivalent to that in the general population. The current analysis adds to the evidence on the survival benefits observed after the Ross procedure beyond the second postoperative decade.

Structural Autograft Deterioration and Reintervention

Deterioration of the autograft was rare in this series, with 80.3% of patients being free from significant regurgitation or dilatation requiring reintervention. When it occurred, structural autograft deterioration followed a typical pattern and involved autograft dilatation, often but not always resulting in autograft regurgitation. Compared with other biological substitutes, the Ross procedure yielded superior durability results with enhanced survival and a markedly delayed deterioration rate. This result was supported by the findings of a recent study from New York and California comparing bioprosthetic, mechanical, and Ross AVR using propensity score matching.[3]

Autograft reinterventions after the unsupported Ross procedure often need to address both valve regurgitation and root dilatation and preferably consist of valve-sparing root replacement using either a remodeling[34] or reimplantation technique.[35] The decision to perform reoperation on an autograft should be mainly based on the presence of progressive autograft regurgitation (more than mild), rather than dilatation of the autograft root alone. Waiting too long before intervening on a progressively regurgitant autograft can result in structural changes in the leaflets, precluding a valve-conserving reoperation.[36]

Modifications on the autograft, ranging from simple annular support to total wrapping techniques,[18,37-39] in an attempt to reduce the risk of autograft dilatation and prevent regurgitation have been proposed. However, this could defeat the wider aim of not using any prosthetic material. The influence of these procedures on clinically relevant outcomes requires longer-term follow-up series. Total inclusion techniques, which do not entail the use of foreign material, have been reported to yield favorable valve durability in long-term follow-up studies.[38]

Functional Class

Most patients (86%) had NYHA class I or II classification at the latest clinical follow-up, which approached 25 years. This observation suggests that the Ross procedure allows patients to live a normal life into the third decade after surgery with few or no symptoms, leading to a better quality of life.

Strengths and Limitations

To date, this study describes the longest clinical follow-up after the Ross procedure in adults, with a median follow-up or 24.1 years and 98% completeness. A total of 45% of patients presented with preoperative AR, 8% had preoperative active endocarditis, and 42% underwent the Ross procedure in a reoperative setting, reflecting the fact that these patients were not selected based on their clinical profiles, representing the entire population undergoing aortic valve replacement.

When interpreting these results, the limitations of this study should be borne in mind. First, this series was a single-surgeon experience, making it difficult to extrapolate these results. However, the technical success factors of the Ross procedure are now better understood, and the operative steps have been clearly delineated,[12,40,41] making the operation reproducible[41,42]; several specialized centers have produced long-term results comparable to ours.[3,43] Nevertheless, renewed interest in the Ross procedure in the past decade should be thoughtfully balanced against the higher technical complexity of a Ross procedure compared with conventional aortic valve replacement. As such, these procedures are ideally performed in Ross centers of excellence to ensure patient safety and excellent long-term outcomes.[44,45] Second, echocardiographic follow-up duration was shorter and less complete (71%) compared with clinical follow-up duration (98%). Third, this study represents a post-hoc analysis of a randomized clinical trial, and outcomes in the cohort that underwent homograft procedures were not reported. Aortic homograft use has nearly disappeared from current practice except for specific indications[46] (eg, endocarditis with root destruction). Therefore, reporting long-term homograft outcomes would be of limited clinical significance to the reader and distract from the specific focus of this study. However, outcomes of homograft procedures might be the subject of future analysis.

Conclusions

This study found that in adults with AVD, the Ross procedure provided excellent survival into the third decade after surgery that was equivalent to that in the general population. Additionally, long-term freedom from reintervention demonstrates that the autograft is a durable aortic valve substitute into late adulthood, showing a delayed but progressive decline in function. These data further support the unique benefits of a living valve substitute in adults and suggest that this effect sustains into the third postoperative decade.

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Invited Commentary

The Longest Reported Outcomes of the Ross Procedure

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The ideal aortic valve substitute is accompanied by long durability, avoidance of anticoagulation, and great valvular hemodynamics. Unfortunately, the 2 major choices for valve prostheses, bioprosthetic and mechanical valves, do not fulfill these ideal valve characteristics. In 1967, to overcome the limitations of mechanical prostheses, Donald Ross, DSc, performed the first Ross procedure, in which he implanted the harvested pulmonary autograft into the aortic position and placed a pulmonary homograft in the pulmonic position.[1] Its primary indication was in growing children to avoid anticoagulation and repeated surgical procedures. With success in the pediatric population, the Ross procedure was expanded to the adult population in the pursuit of an ideal valve prosthesis. Unfortunately, in the early 2000s, autograft dilatation and autograft and homograft reintervention were reported, which hampered the initial excitement of this procedure expanding into the adult population.[2,3] It was not until recently that the Ross procedure regained popularity, mainly due to multiple studies showing superior survival compared with other prostheses and, unlike any other valve substitute, long-term survival equivalent to that of the general population.[4,5] The Ross procedure has lower reintervention rates than bioprosthetic valves and lower thrombotic and hemorrhagic complications than mechanical valves. Today, the Ross procedure is one of the fastest-growing operations in adult cardiac surgery.

Related article page 6

In *JAMA Cardiology*, Notenboom et al[6] report the very long-term outcomes of their previously published randomized clinical study comparing the Ross procedure with aortic homografts. The randomized clinical trial showed superior survival, freedom from reoperation, and quality of life for patients undergoing the Ross procedure at 10 years.[4] In the current study,[6] the authors report the longest published follow-up of the Ross procedure, with a median follow-up of 24.1 years (IQR, 22.6-26.1 years) of the Ross cohort of the randomized clinical trial (n = 108). The clinical follow-up was thorough, with only 3 patients lost to follow-up, although echocardiographic follow-up was available in only 71% of patients. The Ross procedure is typically offered only to young, healthy patients, and this cohort had a median age of 38 years (range, 19-66 years). However, Prof Yacoub, who performed all these operations, was not overly selective, as 45 patients (42%) were undergoing reoperations and 9 (8%) had active endocarditis. There was 1 perioperative death; notably, the 25-year survival was 83.0% (95% CI, 75.5%-91.2%), not different from that of the general population. At 25 years, freedom from any reintervention was 71.1% (95% CI, 61.6%-82.0%), with 80.3% (95% CI, 71.9%-89.6%) freedom from autograft reintervention and 86.3% (95% CI, 79.0%-94.3%) freedom from homograft reintervention. The authors should be congratulated for providing strong evidence that the Ross procedure restores life expectancy in the hands of an excellent surgeon.

Over the past few years, discussion of lifetime management of aortic valve disease has been a hot topic in structural heart disease. This correlates to the rapid expansion of transcatheter aortic valve replacement (TAVR) in younger, low-risk patients, with up to 50% of patients younger than 65 years now receiving a TAVR in the US.[7] The discussion is mainly led by the choice of surgical bioprosthesis vs TAVR in the younger population and their subsequent risk when reintervention is needed.[8] Patients with a life expectancy of 20 years or more who receive a bioprosthesis—either transcatheter or surgical—will nearly certainly require reintervention if they live long enough. A TAVR-first approach is problematic given the uncertainty around the feasibility and functionality of a second TAVR and the risk of surgical explantation of those valves. Valve-in-valve TAVR into a surgical bioprosthetic valve is a low-risk procedure, but its results are entirely predicated on the size of the bioprosthesis. The evidence shown here provides an even stronger argument that the Ross procedure should be considered in the lifetime management of aortic valve disease. The Ross procedure becomes a truly attractive option in younger patients with long life expectancy, particularly given data from the SWEDEHEART (Swedish Web-System for Enhancement and Development of Evidence-Based Care in Heart Disease Evaluated According to Recommended Therapies) study showing that surgical aortic valve replacement shortens life expectancy, more significantly so in the younger population.[9]

Several observations have been made to temper the enthusiasm of the Ross procedure. First, the aortic regurgitation in this cohort worsened over time, potentially leading to late reinterventions.[6] Slow but steady dilatation of the autograft and dysfunction of the neo-aortic valve were observed in this study, although rates of degeneration compare favorably with those for bioprosthetic valves. Reoperations on the autograft have been argued to be complex and risky, and a death was observed in this series. Nevertheless, several reports have shown that reintervention after the Ross procedure