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Valve-Sparing Root Replacement Compared With Composite Valve Graft Procedures in Patients With Aortic Root Dilation

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ABSTRACT

BACKGROUND Although aortic valve-sparing (AVS) operations are established alternatives to composite valve graft (CVG) procedures for patients with aortic root aneurysms, comparative long-term outcomes are lacking.

OBJECTIVES This study sought to compare the results of patients undergoing AVS procedures with those undergoing CVG operations.

METHODS From 1990 to 2010, a total of 616 patients age <70 years and without aortic stenosis underwent elective aortic root surgery (AVS, n = 253; CVG with a bioprosthesis [bio-CVG], n = 180; CVG with a mechanical prosthesis [m-CVG], n = 183). A propensity score was used as a covariate to adjust for unbalanced variables in group comparisons. Mean age was 46 ± 14 years, 83.3% were male, and mean follow-up was 9.8 ± 5.3 years.

RESULTS Patients undergoing AVS had higher rates of Marfan syndrome and lower rates of bicuspid aortic valve than those undergoing bio-CVG or m-CVG procedures. In-hospital mortality (0.3%) and stroke rate (1.3%) were similar among groups. After adjusting for clinical covariates, both bio-CVG and m-CVG procedures were associated with increased long-term major adverse valve-related events compared with patients undergoing AVS (hazard ratio [HR]: 3.4, p = 0.005; and HR: 5.2, p < 0.001, respectively). They were also associated with increased cardiac mortality (HR: 7.0, p = 0.001; and HR: 6.4, p = 0.003). Furthermore, bio-CVG procedures were associated with increased risk of reoperations (HR: 6.9; p = 0.003), and m-CVG procedures were associated with increased risk of anticoagulant-related hemorrhage (HR: 5.6; p = 0.008) compared with AVS procedures.

CONCLUSIONS This comparative study showed that AVS procedures were associated with reduced cardiac mortality and valve-related complications when compared with bio-CVG and m-CVG. AVS is the treatment of choice for young patients with aortic root aneurysm and normal or near-normal aortic cusps. (J Am Coll Cardiol 2016;68:1838–47)
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Aortic valve-sparing (AVS) operations have become established alternatives to composite valve graft (CVG) procedures for patients with aortic root aneurysms and favorable aortic cusp morphology (1-5). Theoretical benefits of AVS procedures include avoiding the complications associated with prosthetic valves, specifically the risks of systemic thromboembolism and lifelong anticoagulation associated with mechanical valves, or the risks of structural valve deterioration (SVD) and need for reoperation associated with bioprosthetic valves. Although valve-sparing root-replacement

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techniques have been available for more than 30 years (6,7), the proportion of AVS operations among patients undergoing root replacement in the United States has remained approximately 15% and is not increasing (8). Reluctance to perform AVS may be caused in part by concerns regarding the durability of these procedures and the lack of comparative data regarding the long-term safety and effectiveness of AVS compared with traditional CVG procedures.

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Several groups have reported their experience with AVS (1–5), but no large series comparing the long-term outcomes after different approaches to the aortic root have been published. The objective of this study was therefore to compare the early and late results of patients undergoing AVS with those of patients undergoing CVG operations with biologic or mechanical aortic valve prostheses.

METHODS

STUDY POPULATION. All patients who underwent elective aortic root replacement procedures at the Peter Munk Cardiac Centre from January 1990 to December 2010 were identified through the cardiovascular surgery database (n = 1,187). We excluded patients with aortic stenosis, age ≥70 years, aneurysm caused by aortic dissection, infective endocarditis, and all nonelective operations. For patients who underwent more than 1 root-replacement procedure, only the index operation was included. Patients who underwent either reimplantation or remodeling procedures were included in the AVS group. Patients undergoing AVS had aortic root aneurysms and normal or near-normal aortic cusp morphology. The operative techniques for AVS procedures have been described in detail (2,9,10). Patients who underwent CVG procedures were included in the mechanical-CVG (m-CVG) and bioprosthetic-CVG (bio-CVG) groups. The final study cohort consisted of 616 patients <70 years of age who underwent elective root replacement for an aortic root aneurysm without aortic stenosis (AVS, n = 253; bio-CVG, n = 180; m-CVG, n = 183). The decision to perform an AVS operation was largely determined by the quality of the aortic cusps and experience of the surgeon.

DATA COLLECTION AND DEFINITIONS. The perioperative clinical data were prospectively collected on all patients undergoing cardiac surgery in our institutional database. Patients were contacted by telephone or electronically to determine morbid outcomes and to confirm vital status. Echocardiogram reports were reviewed and patients' cardiologists contacted to determine valve-related complications. The follow-up period was closed in March 2015. The mean follow-up duration was 9.8 ± 5.3 years; 113 (18.3%) patients were followed up for >15 years, and 16 (2.6%) for >20 years. Clinical follow-up was complete in 95.1% of patients and duration of follow-up was dissimilar between groups ($p < 0.001$). The AVS, bio-CVG, and m-CVG groups had mean follow-up of 8.9 ± 5.1 years, 10.7 ± 5.5 years, and 10.2 ± 5.3 years, respectively. The Research Ethics Board of the University Health Network approved the study and waived the need for individual patient consent.

Valve-related morbidity and mortality were defined according to the multisociety 2008 valve-reporting guidelines (11). Valve-related complications included SVD, nonstructural valve dysfunction, valve thrombosis, thromboembolism (i.e., neurological events and peripheral embolic events), operated valve endocarditis, reintervention, and bleeding. Anticoagulant-related hemorrhage (ARH) was defined as any bleeding event that occurred

ABBREVIATIONS AND ACRONYMS

ARH = anticoagulant-related hemorrhage

AVS = aortic valve sparing

bio-CVG = biologic composite valve graft

CVG = composite valve graft

HR = hazard ratio

MAVRE = major adverse valve-related events

m-CVG = mechanical composite valve graft

SVD = structural valve deterioration

TABLE 1 Baseline Characteristics of Patients Undergoing Aortic Root Replacement

	AVS (n = 253)	bio-CVG (n = 180)	m-CVG (n = 183)	p Value
Age, yrs	44 ± 14	50 ± 15	47 ± 14	<0.001
Male	201 (79.4)	160 (88.9)	152 (83.1)	0.03
Hypertension	89 (35.2)	62 (34.4)	69 (37.7)	0.79
Diabetes	4 (1.6)	7 (3.9)	12 (6.6)	0.03
Dyslipidemia	45 (17.8)	41 (22.8)	33 (18.0)	0.39
Bicuspid aortic valve	25 (10.2)	89 (51.7)	65 (36.5)	<0.001
Marfan syndrome	111 (43.9)	10 (5.6)	19 (10.4)	<0.001
Aortic insufficiency	188 (74.3)	171 (95.0)	165 (90.2)	<0.001
Cerebrovascular disease	6 (2.4)	2 (1.1)	12 (6.6)	0.01
Peripheral vascular disease	1 (0.4)	5 (2.8)	0 (0.0)	0.02
Renal failure	0 (0.0)	0 (0.0)	3 (1.6)	0.05
Severe pulmonary disease	7 (2.8)	3 (1.7)	5 (2.7)	0.80
Atrial fibrillation or flutter	6 (2.4)	6 (3.3)	15 (8.2)	0.01
Smoking history	106 (42.1)	92 (51.1)	81 (44.3)	0.21
Ejection fraction <40%	16 (6.3)	38 (21.1)	41 (22.4)	<0.001
New York Heart Association functional class				<0.001
No restrictions	179 (70.8)	47 (26.1)	58 (31.7)	
Symptoms with exertion	60 (23.7)	76 (42.2)	63 (34.4)	
Symptoms with normal daily activity	11 (4.3)	48 (26.7)	50 (27.3)	
Unprovoked symptoms	3 (1.2)	5 (2.8)	11 (6.0)	

Values are mean ± SD or n (%).

AVS = aortic valve sparing; bio-CVG = bioprosthetic composite valve graft; m-CVG = mechanical composite valve graft.

TABLE 2 Intraoperative Details

	AVS (n = 253)	bio-CVG (n = 180)	m-CVG (n = 183)	p Value
Previous cardiac surgery	17 (6.7)	33 (18.3)	79 (43.2)	<0.001
Concomitant procedures				
Mitral surgery	27 (10.7)	18 (10.0)	27 (14.8)	0.31
Coronary bypass grafting	21 (8.3)	31 (17.2)	32 (17.5)	0.004
Repair of congenital defect	14 (5.5)	5 (2.8)	10 (5.5)	0.36
Surgeon*				<0.001
Surgeon A	227 (89.7)	122 (67.8)	117 (63.9)	
Surgeon B	16 (6.3)	35 (19.4)	32 (17.5)	
Surgeon C	10 (4.0)	23 (12.8)	34 (18.6)	
Type of valve inserted				
St. Jude Mechanical			183 (100.0)	
Freestyle porcine root		90 (50.0)		
Hancock II		26 (14.4)		
Homograft		24 (13.3)		
Toronto stentless root		27 (15.0)		
Other		13 (7.2)		
Cross-clamp time, min	110 ± 23	103 ± 34	102 ± 42	0.02
Total bypass time, min	131 ± 28	127 ± 41	130 ± 52	0.60
Circulatory arrest	19 (7.5)	11 (6.1)	27 (14.8)	0.01

Values are n (%) or mean ± SD. *One of the surgeon categories is a collapse of multiple surgeons.
Abbreviations as in Table 1.

while the patient was taking anticoagulant or antiplatelet drugs, which caused death, hospitalization, permanent injury, or necessitated transfusion. The primary outcome of interest was major adverse valve-related events (MAVRE), a composite introduced by the valve-reporting guidelines to capture all types of valve-related events, and defined as all-inclusive valve-related mortality, valve-related morbidity (SVD, nonstructural valve dysfunction, valve thrombosis, embolism, endocarditis, or ARH), and the need for permanent pacemaker or defibrillator implantation (11).

TABLE 3 In-Hospital Outcomes

	AVS (n = 253)	Bio-CVG (n = 180)	m-CVG (n = 183)	p Value
Death during hospitalization	1 (0.4)	0 (0.0)	1 (0.5)	1.00
Stroke	1 (0.4)	2 (1.1)	5 (2.7)	0.11
Myocardial infarction	1 (0.4)	3 (1.7)	1 (0.5)	0.40
Intra-aortic balloon pump	3 (1.2)	3 (1.7)	7 (3.8)	0.21
Renal failure	0 (0.0)	1 (0.6)	1 (0.5)	0.52
Pulmonary complications	31 (12.3)	12 (6.7)	24 (13.1)	0.09
Permanent pacemaker	2 (0.8)	9 (5.0)	13 (7.1)	0.001
Atrial fibrillation	44 (17.4)	37 (20.6)	32 (17.5)	0.67
Reoperation for bleeding	15 (5.9)	11 (6.1)	13 (7.1)	0.89
Sternal wound infection	0 (0.0)	0 (0.0)	2 (1.1)	0.17
Sepsis	1 (0.4)	3 (1.7)	5 (2.7)	0.15
Hospital length of stay, days	6 (5-8)	6 (5-8)	8 (6-10)	<0.001

Values are n (%) or median (IQR).
IQR = interquartile range; other abbreviations as in Table 1.

All-cause mortality and cause of death was determined by review of patients' medical records and death certificates. In accordance with the valve reporting guidelines (11), we defined valve-related mortality as any death caused by SVD, nonstructural valve dysfunction, valve thrombosis, embolism, bleeding event, or endocarditis; death related to reintervention on the operated valve; or sudden, unexplained death. Cardiac death includes valve-related deaths, sudden unexplained deaths, and deaths from nonvalve-related cardiac causes, such as heart failure, acute myocardial infarction, aortic events, including death from dissection or aortic reintervention, or documented arrhythmias.

STATISTICAL ANALYSES. Categorical variables were reported as frequencies, and continuous variables were reported as mean ± SD or median with interquartile ranges, as appropriate. Patient and surgical characteristics among the 3 groups were compared using F tests (continuous variables) and Fisher exact tests (binary/polytomous variables).

PROPENSITY SCORE ADJUSTMENT FOR BASELINE DIFFERENCES AMONG GROUPS. A propensity score was created to determine the individual patient probability of undergoing AVS instead of m-CVG or bio-CVG using logistic regression. As pointed out in D'Agostino (12,13), the goal of propensity score modeling is to obtain the probability of surgical strategy in relation to background covariates, and to mitigate selection bias; therefore, overparametrization is not a concern. Subsequently, the propensity score model included pre-operative characteristics as independent variables, including age, sex, clinical presentation, family history of heart disease, smoking history, previous surgical and nonsurgical intervention to the heart, the year of the index operation, baseline comorbidities (including severe pulmonary disease, Marfan syndrome, renal failure), valve disease, presence of bicuspid aortic valve, New York Heart Association functional class, and pre-operative use of statins and aspirin. Surgeon and procedure cross-clamp time were not included in the propensity score, because those factors were not instrumental in the selection of surgical strategy. Few missing values in binary or polytomous variables (such as smoking and New York Heart Association functional class) were assumed to be in the reference category (e.g., patients with missing information on smoking history were assumed to be nonsmokers). The propensity score also modeled nonlinear effects of age and the year of the index operation using

smoothing splines. The propensity score was highly associated with the surgical strategy (area under the curve: 0.92; $p < 0.001$), and it was used as a covariate to adjust for baseline differences among groups, as suggested by D'Agostino (12,13).

OUTCOME ANALYSIS. In descriptive outcome analyses, all-cause mortality was analyzed using the Kaplan-Meier method. Between-group differences in the freedom from death were evaluated using log-rank tests. The multivariate Cox proportional hazard model was used to quantify the effects of surgical strategies, adjusting for linear propensity scores, surgeon, cross-clamp time, Marfan syndrome, concomitant coronary bypass graft, and presence of bicuspid aortic valve. The 95% confidence intervals and p values were assessed using Wald statistics. The assumption of proportional hazard was formally assessed using the resampling method described by Lin et al. (14).

Other time-related events (i.e., cardiac-related mortality, MAVREs, aortic valve reoperation, ARH) were analyzed using competing risk models and reported in terms of cumulative incidence rates. In the unadjusted analysis, between-group differences in the cumulative incidence rates were assessed using Gray tests (15). In the adjusted analyses, the same set of covariates was included in the competing risk models. The corresponding 95% confidence intervals and p values were calculated using Wald statistics. In addition, the proportionality assumption for all independent variables was formally assessed for all models using the resampling methods described by Lin et al. (14). Interactions with time were included if a variable showed evidence of nonproportionality. The use of time interaction in Cox hazard regression or extended Cox models has previously been validated in this context (16,17).

A subgroup analysis was performed excluding AVS patients who underwent aortic valve remodeling, given that aortic valve reimplantation is known to be associated with better outcomes in patients with annuloaortic ectasia. In this subgroup analysis, we only compared the aforementioned unadjusted for each outcome variables. Finally, multivariable models were created to adjust for a number of potentially important covariates in the competing risk model. Variables were selected a priori and included in addition to surgical strategy: propensity score, surgeon, cross-clamp time, concomitant coronary bypass, Marfan syndrome, bicuspid aortic valve pathology, and appropriate time interaction. All statistical analyses were performed using SAS

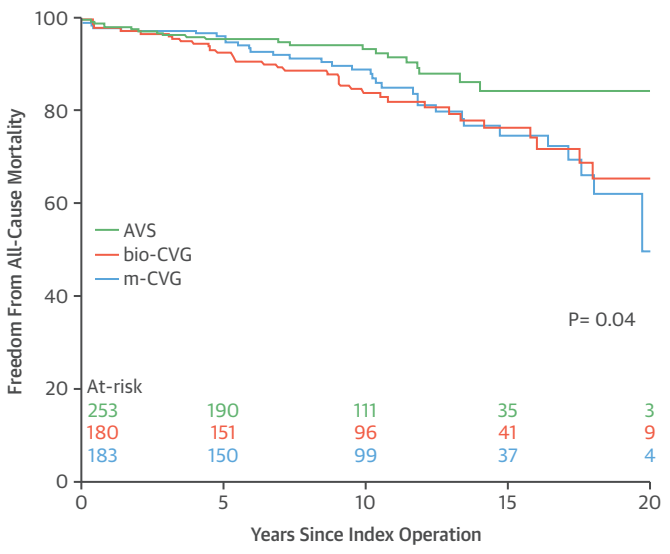
TABLE 4 All-Cause Mortality and Cumulative Incidence Rates at Years 1, 5, 10, and 15

	AVS (n = 253)	Bio-CVG (n = 180)	m-CVG (n = 183)	p Value
Mortality, yrs	21 (8.3)	38 (21.1)	34 (18.6)	
1	2.0 ± 0.9	2.3 ± 1.1	2.2 ± 1.1	0.04
5	4.6 ± 1.4	7.6 ± 2.0	4.0 ± 1.5	
10	6.7 ± 1.8	16.2 ± 3.0	11.2 ± 2.6	
15	15.8 ± 3.8	23.7 ± 4.0	25.3 ± 4.6	
Mortality from cardiac cause, yrs	7 (2.8)	20 (11.1)	24 (13.1)	
1	0.8 ± 0.6	1.7 ± 1.0	1.7 ± 1.0	0.004
5	0.8 ± 0.6	2.9 ± 1.3	3.4 ± 1.4	
10	2.3 ± 1.2	7.4 ± 2.2	9.2 ± 2.4	
15	5.5 ± 2.2	10.2 ± 2.9	18.4 ± 4.1	
Major adverse valve-related events, yrs	20 (7.9)	59 (32.8)	53 (29.0)	
1	1.6 ± 0.8	6.7 ± 1.9	8.8 ± 2.1	<0.001
5	2.9 ± 1.1	10.2 ± 2.3	15.2 ± 2.7	
10	7.4 ± 2.1	22.3 ± 3.4	23.5 ± 3.4	
15	18.9 ± 4.7	38.5 ± 4.9	35.0 ± 4.7	
Aortic valve reoperation, yrs	5 (2.0)	28 (15.6)	2 (1.1)	
1	0.0 ± 0.0	1.1 ± 0.8	0.6 ± 0.6	<0.001
5	0.0 ± 0.0	2.3 ± 1.1	1.1 ± 0.8	
10	3.0 ± 1.5	7.2 ± 2.1	1.1 ± 0.8	
15	4.6 ± 2.2	20.0 ± 4.1	1.1 ± 0.8	
Anticoagulation-related hemorrhage, yrs	5 (2.0)	3 (1.6)	17 (9.3)	
1	0.0 ± 0.0	0.0 ± 0.0	1.7 ± 1.0	<0.001
5	0.9 ± 0.6	0.6 ± 0.6	5.1 ± 1.7	
10	0.9 ± 0.6	1.4 ± 1.0	7.2 ± 2.0	
15	6.3 ± 3.2	2.4 ± 1.4	11.6 ± 3.2	

Values are n (%) or mean ± SD. All-cause mortality estimated using the Kaplan-Meier method and assessment of between-group differences using log-rank tests. Cumulative incidence rates at years 1, 5, 10, and 15 estimated using competing risk models and between-cohort differences assessed using Gray tests.

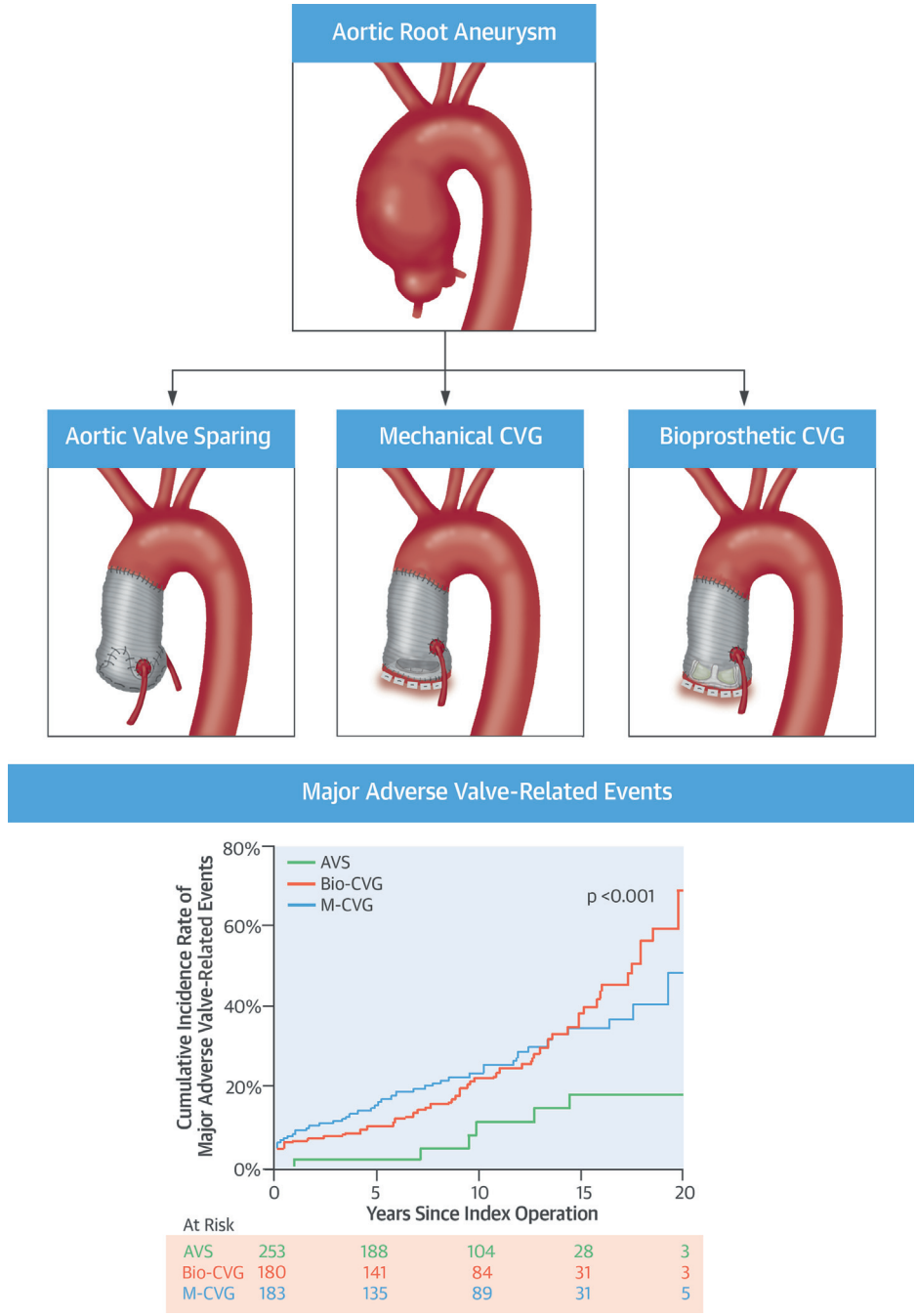
Abbreviations as in Table 1.

FIGURE 1 All-Cause Mortality



All-cause mortality using the Kaplan-Meier method; between-group differences were assessed using log-rank tests. AVS = aortic valve sparing; bio-CVG = bioprosthetic composite valve graft; m-CVG = mechanical composite valve graft.

CENTRAL ILLUSTRATION **Major Adverse Valve-Related Events After Aortic Root Replacement According to Surgical Strategy**



Ouzounian, M. et al. J Am Coll Cardiol. 2016;68(17):1838–47.

Patients who underwent aortic valve-sparing procedures experienced fewer major adverse valve-related events than patients who underwent composite valve graft procedures with either a bioprosthesis or a mechanical prosthesis. These observations suggest that if the aortic valve can be spared, an aortic valve-sparing strategy should be considered for patients undergoing aortic root replacement. AVS = aortic valve sparing; bio-CVG = biologic composite valve graft; CVG = composite valve graft; M-CVG = mechanical composite valve graft.

version 9.4 (SAS Statistical Software, Cary, North Carolina).

RESULTS

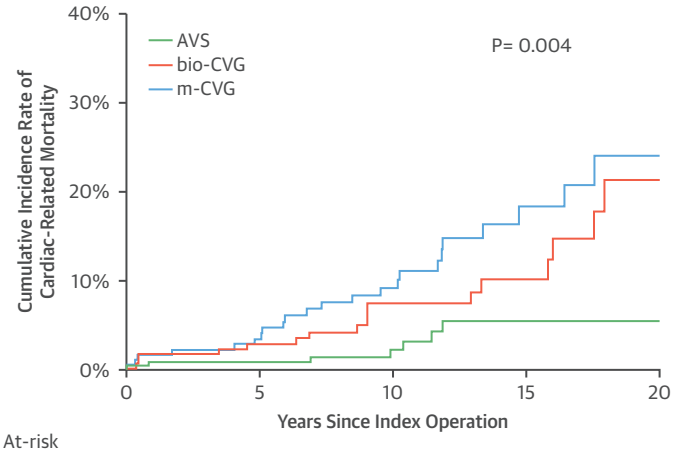
BASELINE CHARACTERISTICS AND INTRAOPERATIVE DETAILS. The baseline characteristics of our final cohort of 616 patients are shown in Table 1. Patients in the 3 cohorts were predominately male, and patients in the AVS cohort were younger and more likely to have preserved left ventricular function and better New York Heart Association functional class. Other notable differences among the groups were in the frequency of Marfan syndrome, which was higher in the valve-sparing group, and frequency of bicuspid aortic valve, which was higher in the CVG groups. Patients who had AVS had either normal or near-normal aortic cusps and a less severe degree of aortic insufficiency. Table 2 summarizes the intraoperative details of patients undergoing root-replacement surgery. Frequency of concomitant coronary bypass and mitral valve surgery were similar in each group. In the valve-sparing group, 200 patients (79%) underwent reimplantation and the remainder root remodeling, a procedure that we now reserve for older patients without annuloaortic ectasia. Patients undergoing AVS had longer cross-clamp times, whereas those receiving m-CVG had more circulatory arrest and previous cardiac surgery than the other 2 groups (Table 2).

IN-HOSPITAL OUTCOMES. The prevalence of in-hospital mortality and stroke rate in the 616 patients were 0.3% and 1.3%, respectively, with 1 death and 1 stroke occurring in the valve-sparing group. The frequency of all early complications was similar among the 3 groups (Table 3), with the exception of permanent pacemaker implantation, which was higher in the m-CVG group, although most of these were in patients with previous cardiac surgery.

LONG-TERM OUTCOMES: UNADJUSTED COMPARISONS BETWEEN SURGICAL STRATEGIES. The unadjusted long-term outcomes of interest stratified by surgical procedure are reported in Table 4. Table 4 reports the cumulative probability of death and the cumulative incidence rates for the other outcomes of interest at 1, 5, 10, and 15 years. Among the groups, all-cause mortality (Figure 1), MAVRE (Central Illustration), and cardiac-related mortality (Figure 2) were lower in patients undergoing AVS procedures. As expected, aortic valve reoperations were higher among patients undergoing bio-CVG (Figure 3), whereas patients undergoing m-CVG experienced more ARH (Figure 4). Long-term rates of endocarditis (AVS, 0.8%; bio-CVG, 2.8%; m-CVG, 2.2%; p = 0.50) and cerebral thromboembolism (stroke and transient ischemic attacks; AVS, 2.0%; bio-CVG, 4.4%; m-CVG, 6.0%; p = 0.21) were equivalent among the 3 surgical strategies. Long-term rates of permanent pacemaker implantation (AVS, 2.8%; bio-CVG, 8.3%; m-CVG, 9.8%; p = 0.01) were lower following AVS.

In the subanalysis, patients undergoing AVS with the remodeling procedure were excluded. The unadjusted results of the subgroup analysis were similar to those of the full sample (data provided in Online Table 1) with some notable differences. Only 2 patients who underwent AVS with the reimplantation technique required aortic valve reoperation. The cumulative incidence rate of aortic valve reoperation patients undergoing AVS with reimplantation was less than one-half of that in the full sample at Year 15 (all AVS, 4.6%; only reimplantation, 2.0%). The risk of aortic valve reoperation at Year 15 following AVS with reimplantation was similar to that of the m-CVG group (1.1%) and remained substantially lower than that of the bio-CVG group (20.0%).

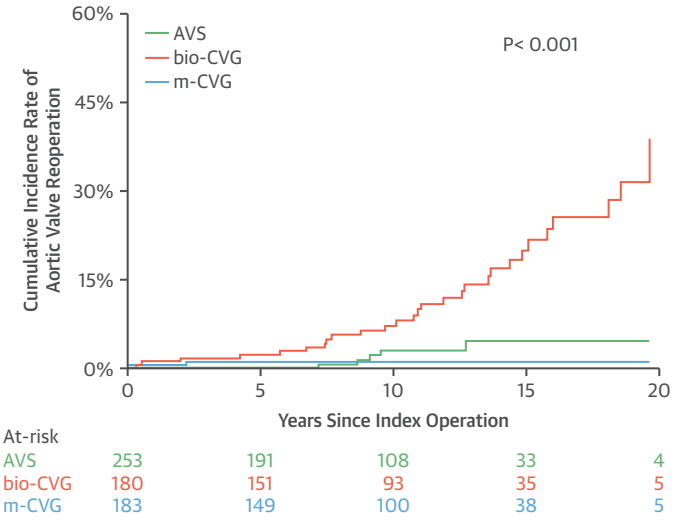
FIGURE 2 Prevalence of Mortality From Cardiac Cause



At-risk					
AVS	253	191	112	36	4
bio-CVG	180	152	97	42	10
m-CVG	183	151	100	38	5

Prevalence of mortality from cardiac cause over time using competing risk methods, and assessment of between-group differences using Gray tests. Mortality from noncardiac-related causes handled using competing risk method (not shown for clarity). Abbreviations as in Figure 1.

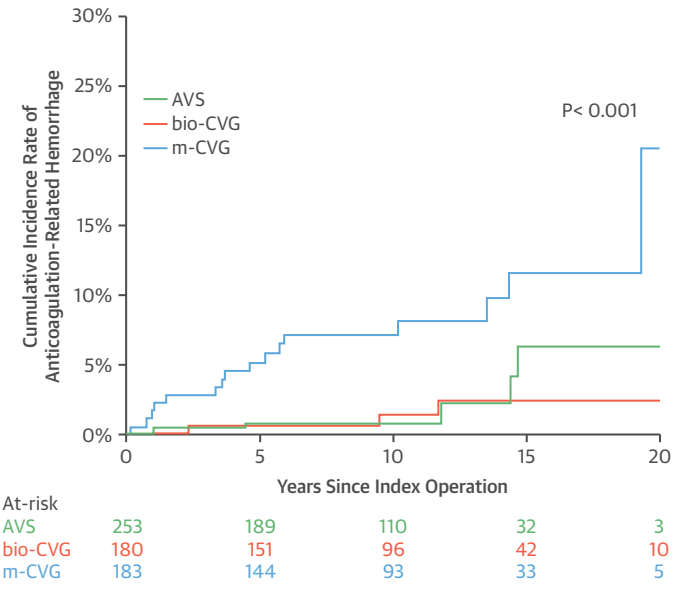
FIGURE 3 Prevalence of Aortic Valve Reoperation



Prevalence of aortic valve reoperation over time using competing risk methods, and assessment of between-group differences using Gray tests. Mortality (all causes) handled using competing risk method (not shown for clarity). Abbreviations as in Figure 1.

LONG-TERM OUTCOMES: MULTIVARIABLE ANALYSES. Figure 5 summarizes the association between surgical strategy and the outcomes of interest, after adjusting for propensity score, surgeon, concomitant coronary bypass, and duration of cross-clamp time in the competing risk models. The complete multivariable models are included in Online Table 2. With the covariate adjustment, all-cause mortality was comparable among the groups; however, both the bio-CVG and m-CVG procedures were associated with increased MAVRE compared with patients undergoing AVS (hazard ratio [HR]: 3.4, p = 0.005; and HR: 5.2, p < 0.001, respectively). They were also associated with increased mortality from cardiac cause (HR: 7.0, p = 0.001; and HR: 6.4, p = 0.003). Furthermore, bio-CVG procedures were associated with increased risk of reoperations on the aortic valve (HR: 6.9, p = 0.003), and m-CVG procedures were associated with increased risk of ARH (HR: 5.6, p = 0.008). There was no significant association between the different surgeons and any of the outcomes of interest.

FIGURE 4 Prevalence of Anticoagulation-Related Hemorrhage



Prevalence of anticoagulation-related hemorrhage over time using competing risk methods, and assessment of between-group differences using Gray tests. Mortality (all causes) handled using competing risk method (not shown for clarity). Abbreviations as in Figure 1.

DISCUSSION

The most important novel finding of this paper is that AVS procedures are associated with improved freedom from cardiac mortality and valve-related morbidities compared with CVG procedures for patients undergoing aortic root replacement (Central Illustration). A few groups have previously compared AVS operations with CVG procedures; however, these studies either had small sample sizes or had limited duration of follow-up (1,4,18-22). To our knowledge, this is the first large series comparing the early and late outcomes following valve-sparing and valve-replacing aortic root surgery.

Because the ideal prosthetic heart valve does not exist, the choice of prosthesis depends primarily on which complication the patient wants to avoid: anticoagulation with a mechanical valve, and SVD with a bioprosthetic valve (23). Although a mechanical CVG has historically been the gold standard operation for young patients needing aortic root replacement, the late complications related to anticoagulation and thromboembolism are not negligible (24,25). Other groups have suggested that in the era of transcatheter valves, bioprosthetic valves should be considered in younger patients (26). However, the probability of reoperation in young patients receiving a bioprosthesis (20% at 15 years in this study) has to be weighed against the increased risk of thromboembolism and ARH with mechanical valves. In addition, several concerns remain with transcatheter valve-in-valve procedures, including valve malposition, coronary obstruction, and poor outcomes in smaller and stenotic bioprosthetic valves, or those that fail

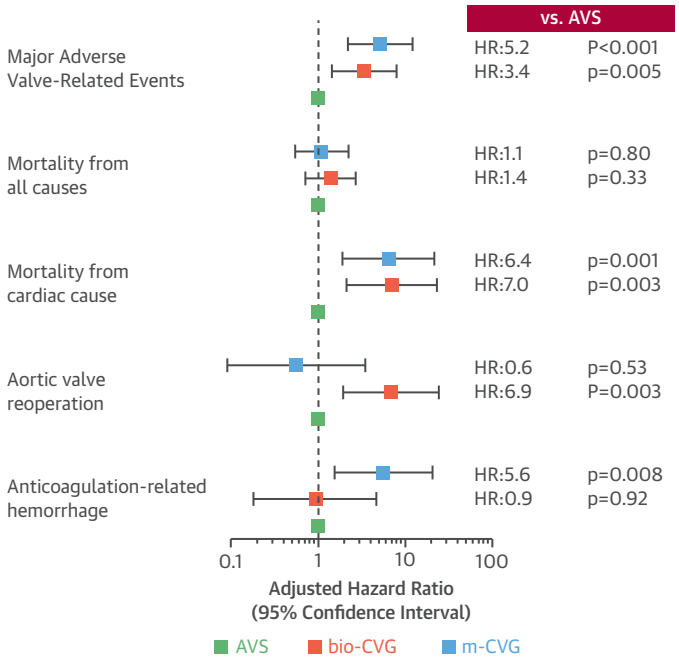
with insufficiency and minimal leaflet calcification (27,28).

Although it may be intuitive that a root-replacement procedure that preserves a patient's native valve would be preferable to a prosthetic valve, the paucity of comparative data, the variable long-term durability data, and the technical complexities of AVS surgery have all likely contributed to the limited uptake of these procedures. Stamou et al. (8) examined trends in aortic root surgery in the United States from 2004 to 2010. The median number of aortic root surgeries per site was only 2, and only 5% of sites performed >16 aortic root surgeries annually. Because the learning curve for AVS surgery is steep and unforgiving of even small technical errors, it is challenging to master the art of AVS surgery and maintain successful and durable outcomes in low-volume centers. Furthermore, the inverse association between procedure volume and mortality has been demonstrated for root replacement (29). We therefore agree with the surgical quality standards laid out by the National Marfan Foundation, stating that AVS procedures should only be performed in centers where the operative mortality is <1% and the 10-year freedom from valve reoperation exceeds 90%. Our results with AVS operations have been exceptionally good, largely because of surgical expertise and the fact that most of our patients had normal or near-normal aortic cusps (2).

Although these data are observational in nature, it is unlikely that a randomized controlled trial addressing this question will ever be performed, given the lack of equipoise in centers experienced with AVS surgery. We suggest that potential candidates for AVS should be referred to larger, experienced centers and not receive a CVG as the default operation.

STUDY LIMITATIONS. This is an analysis of a relatively large cohort of patients undergoing various surgical strategies for aortic root replacement with comprehensive long-term follow-up and careful determination of all valve-related morbidity and mortality. The main limitations of this study stem from its retrospective nature. Although multiple strategies were used to account for differences between the groups, we could not account for other potential unmeasured confounders. Furthermore, because the decision to spare a valve is multifactorial, and dependent on an intraoperative direct examination of the valve and surgical judgment, we do not know how many of the patients who received a prosthetic valve were eligible for an AVS operation.

FIGURE 5 Association Between Surgical Strategy and the Outcomes of Interest Following Multivariate Analysis



Association between surgical strategy and the outcomes of interest following multivariate analysis displayed with patients undergoing AVS as the referent line. HR = hazard ratio; other abbreviations as in **Figure 1**.

We acknowledge that because 2 expert aortic surgeons performed most of the root procedures in this highly selected patient population, these data may not be generalizable to other centers. A recent multicenter prospective cohort study reported an early mortality rate of 3.8% following AVS root replacement (20), and another multicenter registry reported a concerning 1-year failure rate after AVS operations in patients with Marfan syndrome (1). For patients with Marfan syndrome, we recently reported excellent survival and durability after AVS procedures, with mortality and reoperation rates at 15 years of 6.8% and 4.9%, respectively (30). Although other individual centers have also reported excellent results (3,31), a systematic review and meta-analysis by Benedetto et al. (32) found that the probability of reoperation was 4 times higher after the AVS operation than after CVG replacement in patients with Marfan syndrome (1.3%/year vs. 0.3%/year). The variability of these results stresses the importance of consistent reporting of long-term data from centers offering valve-sparing root-replacement procedures.

CONCLUSIONS

In the most comprehensive long-term analysis performed to date of the surgical management of aortic root dilation, AVS procedures were associated with reduced cardiac mortality and valve-related morbid events when compared with bio-CVG and m-CVG. If the aortic valve cusps are normal or near-normal, AVS procedures should be performed in patients with aortic root aneurysm in centers of excellence in aortic surgery.

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PERSPECTIVES

COMPETENCY IN PATIENT CARE AND PROCEDURAL SKILLS: In patients with aortic root aneurysms and normal or nearly normal aortic valve cusps, valve-sparing operations are associated with lower cardiac mortality and valve-related morbidities compared with composite valve-replacing aortic root graft procedures.

TRANSLATIONAL OUTLOOK: In lieu of randomized trials, additional large observational studies with sufficient follow-up are necessary to confirm the advantages of valve-sparing operations over composite valve-replacing root procedures.

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APPENDIX For supplemental tables, please see the online version of this article.