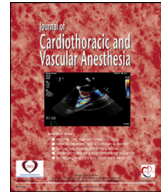


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Editorial

The Ross Procedure for Aortic Valve Disease: Radical or Routine?



The Ross procedure offers the only viable, living valve substitute for the diseased aortic valve, by transposing the pulmonary autograft into the aortic position and replacing the pulmonary valve with a pulmonary homograft (Fig 1).^{1,2} Since it first was described by Donald Ross in 1967, the Ross procedure has experienced fleeting waves of enthusiasm and has undergone multiple iterative improvements in surgical technique and perioperative care. Critics have voiced concerns about reproducibility and durability secondary to increased technical complexity, creation of two-valve disease out of single-valve disease, and potential complexities of reoperations. However, dedicated centers recently have published long-term outcomes that have demonstrated excellent late outcomes with near-normal hemodynamics, high freedom from valve-related complications and need for reoperation, and, most importantly, restored survival out to 20 years comparable to the age- and sex-matched general population.

In the most recent addition of the *Journal of the American College of Cardiology*, Aboud et al. presented the late results of 2,444 patients from the German Ross Registry who had undergone a Ross procedure.³ This multicenter series reported a median follow-up period of 9.2 years (range 0-27.4 years) and represents the largest published series of the Ross procedure to date. The mean age at surgery was 44 ± 12 years and 63% had a bicuspid aortic valve. They employed several techniques for the pulmonary autograft including subcoronary root replacement, and root replacement with additional reinforcement techniques and for the pulmonary valve, a mixture of aortic or pulmonary homografts or biologic valve prostheses. The German Ross registry demonstrated excellent results, with a mean 30-day mortality of 1%. Reoperation occurred in 5% of patients (0.69% per patient-year) for the autograft (aortic valve position) and 4.4% (0.62% per patient-year) for the pulmonary/right ventricular outflow tract graft. The long-term survival of 75.8% at 25 years was similar to the expected survival of the age- and sex-matched general population. They concluded that the “Ross procedure is a very favorable treatment option for nonelderly adults with aortic valve disease” and that it “achieves long-term survival rates similar to that of the general population, and suggests that life expectancy can be largely restored.”

This was yet another study that is adding to the growing body of evidence supporting the use of the Ross procedure for the treatment of aortic valvopathy. There have been several metaanalyses investigating the outcomes following Ross procedures. In 2018, Etnel et al. investigated observational studies of the Ross procedure, including 99 published reports involving 13,129 patients, including both adults and children.⁴ The adult population represented 6,892 patients, with a mean age of 42, across 35 studies. They reported a pooled (adult) early mortality rate of 2.01% (95% CI 1.44-2.82) and a reoperation rate of 0.83% (0.68-1.01) for the autograft and 0.47% (0.37-0.59) for the right ventricular outflow tract.

A study by Um et al., published in 2018, examined trials comparing adults undergoing the Ross procedure versus those undergoing conventional aortic valve repair (AVR) and focused on hemodynamics.⁵ Their study included 13 observational and two randomized trials, 5,336 patients in total (256 in the two randomized trials). The mean follow-up for the observational data was 4.7 years for the observational trials and 8.8 years for the two randomized trials. For both the observational cohort and randomized controlled trials, there was no difference in early mortality relative risk (RR) 0.93 (95% CI 0.47-1.83) for cohort trials versus RR 0.33 (95% CI 0.04-3.15) for randomized controlled trials. There was, however, a difference in late mortality RR 0.49 (95% CI 0.30-0.81) and RR 0.39 (95% CI 0.13-1.16) favoring the Ross procedure. Although the results were compelling, they, unfortunately, were forced to conclude that although favorable toward the Ross procedure, too many trials had moderate-to high-risk of bias to form any specific conclusions.

A study by Mazine et al. looked at the Ross procedure compared to those specifically undergoing a mechanical AVR.⁶ They identified a total of 18 studies including one randomized trial, ten adjusted observational studies, and seven unadjusted observational studies. In total, 3,516 patients were included, 1,552 underwent a Ross procedure, and 1,964 underwent mechanical aortic valve replacement. The median follow-up was 5.8 (3.4-9.2) years. Patients undergoing the Ross procedure had a reduction in the primary outcome of all-cause mortality incidence rate ratios (IRRs) of 0.54; (95% CI, 0.35-

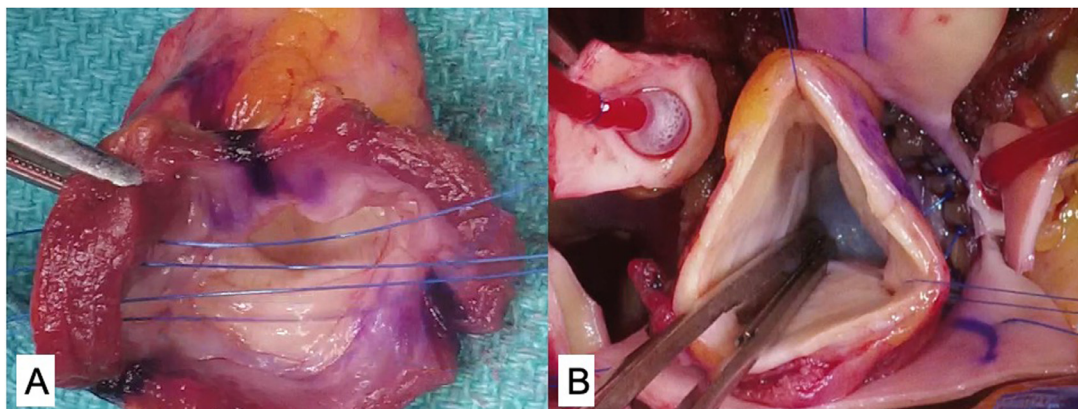


Fig 1. Intraoperative photograph of a harvested pulmonary autograft (A: view from inflow) and in situ as the neo-aortic valve (B: view from outflow).

0.82), which equated to a mortality rate of 0.05%/y versus 0.10%/y favoring the Ross procedure over mechanical AVR. The incidence of valve- or cardiac-related mortality also was lower in the Ross group, with an IRR of 0.42; (95% CI, 0.18-0.97), equating to a mortality of 0.04%/y versus 0.09%/y. There was no significant difference in perioperative mortality, with RR of 0.73 (95% CI, 0.37-1.44). There was a higher rate of reintervention in the Ross patients, with IRR of 1.76 (95% CI, 1.16-2.65), which equates to a reoperation rate of 0.12%/y versus 0.06%/y.

Much of the metaanalysis presented above contain the same trials; that is, to again state that the evidence base primarily was retrospective, involving observational studies and variable follow-up periods. This limitation was appropriately self-identified in all the studies quoted⁷ and may be contributory to the undervalued guideline support for the Ross surgery. The Ross procedure remains a class IIb recommendation in the most recent American College of Cardiology/American Heart Association guidelines and was removed completely from the European guidelines without a recommendation at all.^{8,9} Thus, the recent publication by Aboud et al. confirmed the excellent late durability and survival benefit of the Ross procedure, as reported by others, but these important confirmatory data add value, as it was the largest series published to date and came from multiple centers with very late follow-up. Globally, the Ross procedure remains underutilized, having disappeared completely from most cardiac centers¹⁰; hopefully, this growing evidence will support the ongoing efforts for a Ross renaissance.

The options for treating aortic valve disease truly have multiplied in the last several years. Conventional aortic valve replacement, with standard bioprosthetic or mechanical prosthesis, remained the predominant option for many decades. Sutureless and rapid-deployment prostheses have been developed to reduce myocardial ischemic times and address calcified aortic roots. Surgical techniques have evolved to include less-invasive hemisternotomy and minithoracotomy options; however, bioprosthetic valves continue to suffer from limited durability, restricted hemodynamics, and need for reoperation. Mechanical prostheses continue to decline as valve of choice, are thrombogenic, and require lifelong anticoagulation, and,

thus, are associated with important risks of bleeding and thromboembolic complications. Regardless, young patients who receive either a tissue or mechanical prosthesis experience significantly impaired survival, which should not be overlooked.¹¹ Over the last decade, transcatheter valve prostheses have emerged as an overriding option in elderly patients, with younger patient age thresholds advancing each year.

An important area of great interest is the role of AVR rather than aortic valve replacement in patients with noncalcified, pliable aortic cusps with predominant aortic insufficiency.¹² Aortic valve repair techniques have evolved and matured significantly over the past decade, demonstrating good function and long-lasting durability, with most of the supportive evidence originating from centers of expertise.^{13,14} Arguments for valve repair are similar to those made for the Ross procedure, including optimal hemodynamics, avoidance of anticoagulation, with the additional avoidance of other prosthetic valve-related complications.

In 2020, Buratto et al. published a small but interesting report looking at a series of children who had undergone primary Ross surgery compared to primary AVR with secondary Ross.¹⁵ In a propensity score-matched analysis, they found that secondary Ross procedure was associated with superior ten-year survival and freedom from autograft reoperation than primary Ross and concluded that a primary AVR strategy followed by delayed Ross procedure may provide better long-term survival and pulmonary autograft durability. Although these data would be impossible to generalize to young adults, it does raise the importance of a primary AVR strategy in patients with favorable repair anatomy and that a delayed Ross procedure, if necessary, may provide the optimal strategy in the lifetime management of aortic valve disease in young adults.

The explosive growth in the management of aortic valve disease over the last 20 years, both through the development of new techniques and prosthetic designs, and the reevaluation of older methods, has led to dilemmas and clinical challenges in selecting optimal management strategies for patients. Innovation and procedural advancements have created many options; now personalized aortic valve management strategies must be developed that embrace individual patient preferences

and values while prioritizing valve durability, hemodynamics, freedom from valve-related complications, and, above all else, excellent early and late survival. Current evidence remains limited by small, retrospective, single-center series with limited follow-up. However, Aboud et al. have provided tantalizing evidence, in a large multicenter study with 25-year follow-up, that patients indeed may benefit from a Ross procedure, as it is associated with very good valve durability, high freedom from valve-related complications, and excellent early and late survival, comparable to the age- and sex-matched general population. The profession must continue to raise the bar and develop larger, multicenter prospective randomized studies to confirm the small retrospective observational articles currently populating the evidence base.

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