Perioperative and Long-Term Outcomes of Ross versus Mechanical Aortic Valve Replacement

Chelsea Wenos¹, Jeremy Herrmann¹, Lava Timsina¹, Parth M. Patel¹, John W. Fehrenbacher¹, and John Brown¹

¹Indiana University Department of Surgery

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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 to 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 < 0.01). Overall survival (p = 0.93), freedom from reintervention and valve dysfunction free survival (p = 0.91) 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 expertise, the Ross procedure should be strongly considered in select patients requiring aortic valve replacement.

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*Chelsea D. Wenos, MD¹;*Jeremy L. Herrmann, MD^{1,2}; Lava R. Timsina, MPH, PhD^{1,3}; Parth M. Patel, MD¹; John W. Fehrenbacher, MD^{1,4} and John W. Brown, MD^{1,2}

¹Indiana University School of Medicine, Indianapolis, IN, Division of Thoracic and Cardiovascular Surgery²Riley Children's Health, Indiana University Health, Indianapolis, IN ³Indiana University School of Medicine, Center for Outcomes Research in Surgery, Indianapolis, IN, Department of Surgery ⁴Indiana University Health Methodist Hospital, Indianapolis, IN, Division of Cardiothoracic Surgery *Co-authors

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Corresponding Author: Chelsea D. Wenos, MD who can be reached at chelsea.wenos@unmc.edu

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Methods Data were retrospectively collected for patients 18 to 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 < 0.01). Overall survival (p = 0.93), freedom from reintervention and valve dysfunction free survival (p = 0.91) 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 expertise, the Ross procedure should be strongly considered in select patients requiring aortic valve replacement.

Word count: 250

INTRODUCTION The optimal type of aortic valve replacement for young and middle-aged adults continues to serve as a

challenging clinical judgement 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.¹⁻³ 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.⁴ 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 long-term outcomes with respect to operative mortality, freedom from major complications, freedom from reintervention and overall survival.⁵⁻⁷ 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).⁸⁻¹¹

Several recent studies have added further support to the use of the Ross procedure in young and middle-aged adults. A propensity-matched analysis from the University of Toronto including 208 pairs of patients who underwent the Ross procedure or mechanical aortic valve replacement (mAVR) demonstrated equivalent select perioperative outcomes, freedom from valve deterioration and reintervention and overall survival. ¹² 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. ¹³Neither 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. 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. Moreover, according to the most recent AHA/ACC guidelines, mechanical prostheses are recommended for most patients less than 50 years of age undergoing aortic valve replacement.

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.

METHODS

Data for all patients age 18 to 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. Demographics, perioperative, operative and postoperative variables were collected from the electronic medical record. Primary endpoints included overall survival and freedom from re-intervention of either aortic or pulmonic valves. Valve dysfunction, defined as moderate insufficiency or greater at the aortic or pulmonic valve, aortic valve gradient > 20 mm Hg or pulmonic valve gradient > 40 mm Hg, 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 anti-hypertensive, 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 follow-up of less than one year were excluded from the study in order to accurately predict post-operative and long-term complications. Prior to propensity score matching, there was significant disparity appreciated between the two groups; however, this difference became insignificant following matching (see Supplementary Figure 1). 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 in order to compare the survival function between Ross and mAVR over a ten-year follow-up period. All analyses were performed using Stata MP 16.1 (StataCorp LLC; College Station, TX).

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 m² with SD of 0.29 m². 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 prior to their index Ross or mAVR. respectively (Supplementary Table 1). 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 prior to surgery. The most frequently observed indication for surgery was the presence of a bicuspid aortic valve at 54.7% followed closely by a ortic 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 = 0.01) or ascending aortic aneurysm (p = 0.02) 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 < 0.01). The most common type of aortic prosthesis employed for mAVR was St. Jude (St. Jude Medical Inc.; Saint Paul, MN) while the most frequent type of pulmonic prosthesis utilized for the pulmonary autograft technique was CryoLife SynerGraft (CryoLife Inc.; Kennesaw, GA). 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 thirty 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 post-operative characteristics and outcomes can be found in Table 2.

Of the matched Ross patients, three required reintervention of either the aortic or pulmonic valves (Supplementary Table 2). 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 fifteen years later. The other patient acquired severe aortic insufficiency secondary to endocarditis necessitating a Bentall procedure. One-, five- and ten-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 = 0.91).

Median time-to-follow-up was 7.3 (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 -23.0 mm Hg and -12.5 mm Hg, respectively (p < 0.01). No statistically significant differences were appreciated for the remaining echocardiographic variables at time of last follow-up including left ventricular ejection fraction, peak and mean pulmonic valve gradients, sinus of Valsalva and ascending aorta diameters. One-, five- and ten-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 = 0.91). Major hemorrhage (intracranial, gastrointestinal, genitourinary and nasal) requiring anticoagulation reversal, blood product administration and/or hospitalization as well as stroke events were significantly more frequent in the mAVR population (p < 0.01). One-, five- and ten-year major hemorrhage free survival

following Ross or mAVR was 100% and 94%, 100% and 80% and 83% and 61%, respectively (Figure 3). Similarly, one-, five- and ten-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 = 0.46).

Late mortality amongst both Ross (n=3) and mAVR (n=4) patients was rare (Table 4). 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 hemorrhage had experienced several prior cerebrovascular insults secondary to a vegetative aortic valve thrombus. One-, five- and ten-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=0.93).

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 mechanical aortic valve replacement in the United States. ^{21,22} 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 cardiopulmonary bypass and cross-clamp times, this series demonstrated similar perioperative outcomes including time to extubation, cardiovascular intensive care unit and hospital length of stay, renal failure and readmission. Additionally, no early mortality (within thirty 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 ten years. ¹² This finding was extended to the pulmonary homograft with only one Ross patient requiring replacement and another percutaneous balloon valvuloplasty. Furthermore, this study demonstrated significantly lower peak and mean aortic valve gradients at time of last follow-up for Ross patients with similar overall pulmonic valve function, suggesting not only stability of the pulmonary homograft but also superior aortic valve hemodynamics following the Ross procedure.

In accordance with several prior studies, mechanical aortic valve replacement was associated with significantly more major hemorrhage and stroke events compared to the Ross procedure. ^{12,22} It is important to note that a St. Jude aortic valve prosthesis (St. Jude Medical Inc.; Saint Paul, MN) was implanted into 66% of mAVR patients included in this study. Interim results of the Prospective Randomized On-X Anticoagulation Clinical Trial (PROACT) indicate that the Food and Drug Administration (FDA)-approved On-X mechanical valve can be safely managed with a reduced international normalized ratio (INR) goal of 1.5-2.0 when implanted in the aortic position. ²³ This resulted in significantly fewer major and minor bleeding events without associated increase in thromboembolism. Additionally, a propensity-matched cohort study performed by Mokhles and colleagues demonstrated equivalent bleeding and thromboembolic events with no difference in overall survival at eight years when patients adhered to optimal anticoagulation self-management. ^{24,25} 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 meta-analysis. ^{12,13,22} 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., these profoundly distinct aortic valve replacement strategies do not easily lend

themselves to random treatment allocation secondary to surgeon and patient preferences.²⁶ 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 mechanical aortic valve replacement 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.

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Tables:

Table 1	Table 1	Table 1	Table 1	Table 1
Demographics	Demographics	Demographics	Demographics	Demographics
and preoperative	and preoperative	and preoperative	and preoperative	and preoperative
characteristics of	characteristics of	characteristics of	characteristics of	characteristics of
adults who	adults who	adults who	adults who	adults who
underwent Ross	underwent Ross	underwent Ross	underwent Ross	underwent Ross
or mAVR	or mAVR	or $mAVR$	or $mAVR$	or mAVR
	Ross (n = 32)	mAVR (n = 32)	Total (n = 64)	p value
Age, mean (SD)	36.88 (10.64)	37.38 (9.28)	37.13 (9.91)	0.87
Sex				0.99
Male	22 (68.75)	22(68.75)	44 (68.75)	
Female	10 (31.25)	10 (31.25)	20 (31.25)	
Body surface area	2.06 (0.20)	$2.06 \ (0.35)$	2.06(0.29)	0.60
(m^2) , mean (SD)				
Cardiovascular	Cardiovascular	Cardiovascular	Cardiovascular	Cardiovascular
risk factors	risk factors	risk factors	risk factors	risk factors
Obesity	3(9.38)	3(9.38)	6(9.38)	> 0.99
Smoker	17 (53.13)	17 (53.13)	34 (53.13)	> 0.99

Hypertension Hyperlipidemia Diabetes mellitus Comorbidities Atrial	16 (50.00) 4 (12.50) 1 (3.13) Comorbidities 6 (18.75)	15 (46.88) 3 (9.38) 1 (3.13) Comorbidities 5 (15.63)	31 (48.44) 7 (10.94) 2 (3.13) Comorbidities 11 (17.19)	0.81 0.65 > 0.99 Comorbidities 0.76
fibrillation/flutter Transient ischemic attack/stroke	3 (9.38)	4 (12.50)	7 (10.94)	0.70
Peripheral vascular disease	1 (3.13)	1 (3.13)	2 (3.13)	> 0.99
Chronic obstructive pulmonary disease	1 (3.13)	0 (0.00)	1 (1.56)	
Previous	Previous	Previous	Previous	Previous
cardiac	cardiac	cardiac	cardiac	cardiac
intervention	intervention	intervention	intervention	intervention
Surgical	9 (28.13)	10(31.25)	19(29.69)	0.78
Catheter-based	4(12.50)	1(3.13)	5 (7.81)	0.35
New York				> 0.99
Heart				
Association				
functional				
classification	7 (01 00)	0 (05 00)	15 (00 44)	
I	7 (21.88)	8 (25.00)	15 (23.44)	
II	5 (15.63)	6 (18.75)	11 (17.19)	
III	6 (18.75)	3(9.38)	9 (14.06)	
IV Clinical	3 (9.38)	2 (6.25)	5 (7.81)	Clinical
	Clinical	Clinical	Clinical	Clinical
presentation	presentation	presentation	presentation	$\mathbf{presentation}$ 0.62
Dyspnea Fatigue	14 (43.75) 11 (34.38)	16 (50.00) 13 (40.63)	30 (46.88) 24 (37.50)	0.62
Chest	9 (28.13)	10 (31.25)	19 (29.69)	0.74
pain/angina	9 (20.19)	10 (31.20)	19 (29.09)	0.74
Palpitations	7 (21.88)	3 (9.38)	10 (15.63)	0.20
Congestive heart	4 (12.50)	4 (12.50)	8 (12.50)	> 0.99
failure	- ()	- ()	()	, ,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,
Presyncope/syncope	3 (9.38)	1 (3.13)	4 (6.25)	0.31
Asymptomatic	6 (18.75)	7 (21.88)	13 (20.31)	0.78
Indication	Indication	Indication	Indication	Indication
Aortic stenosis	5 (15.63)	4 (12.50)	9 (14.06)	0.74
Aortic	12 (37.50)	20 (62.50)	32 (50.00)	0.05
insufficiency				
Mixed	15 (46.88)	6 (18.75)	21 (32.81)	0.02
Bicuspid aortic valve	23 (71.88)	12 (37.50)	35 (54.69)	0.01
Ascending aortic aneurysm	16 (50.00)	6 (18.75)	22 (34.38)	0.02
Endocarditis/rheumat heart disease	ti 6 (18.75)	10 (31.25)	16 (25.00)	0.28

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

Table 2	Table 2	Table 2	Table 2	
Operative and	Operative and	Operative and	Operative and	
early	early	early	early	
post-operative	post-operative	post-operative	post-operative	
characteristics of	characteristics of	characteristics of	characteristics of	
adults who	adults who	adults who	adults who	
underwent Ross	underwent Ross	underwent Ross	underwent Ross	
or mAVR	or mAVR	or mAVR	or mAVR	
01 11111110	Ross $(n = 32)$	mAVR (n = 32)	Total $(n = 64)$	p value
Cardiopulmonary	262.86 (77.64)	176.77 (87.95)	225.73 (92.08)	< 0.01
bypass time (min)	()	()	()	
Cross-clamp time	207.97 (47.05)	123.69 (57.31)	168.13 (66.87)	< 0.01
(min)		, ,	, ,	
Concomitant	Concomitant	Concomitant	Concomitant	Concomitant
$\mathbf{procedure}, n$				
(%)	(%)	(%)	(%)	(%)
Aortic arch	6 (18.75)	5(15.63)	11 (17.19)	
replacement				
(hemiarch)				
Mitral valve	$0\ (0.00)$	8 (25.00)	8 (12.50)	
replacement		- (- ()	
Bentall procedure	- (0.0%)	8 (25.00)	8 (12.50)	
Mitral valve	2(6.25)	2(6.25)	4(6.25)	> 0.99
repair	0 (0 00)	1 (0.10)	1 (0.05)	0.01
Coronary artery	3(9.38)	1(3.13)	4(6.25)	0.31
bypass grafting	12.91 (5.73)	11 01 (6 16)	19 26 (5 99)	0.71
Time to extubation (h)	12.91 (0.75)	11.81 (6.16)	12.36 (5.88)	0.71
Cardiovascular	2.53 (0.95)	2.47 (1.50)	2.5 (1.25)	0.92
intensive care unit	2.55 (0.95)	2.47 (1.50)	2.0 (1.20)	0.92
length of stay (d)				
Hospital length of	9.87 (7.37)	13.16 (21.98)	11.54 (16.45)	0.43
stay (d)	0.01 (1.01)	10.10 (21.00)	11.01 (10.10)	0.10
200J (a)				

Early mortality (< 30 d), n (%)	0 (0.00)	0 (0.00)	0 (0.00)	
Early complications, n (%)	Early complications, n (%)	Early complications, n (%)	Early complications, n (%)	Early complications, n
Arrhythmia requiring medication or cardioversion	5 (15.63)	0 (0.00)	5 (7.81)	0.053
Pleural effusion	3(9.38)	1(3.13)	4(6.25)	0.31
Renal failure	2(6.25)	2(6.25)	4(6.25)	> 0.99
Readmission within 30 days	3 (9.38)	0 (0.00)	3 (4.69)	> 0.99
Pericardial effusion	2 (6.25)	0 (0.00)	2 (3.13)	
Hemorrhage requiring re-exploration	0 (0.00)	2 (6.25)	2 (3.13)	
Variables	Variables	Variables	Variables	Variables
expressed as	expressed as	expressed as	expressed as	expressed as
mean (standard	mean (standard	mean (standard	mean (standard	mean (standard
deviation) unless	deviation) unless	deviation) unless	deviation) unless	deviation) unless
otherwise	otherwise	otherwise	otherwise	otherwise
specified. PDA,	specified. PDA,	specified. PDA,	specified. PDA,	specified. PDA,
patent ductus	patent ductus	patent ductus	patent ductus	patent ductus
arteriosus; ICD,	arteriosus; ICD,	arteriosus; ICD,	arteriosus; ICD,	arteriosus; ICD,
implantable	implantable	implantable	implantable	implantable
cardioverter-	cardioverter-	cardioverter-	cardioverter-	cardioverter-
defibrillator.	defibrillator.	defibrillator.	defibrillator.	defibrillator.

Table 3 Late complications of adults who underwent Ross or mAVR

Time-to-follow-up $(y)^a$

New York Heart Association functional classification^b

$\bf Echocardiogram^a$

Left ventricular ejection fraction (%)

Peak aortic valve gradient (mm Hg)

Mean aortic valve gradient (mm Hg)

Peak pulmonic valve gradient (mm Hg)

Mean pulmonic valve gradient (mm Hg)

Sinus of Valsalva (mm)

Ascending aorta (mm)

Late complications bc

Bleeding

Stroke

Endocarditis

Arrhythmia

Aortic root dilatation

Ascending aortic dilatation

${\bf Table~4}~{\bf Late~mortality~of~adults~who~underwent~Ross~or~mAVR$

Late mortality

Interval from index operation (y), mean (SD)

Cause

 ${\bf Thromboembolism}$

Massive hemorrhage

Heart failure

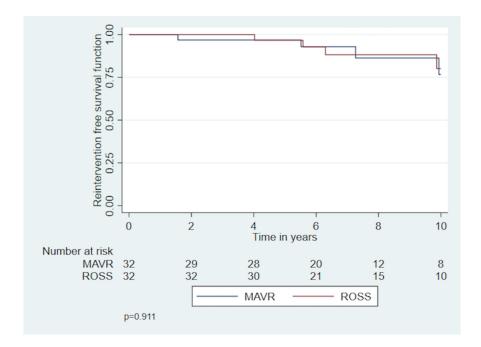
Ventricular tachycardia/fibrillation

Other

Unknown

Variables expressed as number (%) unless otherwise specified. Other cause of death was a rtic dissection and septic shock.

Figures:



 $Figure\ 1$ Kaplan-Meier freedom from reintervention.

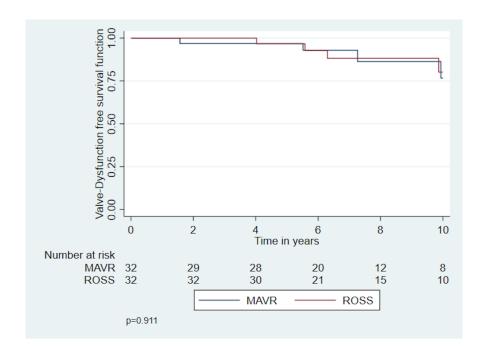
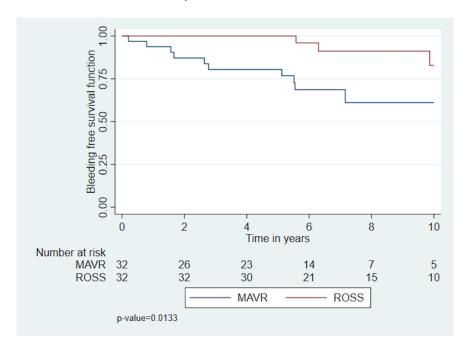


Figure 2 Kaplan-Meier freedom from valve dysfunction.



 $Figure\ \mathcal 3$ Kaplan-Meier freedom from major hemorrhage.

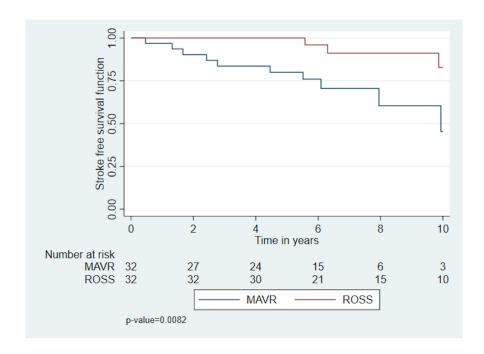
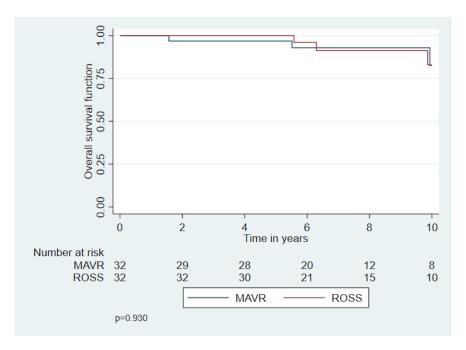


Figure 4 Kaplan-Meier freedom from stroke.



 $Figure\ 5\ {\rm Kaplan\text{-}Meier\ overall\ survival}.$