DOI: 10.1111/jocs.16831

### ORIGINAL ARTICLE

## CARDIAC SURGERY WILEY

# Perioperative and long-term outcomes of Ross versus mechanical aortic valve replacement

Chelsea D. Wenos MD<sup>1</sup> <sup>[5]</sup> | Lava R. Timsina MPH, PhD<sup>1,3</sup> John W. Brown MD<sup>1,2</sup>

<sup>1</sup>Division of Thoracic and Cardiovascular Surgery, Indiana University School of Medicine, Indianapolis, Indiana, USA

<sup>2</sup>Divison of Pediatric Cardiothoracic Surgery, Riley Children's Health, Indiana University Health, Indianapolis, Indiana, USA

<sup>3</sup>Department of Surgery, Indiana University School of Medicine, Center for Outcomes Research in Surgery, Indianapolis, Indiana, USA

<sup>4</sup>Division of Cardiothoracic Surgery, Indiana University Health Methodist Hospital, Indianapolis, Indiana, USA

#### Correspondence

Chelsea D. Wenos, MD, Division of Thoracic and Cardiovascular Surgery, Indiana University School of Medicine, Indianapolis, IN, USA. Email: chelsea.wenos@unmc.edu

| Jeremy L. Herrmann  $MD^{1,2}$  |  $p^{1,3}$  | Parth M. Patel  $MD^1$  | John W. Fehrenbacher  $MD^{1,4}$  |

### Abstract

**Background**: The ideal aortic valve replacement strategy in young- and middle-aged adults remains up for debate. Clinical practice guidelines recommend mechanical prostheses for most patients less than 50 years of age undergoing aortic valve replacement. However, risks of major hemorrhage and thromboembolism associated with long-term anticoagulation may make the pulmonary autograft technique, or Ross procedure, a preferred approach in select patients.

**Methods:** Data were retrospectively collected for patients 18–50 years of age who underwent either the Ross procedure or mechanical aortic valve replacement (mAVR) between January 2000 and December 2016 at a single institution. Propensity score matching was performed and yielded 32 well-matched pairs from a total of 216 eligible patients.

**Results:** Demographic and preoperative characteristics were similar between the two groups. Median follow-up was 7.3 and 6.9 years for Ross and mAVR, respectively. There were no early mortalities in either group and no statistically significant differences were observed with respect to perioperative outcomes or complications. Major hemorrhage and stroke events were significantly more frequent in the mAVR population (p < .01). Overall survival (p = .93), freedom from reintervention and valve dysfunction free survival (p = .91) were equivalent.

**Conclusions:** In this mid-term propensity score-matched analysis, the Ross procedure offers similar perioperative outcomes, freedom from reintervention or valve dysfunction as well as overall survival compared to traditional mAVR but without the morbidity associated with long-term anticoagulation. At specialized centers with sufficient expertize, the Ross procedure should be strongly considered in select patients requiring aortic valve replacement.

Chelsea D. Wenos and Jeremy L. Herrmann are co-authors.

Institutional Review Board (IRB) Approval/Waiver: #1801868334.

This is an open access article under the terms of the Creative Commons Attribution-NonCommercial-NoDerivs License, which permits use and distribution in any medium, provided the original work is properly cited, the use is non-commercial and no modifications or adaptations are made. © 2022 The Authors. *Journal of Cardiac Surgery* published by Wiley Periodicals LLC.

KEYWORDS

replacement, valve repair

### 1 | INTRODUCTION

The optimal type of aortic valve replacement for young and middleaged adults continues to serve as a challenging clinical judgment for cardiothoracic surgeons. Mechanical prostheses generally exhibit longer durability but require long-term anticoagulation which carries elevated risks of bleeding and thromboembolic events at approximately 1% per patient-year.<sup>1-3</sup> While bioprosthetic valves do not require long-term anticoagulation on the basis of their tissue substrate, they exhibit shorter durability particularly amongst younger patients. An alternative to traditional aortic valve replacement is the pulmonary autograft technique, or Ross procedure.<sup>4</sup> First described in 1967, the Ross procedure involves excising a patient's dysfunctional aortic valve and replacing it with their native pulmonic valve which, in turn, is replaced with a separate bioprosthesis. Thus, the major advantage of the Ross procedure includes avoidance of long-term anticoagulation and durability of the autograft in the aortic position. Longitudinal follow-up of adults who have undergone the Ross procedure at our institution has shown excellent mid- and longterm outcomes with respect to operative mortality, freedom from major complications, freedom from reintervention and overall survival.<sup>5-7</sup> The Ross procedure may also confer comparable survival to age- and sex-matched controls in the general population, a finding that has consistently not been extended to mechanical aortic valve replacement (mAVR).<sup>8–12</sup>

Several recent studies have added further support to the use of the Ross procedure in young and middle-aged adults. A propensitymatched analysis from the University of Toronto including 208 pairs of patients who underwent the Ross procedure or mAVR demonstrated equivalent select perioperative outcomes, freedom from valve deterioration and reintervention and overall survival.<sup>13</sup> Most notably, the Ross procedure exhibited superior freedom from stroke and major hemorrhage as well as cardiac- and valve-related mortality. Similarly, an Australian propensity-score matched study of 275 pairs revealed superior survival at 20 years following the Ross procedure compared to mAVR.<sup>14</sup> Neither study thoroughly addressed early morbidity associated with the Ross procedure and cited that the vast majority of Ross procedures were performed by a single surgeon, limiting generalizability.

Despite these advantages, the technical complexity, longer operative times and concern for future complications involving two, replaced valves has limited utilization of the Ross procedure. In earlier experiences with the Ross procedure, neo-aortic root dilatation was observed, possibly a result of exposure of the native pulmonary valve to left-sided systemic pressures.<sup>15-18</sup> Accordingly, many centers (including our own) have adopted strategies involving external reinforcement of the autograft root and replacement of the ascending aorta, if dilated, to mitigate this.<sup>7,19</sup> Moreover, according to the most recent AHA/ACC guidelines, mechanical prostheses are recommended for most patients less than 50 years of age undergoing a ortic valve replacement.<sup>20</sup>

While a randomized trial to evaluate these two aortic valve replacement strategies is largely unfeasible secondary to patient and/or surgeon preference, we sought to employ propensity score matching order to generate a matched cohort of patients to compare both perioperative and long-term outcomes of the Ross procedure compared to mAVR in young and middle-age adults at a single institution. As previously reported in the literature, we hypothesized that the Ross procedure offers superior overall survival and equivalent durability without increased perioperative or long-term morbidity.

### 2 | METHODS

Data for all patients age 18-50 years of age who underwent either mAVR (with or without root replacement) or the Ross procedure between the years 2000 and 2016 at Indiana University affiliated hospitals were retrospectively gathered following Institutional Review Board approval. The technique employed for autograft implantation included root replacement with reimplantation of the coronaries as well as annular and distal graft reinforcement with pledgeted sutures and strips of Dacron.<sup>10</sup> Demographics, perioperative, operative, and postoperative variables were collected from the electronic medical record. Primary endpoints included overall survival and freedom from reintervention of either aortic or pulmonic valves. Valve dysfunction, defined as moderate insufficiency or greater at the aortic or pulmonic valve, aortic valve gradient >20 mmHg or pulmonic valve gradient >40 mmHg, as well as perioperative and long-term complications including bleeding, stroke, endocarditis and arrhythmia served as secondary endpoints.

One-to-one propensity score weight bivariate analysis was performed using a caliper width of 0.05. Variables for propensity score matching at the time of index operation (mAVR or Ross) included: age, sex, year of surgery, previous cardiac intervention, clinical presentation (chest pain/angina, presyncope/syncope, dyspnea, fatigue and congestive heart failure), New York Heart Association (NYHA) functional classification, cardiovascular risk factors (obesity, any tobacco use, hypertension, hyperlipidemia, and diabetes mellitus), total number of comorbidities, prescribed antihypertensive, statin or aspirin medications and total number of concomitant procedures performed in addition to aortic valve replacement. This yielded 32 well-matched pairs from a total database of 216 eligible patients (Ross = 125, mAVR = 91). A total of 19 subjects with inadequate clinical follow-up of less than 1 year were excluded from the study to accurately predict postoperative and long-term complications. However, patients were otherwise included in the study including four mechanical aortic valve patients who were seen

in follow-up but did not have echocardiography performed postoperatively. Before propensity score matching, there was significant disparity appreciated between the two groups; however, this difference became insignificant following matching (see Table S1 and Figure S1). Thus, any difference between the two groups after matching are assumed to be the result of treatment differences, i.e., type of index operation (mAVR or Ross).

Bivariate analyses were performed using the matched pairs of data. Mean (standard deviation) and frequency (percentage) were employed for continuous and discrete variables as appropriate. The test of significance between the two groups was evaluated for these variables using conditional logistic regressions. Similarly, operative outcomes and late complications for the matched pairs were assessed using conditional logistic regressions for binary variables and propensity score weighted linear regressions for continuous variables. Log rank tests were employed for time-to-event analyses regarding overall survival and complication-free survival to compare the survival function between Ross and mAVR over a 10-year follow-up period. All analyses were performed using Stata MP 16.1 (StataCorp LLC).

### 3 | RESULTS

Of the 32 matched pairs, the mean age was 37.1 years and 22 patients (68.8)% were male. Mean body surface area of the cohort was  $2.06 \text{ m}^2$  with SD of  $0.29 \text{ m}^2$ . The most common cardiovascular risk factors observed for all included patients were any tobacco use and hypertension at 53.1% and 48.4%, respectively. Atrial flutter/fibrillation and transient ischemic attack/stroke were the most commonly observed comorbidities but only at 17.2% and 10.9% of the cohort, respectively. Of the study population, 26.7% and 7.8% underwent previous surgical or catheter-based cardiac interventions before their index Ross or mAVR, respectively (Table S2). The most common clinical presentations were dyspnea, fatigue and chest pain/angina at 46.9%, 37.5%, and 29.7%, respectively. Furthermore, of those patients for whom NYHA stages could be deduced from the electronic medical record, 65% were classified as either functional class I or II before surgery. The most frequently observed indication for surgery was the presence of a bicuspid aortic valve at 54.7% followed closely by aortic insufficiency at 50%, although it should be noted that these were not mutually exclusive. There were no statistically significant differences between those patients who underwent the Ross procedure and mAVR with respect to the demographic and preoperative characteristics discussed here and found in Table 1. The only exception to this was with respect to indication, with the presence of either a bicuspid aortic valve (p = .01) or ascending aortic aneurysm (p = .02) being significantly more common indications for the Ross procedure than mAVR.

The Ross procedure was associated with significantly longer cardiopulmonary bypass and cross-clamp times (p < .01). The most common type of aortic prosthesis employed for mAVR was St. Jude (St. Jude Medical Inc.) while the most frequent type of pulmonic

CARDIAC SURGERY -WILEY

prosthesis utilized for the pulmonary autograft technique was CryoLife SynerGraft (CryoLife Inc.). Concomitant procedures at the time of Ross or mAVR included aortic arch replacement (17.2%), mitral valve replacement (n = 8; 12.5%) and root replacement (Bentall procedure, n = 8; 12.5%). There were no statistically significant differences with respect to time to extubation, cardiovascular intensive care unit or hospital length of stay between the two groups. No early mortality (within 30 days) was observed for either group and there were no statistically significant differences between the groups regarding early complications including arrhythmia (approaching significance), acute renal failure (documented by nephrology or requiring dialysis) or readmission. Additional operative and early postoperative characteristics and outcomes can be found in Table 2.

Of the matched Ross patients, three required reintervention of either the aortic or pulmonic valves (Table S3). One patient developed aortic insufficiency as well as mitral regurgitation necessitating aortic valve replacement and mitral valve repair. Another patient acquired severe pulmonic insufficiency and ascending aortic aneurysm requiring pulmonic valve and ascending aortic replacement. The third underwent endovascular pulmonic valve repair for pulmonic stenosis. Two mAVR patients required reintervention of the aortic valve. The first developed severe aortic and mitral insufficiency requiring a Bentall procedure and mitral valve replacement. This was ultimately succeeded by repeat transcatheter aortic valve replacement 15 years later. The other patient acquired severe aortic insufficiency secondary to endocarditis necessitating a Bentall procedure. 1-, 5-, and 10-year reintervention-free survival following Ross or mAVR was 100% and 100%, 97% and 97% and 80% and 77%, respectively (Figure 1). There was no statistically significant difference in reintervention free survival between the two groups (p = .91).

Median time-to-follow-up was 7.3 (interguartile range [IQR]: 5.7-11.7) and 6.9 (IQR: 5.6-10.0) years for Ross and mAVR, respectively. For those patients who developed complications, NYHA functional classification did not differ significantly between the groups (Table 3). Peak and mean aortic valve gradients at time of last follow-up were significantly lower for Ross patients at 8.2 and 4.5 mmHg, respectively (p < .01). Pulmonic valve hemodynamics amongst Ross patients approached clinical significance with higher peak and mean pulmonic valve gradients of 16.0 mmHg (p = .06) and 10.0 mmHg (p = .051), respectively (Table 4). Sinus of Valsalva diameter was significantly higher for Ross patients at 37.71 mm (p = .018). No statistically significant differences were appreciated for the remaining echocardiographic variables at time of last follow-up including left ventricular ejection fraction and ascending aorta diameters. 1-, 5-, and 10-year freedom from valve dysfunction following Ross or mAVR was 100% and 100%, 97% and 97% and 80% and 77%, respectively (Figure 2). There was no statistically significant difference with respect to valve dysfunction free survival between the two groups (p = .91). Major hemorrhage (intracranial, gastrointestinal, genitourinary, and nasal) requiring anticoagulation reversal, blood product administration and/or hospitalization as well

### TABLE 1 Demographics and preoperative characteristics of matched adults who underwent Ross or mAVR

WENOS	ΕT	AL.
-------	----	-----

	Ross (n = 32)	mAVR ( <i>n</i> = 32)	Total (n = 64)	p value
Age, mean ( <i>SD</i> )	36.88 (10.64)	37.38 (9.28)	37.13 (9.91)	.87
Sex				.99
Male	22 (68.75)	22 (68.75)	44 (68.75)	
Female	10 (31.25)	10 (31.25)	20 (31.25)	
Body surface area (m <sup>2</sup> ), mean (SD)	2.06 (0.20)	2.06 (0.35)	2.06 (0.29)	.60
Cardiovascular risk factors				
Obesity	3 (9.38)	3 (9.38)	6 (9.38)	>.99
Smoker	17 (53.13)	17 (53.13)	34 (53.13)	>.99
Hypertension	16 (50.00)	15 (46.88)	31 (48.44)	.81
Hyperlipidemia	4 (12.50)	3 (9.38)	7 (10.94)	.65
Diabetes mellitus	1 (3.13)	1 (3.13)	2 (3.13)	>.99
Comorbidities				
Atrial fibrillation/flutter	6 (18.75)	5 (15.63)	11 (17.19)	.76
Transient ischemic attack/stroke	3 (9.38)	4 (12.50)	7 (10.94)	.70
Peripheral vascular disease	1 (3.13)	1 (3.13)	2 (3.13)	>.99
Chronic obstructive pulmonary disease	1 (3.13)	0 (0.00)	1 (1.56)	
Previous cardiac intervention				
Surgical	9 (28.13)	10 (31.25)	19 (29.69)	.78
Catheter-based	4 (12.50)	1 (3.13)	5 (7.81)	.35
New York Heart Association functional classification				>.99
1	7 (21.88)	8 (25.00)	15 (23.44)	
П	5 (15.63)	6 (18.75)	11 (17.19)	
ш	6 (18.75)	3 (9.38)	9 (14.06)	
IV	3 (9.38)	2 (6.25)	5 (7.81)	
Clinical presentation				
Dyspnea	14 (43.75)	16 (50.00)	30 (46.88)	.62
Fatigue	11 (34.38)	13 (40.63)	24 (37.50)	.62
Chest pain/angina	9 (28.13)	10 (31.25)	19 (29.69)	.74
Palpitations	7 (21.88)	3 (9.38)	10 (15.63)	.20
Congestive heart failure	4 (12.50)	4 (12.50)	8 (12.50)	>.99
Presyncope/syncope	3 (9.38)	1 (3.13)	4 (6.25)	.31
Asymptomatic	6 (18.75)	7 (21.88)	13 (20.31)	.78
ndication				
Aortic stenosis	5 (15.63)	4 (12.50)	9 (14.06)	.74
Aortic insufficiency	12 (37.50)	20 (62.50)	32 (50.00)	.05
Mixed	15 (46.88)	6 (18.75)	21 (32.81)	.02
Bicuspid aortic valve	23 (71.88)	12 (37.50)	35 (54.69)	.01
Ascending aortic aneurysm	16 (50.00)	6 (18.75)	22 (34.38)	.02
Endocarditis/rheumatic heart disease	6 (18.75)	10 (31.25)	16 (25.00)	.28

Note: Variables expressed as number (%) unless otherwise specified. Degree of aortic insufficiency this was collected as none (0), mild (1), moderate (2), severe (3) with the associated numerical values denoted in parentheses.

Abbreviations: mAVR, mechanical aortic valve replacement; SD, standard deviation.

# CARDIAC SURGERY -WILEY-

#### TABLE 2 Operative and early postoperative characteristics of adults who underwent Ross or mAVR

	$D_{a}$ ( $u = 22$ )	$m(\Lambda)/D(m-22)$	$\mathbf{T}_{abal} (u = (A)$	
	Ross (n = 32)	mAVR ( <i>n</i> = 32)	Total (n = 64)	p value
Cardiopulmonary bypass time (min), 95% Cl	233.33, 292.39	137.28, 215.77	199.83, 251.62	<.01
Cross-clamp time (min), 95% CI	190.07, 225.86	100.54, 146.84	150.05, 186.20	<.01
Concomitant procedure, n (%)				
Aortic arch replacement (hemiarch)	6 (18.75)	5 (15.63)	11 (17.19)	
Mitral valve replacement	0 (0.00)	8 (25.00)	8 (12.50)	
Bentall procedure	-	8 (25.00)	8 (12.50)	
Mitral valve repair	2 (6.25)	2 (6.25)	4 (6.25)	>.99
Coronary artery bypass grafting	3 (9.38)	1 (3.13)	4 (6.25)	.31
Time to extubation (h), 95% CI	9.85, 15.96	8.53, 15.09	10.24, 14.48	.71
Cardiovascular intensive care unit length of stay (d), 95% CI	2.06, 3.00	1.75, 3.20	2.08, 2.92	.92
Hospital length of stay (d), 95% Cl	7.11, 12.62	5.10, 21.22	7.33, 15.75	.43
Early mortality (<30 days), n (%)	0 (0.00)	0 (0.00)	0 (0.00)	
Early complications, n (%)				
Arrhythmia requiring medication or cardioversion	5 (15.63)	0 (0.00)	5 (7.81)	.053
Pleural effusion	3 (9.38)	1 (3.13)	4 (6.25)	.31
Renal failure	2 (6.25)	2 (6.25)	4 (6.25)	>.99
Readmission within 30 days	3 (9.38)	0 (0.00)	3 (4.69)	>.99
Pericardial effusion	2 (6.25)	0 (0.00)	2 (3.13)	
Hemorrhage requiring reexploration	0 (0.00)	2 (6.25)	2 (3.13)	

Note: Variables expressed as mean (standard deviation) unless otherwise specified.

Abbreviations: CI, confidence interval; ICD, implantable cardioverter-defibrillator; mAVR, mechanical aortic valve replacement; PDA, patent ductus arteriosus.

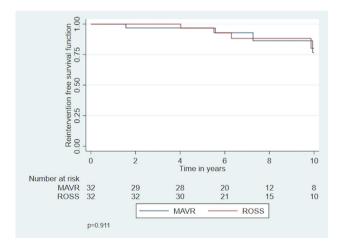


FIGURE 1 Kaplan-Meier freedom from reintervention

as stroke events were significantly more frequent in the mAVR population (p < .01). 1-, 5-, and 10-year major hemorrhage free survival following Ross or mAVR was 100% and 94%, 100% and 80% and 83% and 61%, respectively (Figure 3). Similarly, 1-, 5-, and 10-year stroke free survival following Ross or mAVR was 100% and 97%, 100% and 80% and 83% an 45% (Figure 4). With respect to freedom from all complications including endocarditis, arrhythmia, aortic root and ascending aortic dilatation, no significant differences were appreciated between the two groups (p = .46).

Late mortality amongst both Ross (n = 3) and mAVR (n = 4) patients was rare (Table 5). Heart failure and ventricular tachycardia/ fibrillation were the cited causes of death for two of the Ross subjects with unknown cause for the remaining patient. Cause of death following mAVR included massive hemorrhage and aortic dissection with septic shock, with unknown cause for the remaining two subjects. The mAVR patient that sustained a lethal intracerebral

	Any complica Estimates	Any complications at follow-up		
	for Ross	95% CI	p value	
Time-to-follow-up (year) <sup>a</sup>	-0.64	-3.28, 1.99	.62	
New York Heart Association functional classification <sup>b</sup>	0.36	0.09, 1.44	.15	
Late complications <sup>b</sup> , <sup>c</sup>				
Bleeding	0.03	0, 0.24	<.01	
Stroke	0.06	0.00, 0.51	<.01	
Endocarditis	0.17	0, 1.66	.13	
Arrhythmia	1.63	0.34, 9.01	.73	
Aortic root dilatation	4.10	0.99, 18.96	.052	
Ascending aortic dilatation	6.37	0.70, 315.12	.13	

**TABLE 3** Late complications of adults who underwent Ross or mAVR

Note: Among patients who had any complication at follow-up, variables expressed above as:

<sup>a</sup>Matched β-coefficients or

<sup>b</sup>Matched odds ratio.

<sup>c</sup>Exact weight logistical regression.

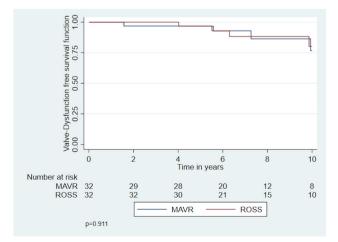
Abbreviations: CI, confidence interval; mAVR, mechanical aortic valve replacement.

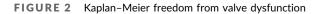
	Ross (n = 32)	mAVR ( <i>n</i> = 32)	p value
Time-to-follow-up (year), median (IQR)	6 (4.4–8.6)	5.6 (3.6-9.2)	
Left ventricular ejection fraction (%)	57.75 (13.67)	53.36 (10.43)	.155
Peak aortic valve gradient (mmHg)	8.18 (2.99)	29.87 (19.06)	<.01
Mean aortic valve gradient (mmHg)	4.47 (1.45)	15.82 (11.77)	<.01
Peak pulmonic valve gradient (mmHg)	15.97 (9.51)	8.2 (4.35)	.06
Mean pulmonic valve gradient (mmHg)	9.95 (7.20)	4.17 (2.36)	.051
Sinus of Valsalva (mm)	37.71 (7.96)	32.10 (7.55)	.018
Ascending aorta (mm)	36.34 (6.12)	33.92 (9.26)	.905

TABLE 4Echocardiographic variablesat last follow-up of adults who underwentRoss or mAVR

*Note*: Variables expressed as mean (*SD*) with *p* values from generalized regression on matched data with robust standard error, unless otherwise specified.

Abbreviations: IQR, interquartile range; mAVR, mechanical aortic valve replacement.





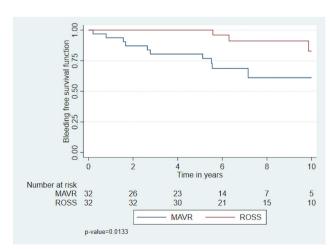
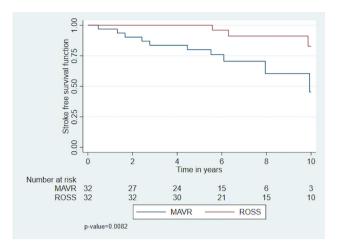


FIGURE 3 Kaplan-Meier freedom from major hemorrhage



**FIGURE 4** Kaplan-Meier freedom from stroke

TABLE 5	Late mortality	of adults who und	derwent Ross or mAVR
IADLEJ	Late mortant	/ OF adults who und	JEIWEIIL KUSS UI IIIAVK

	Ross (n = 32)	mAVR (n = 32)	Total (n = 64)	
Late mortality	3 (9.38)	4 (12.5)	7 (10.94)	
Interval from index operation (year), mean (SD)	7.27 (2.31)	6.78 (4.05)	6.99 (3.17)	
Cause				
Thromboembolism	0 (0.00)	0 (0.00)	0 (0.00)	
Massive hemorrhage	0 (0.00)	1 (25.00)	1 (14.29)	
Heart failure	1 (50.00)	0 (0.00)	1 (14.29)	
Ventricular tachycardia/ fibrillation	1 (50.00)	0 (0.00)	1 (14.29)	
Other	0 (0.00)	1 (25.00)	1 (14.29)	
Unknown	1 (0.00)	2 (50.00)	2 (28.57)	

Note: Variables expressed as number (%) unless otherwise specified. Other cause of death was aortic dissection and septic shock. Abbreviation: mAVR, mechanical aortic valve replacement.

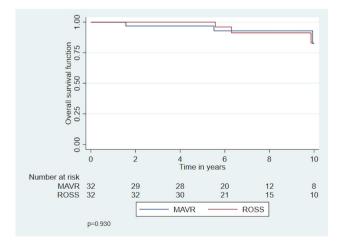


FIGURE 5 Kaplan-Meier overall survival

CARDIAC SURGERY -WILEY

hemorrhage had experienced several prior cerebrovascular insults secondary to a vegetative aortic valve thrombus. 1-, 5-, and 10-year survival following Ross or mAVR was 100% and 100%, 100% and 97% and 83% and 83%, respectively (Figure 5). No significant difference regarding overall survival was observed (p = .93).

### 4 | CONCLUSIONS

To the best of our knowledge, this is the first study in over two decades documenting the experience of the Ross procedure compared to mAVR in the United States.<sup>21,22</sup> The technical complexity, longer operative times and dual valve manipulation of the Ross procedure have often been cited as its weaknesses, resulting in apprehension and ultimately diminished use of this aortic valve replacement strategy in recent years. Despite longer cardio-pulmonary bypass and cross-clamp times, this series demonstrated similar perioperative outcomes including time to extubation, cardio-vascular intensive care unit and hospital length of stay, renal failure and readmission. Additionally, no early mortality (within 30 days) was observed for either group, indicating that the complex and lengthy nature of the Ross procedure does not appear to translate into worse early postoperative outcomes.

As has been previously reported in the literature, the Ross procedure was also found to offer equivalent freedom from reintervention and valve dysfunction compared to mAVR at 10 years.<sup>13</sup> This finding was extended to the pulmonary homograft with only one Ross patient requiring replacement and another percutaneous balloon valvuloplasty. As would be expected, there was a trend towards significance with respect to higher peak mean pulmonic valve gradients following the Ross procedure. Nevertheless, this did not translate to differences in reintervention of either valve between the two groups. Furthermore, this study demonstrated significantly lower peak and mean aortic valve gradients at time of last follow-up for Ross patients, suggesting not only stability of the pulmonary homograft but also superior aortic valve hemodynamics following the Ross procedure. Sinus of Valsalva diameters were significantly higher following the Ross procedure compared to their mAVR pairs but this was not extended to the ascending aorta, suggesting durability of the aortic root with our reinforcement technique. Despite these encouraging findings, it is important to clarify the similar rates of valve dysfunction and reoperations highlighted in Figures 1 and 2. As has been reported in prior Ross series, many patients develop valve dysfunction that do not ultimately go on to require reoperation, an observation that is at odds with these results. This is most likely due to the shorter time to echocardiographic follow-up relative to clinical follow-up observed in this study across both cohorts. Median (interquartile range) times to echocardiographic and clinical follow-up for Ross patients were 6 years (4.4-8.6) and 7.3 years (5.7-11.7), respectively. Likewise median times for mAVR patients were 5.6 years (3.6-9.2) and 6.9 years (5.6-10.0), respectively. These differences may have resulted in an underestimation of the true rates of valve dysfunction.

In accordance with several prior studies, mAVR was associated with significantly more major hemorrhage and stroke events compared to the Ross procedure.<sup>13,22</sup> It is important to note that a St. Jude aortic valve prosthesis (St. Jude Medical Inc.) was implanted into 66% of mAVR patients included in this study. Interim results of the Prospective Randomized On-X Anticoagulation Clinical Trial indicate that the Food and Drug Administration-approved On-X mechanical valve can be safely managed with a reduced international normalized ratio goal of 1.5-2.0 when implanted in the aortic position.<sup>23</sup> This resulted in significantly fewer major and minor bleeding events without associated increase in thromboembolism. Additionally, a propensity-matched cohort study performed by Mokhles<sup>24</sup> and colleagues demonstrated equivalent bleeding and thromboembolic events with no difference in overall survival at 8 years when patients adhered to optimal anticoagulation selfmanagement.<sup>25</sup> This highlights the importance of discussing valve replacement options with patients as well as appropriate patient selection by surgeons.

Despite the significantly reduced major hemorrhage and stroke free survival observed amongst mAVR patients, this did not translate into a significant difference in overall survival between the two groups, an observation that is at odds with similar propensity-matched studies and a recent metaanalysis.<sup>13,14,22</sup> Given that survival benefits in those studies were reported at 20 years, our negative finding is likely the result of an inadequate median follow-up period of 7.33 (IQR: 5.7-11.7) and 6.89 (IQR: 5.6-10.0) years for Ross and mAVR, respectively. Additional limitations of this study include its small sample size that is presumably insufficiently powered to detect survival differences. While randomization was successfully conducted in one clinical trial by Doss et al.,<sup>26</sup> these profoundly distinct aortic valve replacement strategies do not easily lend themselves to random treatment allocation secondary to surgeon and patient preferences.<sup>26</sup> Nevertheless, this is another limitation of the current study for which propensity score weight bivariate analysis was a practical alternative. Even with these limitations, our results may be more generalizable than other studies as multiple surgeons (four) performed the Ross procedures.

In conclusion, the current study demonstrates that the Ross procedure offers equivalent perioperative outcomes, freedom from reintervention, freedom from valve dysfunction and overall survival compared to traditional mAVR in young and middle-aged adults but without the need for long-term anticoagulation. Thus, the Ross procedure should be strongly considered in select patients requiring aortic valve replacement at specialized centers.

#### ACKNOWLEDGMENTS

The authors wish to acknowledge the support of the Riley Clinical Data and Outcomes Center.

#### CONFLICT OF INTEREST

The authors declare no conflict of interest.

#### ORCID

Chelsea D. Wenos D https://orcid.org/0000-0001-7197-7693

#### REFERENCES

- Bouhout I, Stevens LM, Mazine A, et al. Long-term outcomes after elective isolated mechanical aortic valve replacement in young adults. J Thorac Cardiovasc Surg. 2014;148:1341-1346.
- Goldstone AB, Chiu P, Baiocchi M, et al. Mechanical or biologic prostheses for aortic-valve and mitral-valve replacement. N Engl J Med. 2017;377:1847-1857.
- Hirji SA, Kolkailah AA, Ramirez-Del Val F, et al. Mechanical versus bioprosthetic aortic valve replacement in patients aged 50 years and younger. Ann Thorac Surg. 2018;106:1113-1120.
- Ross DN. Replacement of aortic and mitral valves with a pulmonary autograft. Lancet. 1967;2:956-958.
- Brown JW, Ruzmetov M, Fukui T, Rodefeld MD, Mahomed Y, Turrentine MW. Fate of the autograft and homograft following Ross aortic valve replacement: reoperative frequency, outcome, and management. J Heart Valve Dis. 2006;15:253-260.
- Brown JW, Ruzmetov M, Shahriari A, Rodefeld MD, Mahomed Y, Turrentine MW. Midterm results of Ross aortic valve replacement: a single-institution experience. *Ann Thorac Surg.* 2009;88:601-608.
- Brown JW, Ruzmetov M, Shahriari A, Rodefeld MD, Turrentine MW, Mahomed Y. The Ross full root replacement in adults with bicuspid aortic valve disease. J Heart Valve Dis. 2011;20:332-340.
- Charitos El, Stierle U, Hanke T, Schmidtke C, Sievers HH, Richardt D. Long-term results of 203 young and middle-aged patients with more than 10 years of follow-up after the original subcoronary operation. *Ann Thorac Surg.* 2012;93:495-502.
- David TE, David C, Woo A, Manlhiot C. The Ross procedure: outcomes at 20 years. J Thorac Cardiovasc Surg. 2014;147:85-93.
- Herrmann JL, Stram AR, Brown JW. Ross procedure: how to do it and how to teach it. World J Pediatr Congenit Heart Surg. 2019;10: 624-627.
- 11. Mastrobuoni S, de Kerchove L, Solari S, et al. The Ross procedure in young adults: over 20 years of experience in our institution. *Eur J Cardiothorac Surg.* 2016;49:507-512.
- Bouhout I, Stevens LM, Mazine A, et al. Long-term outcomes after elective isolated mechanical aortic valve replacement in young adults. J Thorac Cadiovasc Surg. 2014;148:1341-13456.
- Mazine A, David TE, Rao V, et al. Long-term outcomes of the Ross procedure versus mechanical aortic valve replacement. *Circulation*. 2016;134:576-585.
- 14. Buratto E, Shi WY, Wynne R, et al. Improved survival after the Ross procedure compared with mechanical aortic valve replacement. *J Am Coll Cardiol*. 2018;71:1337-1344.
- Tantengco MV, Humes RA, Clapp SK, et al. Aortic root dilation after the Ross procedure. Am J Cardiol. 1999;83:915-920.
- Solymar L, Südow G, Holmgren D. Increase in size of the pulmonary autograft after the Ross operation in children: growth or dilation? *J Thorac Cardiovasc Surg.* 2000;119:4-9.
- 17. David TE, Omran A, Ivanov J, et al. Dilation of the pulmonary autograft after the Ross Procedure. *J Thorac Cardiovasc Surg.* 2000;119:210-220.
- Laudito A, Brook MM, Suleman S, et al. The Ross procedure in children and young adults: a word of caution. J Thorac Cardiovasc Surg. 2001;122:147-153.
- 19. Brown JW, Fehrenbacher JW, Ruzmetov M, Shahriari A, Miller J, Turrentine MW. Ross root dilation in adult patients: is preoperative aortic insufficiency associated with increased late autograft reoperation? *Ann Thorac Surg.* 2011;92:74-81.
- 20. Nishimura RA, Otto CM, Bonow RO, et al. 2014 AHA/ACC guideline for the management of patients with valvular heart disease: executive summary. *Circulation*. 2014;129:2440-2492.

# CARDIAC SURGERY -WILEY

- Jaggers J, Harrison JK, Bashore TM, David RD, Glower DD, Ungerleider RM. The Ross procedure: shorter hospital stay, decreased morbidity, and cost effective. Ann Thorac Surg. 1998;65: 1553-1558.
- Mazine A, Rocha RV, El-Hamamsy I, et al. Ross procedure vs mechanical aortic valve replacement in adults: a systematic review and meta-analysis. JAMA Cardiol. 2018;3:978-987.
- 23. Puskas J, Gerdisch M, Nichols D, et al. Reduced anticoagulation after mechanical aortic valve replacement: interim results from the prospective randomized On-X valve anticoagulation clinical trial randomized Food and Drug Administration investigational device exemption trial. J Thorac Cardiovasc Surg. 2014;147:1202-1211.
- Mokhles MM, Körtke H, Stierle U, et al. Survival comparison of the Ross procedure and mechanical valve replacement with optimal selfmanagement anticoagulation therapy: propensity-matched cohort study. *Circulation*. 2011;123:31-38.
- 25. Koertke H, Minami K, Boethig D, et al. INR self-management permits lower anticoagulation levels after mechanical heart valve replacement. *Circulation*. 2003;108:75-78.

 Doss M, Wood JP, Martens S, Wimmer-Greinecker G, Moritz A. Do pulmonary autografts provide better outcomes than mechanical valves? A prospective randomized trial. *Ann Thorac Surg.* 2005;80: 2194-2198.

#### SUPPORTING INFORMATION

Additional supporting information can be found online in the Supporting Information section at the end of this article.

How to cite this article: Wenos CD, Herrmann JL, Timsina LR, Patel PM, Fehrenbacher JW, Brown JW. Perioperative and long-term outcomes of Ross versus mechanical aortic valve replacement. *J Card Surg.* 2022;37:2963-2971. doi:10.1111/jocs.16831