Valve-sparing root replacement and composite valve graft replacement in patients with aortic regurgitation: From the Japan Cardiovascular Surgery Database

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ABSTRACT

Objectives: The advantage of valve-sparing root replacement (VSRR) over aortic root replacement with a composite valve graft (CVG) remains unclear. We compared these 2 procedures with regard to early outcomes with propensity score matching using the Japan Cardiovascular Surgery Database.

Methods: Of 5303 patients from the Japan Cardiovascular Surgery Database who had undergone aortic root replacement in 2008 to 2017, emergent/urgent or redo cases and those with infective endocarditis or aortic stenosis were excluded (included $n = 3841$). Two propensity score–matched groups treated with VSRR or CVG replacement ($n = 1164$ each) were established.

Results: Overall, VSRR was more frequently performed for younger patients with Marfan syndrome with lower operative risk and aortic regurgitation grade compared with CVG replacement. After matching, a weaker but similar trend still existed in baseline characteristics. Although more concomitant procedures were performed in the CVG group, myocardial ischemia and cardiopulmonary bypass time was significantly longer in the VSRR group (median, 193 and 245 minutes) than the CVG group (172 and 223 minutes, both $P < .01$). The CVG group was associated with a significantly greater incidence of postoperative stroke (2.5% vs 1.1%, $P = .01$) and prolonged ventilation >72 hours (7.0% vs 4.6%, $P = .02$). In-hospital mortality rates were significantly greater in the CVG group (1.8%) than the VSRR group (0.8%, $P = .02$).

Conclusions: In overall Japanese institutions, VSRR was more frequently performed for patients at low risk and was associated with better morbidity and mortality rates than CVG replacement. After matching, VSRR was also associated with better morbidity and mortality rates despite longer procedure time. (J Thorac Cardiovasc Surg 2019;158:1501-11)

Annual number of patients undergoing root replacement with or without valve preservation.

Central Message

A nationwide Japanese database survey indicated that valve-sparing root replacement was associated with longer procedure time but lower in-hospital mortality than composite valve graft replacement.

Perspective

According to a nationwide Japanese database, valve-sparing root replacement was performed more frequently in low-risk cases with better mortality/morbidity rates compared with composite valve graft replacement. After matching, they showed similar excellent early mortality/morbidity rates, although the former was associated with significantly longer procedure time but lower in-hospital mortality.

See Commentaries on pages 1512 and 1514.

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Surgical intervention for aortic root aneurysm with or without aortic valve regurgitation (AR) was first reported by Wheat and colleagues in 1964.¹ However, future potential expansion of the remnant aortic wall was a matter of great concern in their technique. Since Bentall and de Bono

Scanning this QR code will take you to the article title page to access supplementary information.

Abbreviations and Acronyms

AR	= aortic valve regurgitation
CABG	= coronary artery bypass grafting
CVG	= composite valve graft
CVG-B	= biological composite valve graft
CVG-M	= mechanical composite valve graft
JCVSD	= Japan Cardiovascular Surgery Database
MFS	= Marfan syndrome
SMD	= standardized mean difference
VSRR	= valve-sparing root replacement

advocated total replacement of the aortic root with a composite valve graft (CVG) in 1968,² this has become the gold standard treatment method, referred to as the Bentall procedure. However, the majority of patients are relatively young, so the requirement for lifelong anticoagulation has emerged as another concern. The Ross procedure using an autologous pulmonary valve can eliminate the need for anticoagulation and provides durable long-term outcome; however, the high degree of operative invasiveness and future potential risk of reoperation associated with the use of a valved conduit in the pulmonary position remain inherent disadvantages of this method. Stentless bioprosthesis or biological composite valve graft (CVG-B) can also eliminate the need for anticoagulation but are not recommended for young patients because of their short durability.

The majority of cases with root dilatation have aortic cusps, which may be stretched but not degenerated, and can theoretically be preserved when aortic root replacement is indicated. Technical developments over the past 25 years have resolved this dilemma with 2 types of valve-sparing root replacement (VSRR): reimplantation of the aortic valve (hereinafter referred to as reimplantation) proposed by David and Feindel in 1992³ and remodeling of the aortic root (hereinafter referred to as remodeling) advocated by Sarsam and Yacoub in 1993.⁴ Although they both have a number of advantages and disadvantages, these procedures can eliminate the need for anticoagulation and provide physiological hemodynamics through technical refinements and therefore are associated with good long-term outcome.^{5,6}

The numbers of VSRR and Bentall procedures using CVG-B have increased, whereas those of Bentall procedures using mechanical composite valve graft (CVG-M) have decreased in the United States.^{7,8} Each procedure has been shown to provide acceptable early outcomes. However, details regarding the advantages or disadvantages of one procedure over the others have not exactly been reported. With the exception of only one single-institution study comparing small numbers of cases using propensity score matching, the majority of reports compared inhomogeneous cohorts.⁸ The present study

was performed to compare clinical outcomes associated with VSRR and the Bentall procedure using propensity score-adjusted analysis based on the nationwide Japan Cardiovascular Surgery Database (JCVSD).

PATIENTS AND METHODS

The JCVSD was established in 2000 to evaluate outcomes of cardiovascular surgery in Japan by prospectively collecting more than 300 variables from 581 institutions (as of October 2017). The number of participating institutions registering at least 1 VSRR or CVG replacement case per year over time is indicated in Figure 1. The institutional review board at each institution has approved the data collection for the JCVSD, and the Data Utilization Committee of the JCVSD approved the use of data for the current study (#A0063). Patients have been given opt-out participant information instead of giving written informed consent based on the ethical policy of National Clinical Database (http://www.ncd.or.jp/about/ethical_considerations.html). The further detailed information about the JCVSD has previously been described^{E1,E2} and available online at <http://www.jacvds.umin.jp>.

We first accessed the JCVSD records and identified 5303 surgical cases of elective aortic root replacement using either a valve-sparing method ($n = 1518$) or a composite valve graft ($n = 3785$) between 2008 and 2017. Cases of redo surgery ($n = 1089$) and those of patients with infective endocarditis ($n = 186$) or aortic stenosis ($n = 403$) were excluded. There were still many inhomogeneities between patients undergoing VSRR ($n = 1345$) and CVG replacement ($n = 2496$) (Table 1). Therefore, we established a propensity score-matched sample ($n = 1155$ each) in which to compare the outcomes of VSRR and CVG replacement (Figure 2 and Table 1). The distributions of the year of the operations and operative procedures are shown in Tables 1 and 2. The number of operations increased each year with the increased number of participating institutions over time (Figure 1). Since 2014, the number of CVG-B procedures has exceeded that of CVG-M. Among VSRR cases, remodeling and reimplantation have been distinguished in the database only since 2017. In 2017, remodeling and reimplantation were performed in 109 of 276 (39.5%) and 167 of 276 cases (60.5%), respectively. The geometric size of the proximal aorta has been recorded only since 2013 and morphology of the aortic valve (eg, bicuspid aortic valve) only since 2016. Since 2013, maximum diameter in the short axis of the proximal aorta was less than 40 mm in 38 (1.9%), 40 to 49 mm in 509 (24.8%), 50 to 59 mm in 973 (47.4%), and 60 mm or more in 534 cases (26.0%) among 2054 cases with valid record of the diameter. Since 2016, 17 unicuspid (1.5%), 126 bicuspid (11%), 993 tricuspid (87%), and 2 quadricuspid (0.2%) aortic valves were registered (unknown: 9, 0.8%) among 1147 cases. These partially available variables were not included in the propensity score matching.

Propensity Score Matching

We used propensity score matching to account for covariates that may have influenced whether VSRR or CVG replacement was selected for treatment. Each patient's estimated propensity score, which is the likelihood that the patient would be treated by VSRR, was calculated by a multivariable logistic model using preselected 29 preoperative variables as independent variables, as described in Appendix E1. Interaction terms were used only between Marfan syndrome (MFS) and age. We then matched patients who underwent VSRR with those who underwent CVG replacement in a 1:1 ratio using greedy (nearest neighbor) matching with a caliper width equal to 0.25 standard deviation of the propensity score (0.050688) (Cohort A). Mirror histograms before and after matching of the propensity scores in each group are shown in Figure E1.

Statistical Analysis

In most variables, the proportion of missing values was less than 0.1%, although some variables were recorded only for cases in the later part of the

FIGURE 1. Annual distribution of the cases undergoing aortic root replacement according to the operative procedures and the number of participating institutions registering at least 1 aortic root replacement case per year (white numbers). VSRR, Valve-sparing root replacement; CVG-B, biological composite valve graft; CVG-M, mechanical composite valve graft.

study period, which are all specifically described in the manuscript. Distribution of each variable was summarized excluding missing values. For multivariable analyses, both propensity score and logistic regression for predicting outcomes, missing values were replaced with the mode in categorical variables and the median in continuous variables.

All continuous variables were tested for normality. Hypothesis of normality was rejected with all continuous variables but body mass index. When not otherwise specified, median with interquartile range, not mean with standard deviation, was used to represent distribution of continuous variables. As a measure of imbalance between groups, before and after matching, standardized mean difference (SMD) was used. For comparing values between unmatched treatment groups, the Mann–Whitney–Wilcoxon test was used for continuous variables and Pearson χ^2 test for categorical variables. Between matched groups, a paired *t* test was used for continuous variables and the McNemar test for categorical variables. Independent variables for logistic regression were selected based on existing literature and clinical experiences. Calculation of propensity scores and matching of cases based on propensity scores were conducted using R version 3.5.1 (R Foundation for Statistical Computing, Vienna, Austria) and MatchIt package version 3.0.2 (Daniel Ho and colleagues). All other statistical analyses were performed with JMP Pro Version 14.2.0 (SAS Institute Inc, Cary, NC). $P < .05$ was taken to indicate statistical significance.

RESULTS

Preoperative Patient Characteristics

Before matching, patients in the VSRR group were significantly younger (55 years) and had fewer cardiovascular risk factors than patients in the CVG group (65 years) (Table 1). In addition, more patients in the VSRR group suffered from MFS (47.1%) than in the CVG group (17.8%) (Table 1). In contrast, more patients in the CVG group suffered from AR grade III (38.8%) or grade IV (44.8%) and New York Heart Association class III or IV (7.1%) than in the VSRR group (29.7%, 36.2%, and 2.7%, respectively).

After matching, there were still similar but weaker differences in preoperative patient characteristics between the 2 groups (Table 1). Patients in the VSRR group were still younger with more MFS than those in the CVG group. A SMD plot indicating the bias reduction after matching is shown in Figure E2.

Operative Variables

Before matching, operation time, cardiopulmonary bypass time, and aortic crossclamping time were significantly longer in the VSRR group (411, 245, and 194 minutes, respectively) than in the CVG group (399, 223, and 172 minutes, respectively, all $P < .01$). Aortic arch replacement, coronary artery bypass grafting (CABG), and mitral valve surgery were performed significantly more frequently in the CVG group (29.4%, 13.6%, and 10.0%) than the VSRR group (19.5%, 7.9%, and 8.0%, $P < .01$, $P < .01$, and $P < .05$, respectively). Homologous blood transfusion was performed more frequently in the CVG group (79.7% vs 66.1%, respectively, $P < .01$), whereas autologous blood transfusion was performed more frequently in the VSRR group (22.0% vs 35.1%, respectively, $P < .01$) (Table 2).

After matching, cardiopulmonary bypass time and aortic crossclamping time were still significantly longer in the VSRR group (245 minutes and 193 minutes, respectively) than in the CVG group (223 minutes and 172 minutes, respectively, both $P < .01$). Aortic arch replacement and CABG were still performed significantly more frequently in the CVG group (29.5% and 13.4%) than the VSRR group (19.6% and 8.1%, both $P < .01$, respectively). The rates of homologous blood transfusion were still

TABLE 1. Patients' clinical characteristics, per study group

Variable	Total	VSRR	CVG		VSRR	CVG	
N	3841	1345	2496	SMD	(matched) 1155	(matched) 1155	SMD (matched)
Year of operation							
2008-2009	434 (11.3%)	121 (9.0%)	313 (12.5%)	-0.115	103 (8.9%)	117 (10.1%)	-0.041
2010-2011	562 (14.6%)	153 (11.4%)	409 (16.4%)	-0.145	144 (12.5%)	135 (11.7%)	0.024
2012-2013	807 (21.0%)	269 (20.0%)	538 (21.6%)	-0.038	241 (20.9%)	238 (20.6%)	0.006
2014-2015	891 (23.2%)	324 (24.1%)	567 (22.7%)	0.032	266 (23.0%)	268 (23.2%)	-0.004
2016-2017	1147 (29.9%)	478 (35.5%)	669 (26.8%)	0.189	401 (34.7%)	397 (34.4%)	0.007
Age, (y)	63 (49-70)	55 (41-66)	65 (54-73)	-0.629	58 (44-67)	60 (47-68)	-0.154
Sex (male)	3036 (79.0%)	1049 (78.0%)	1987 (79.6%)	-0.040	912 (79.0%)	930 (80.5%)	-0.039
BSA, m ²	1.71 (1.58-1.84)	1.75 (1.62-1.88)	1.70 (1.56-1.82)	0.307	1.74 (1.61-1.86)	1.74 (1.61-1.86)	0.019
BMI	22.6 (20.2-25.0)	22.6 (20.0-25.1)	22.6 (20.3-25.0)	-0.035	22.8 (20.2-25.3)	22.9 (20.5-25.3)	-0.088
Current smoker*	435 (11.3%)	118 (8.8%)	317 (12.7%)	-0.127	113 (9.8%)	125 (10.8%)	-0.034
Diabetes mellitus with medication	195 (5.1%)	67 (5.0%)	128 (5.1%)	-0.007	65 (5.6%)	62 (5.4%)	0.011
Hypertension	2538 (66.1%)	798 (59.3%)	1740 (69.7%)	-0.219	720 (62.3%)	741 (64.2%)	-0.039
Hyperlipidemia	1028 (26.8%)	334 (24.8%)	694 (27.8%)	-0.068	308 (26.7%)	318 (27.6%)	-0.020
CKD†	419 (10.9%)	119 (8.8%)	300 (12.0%)	-0.104	114 (9.9%)	126 (10.9%)	-0.034
Hemodialysis	51 (1.3%)	17 (1.3%)	34 (1.4%)	-0.009	16 (1.4%)	22 (1.9%)	-0.041
COPD	604 (15.7%)	207 (15.4%)	397 (15.9%)	-0.014	175 (15.2%)	192 (16.6%)	-0.041
Atrial fibrillation	357 (9.3%)	86 (6.4%)	271 (10.9%)	-0.160	82 (7.1%)	94 (8.1%)	-0.039
Triple-vessel coronary disease	52 (2.1%)	11 (1.5%)	41 (2.4%)	-0.070	11 (1.6%)	14 (1.9%)	-0.025
Angina pectoris CCS ≥2	74 (1.9%)	15 (1.1%)	59 (2.4%)	-0.096	15 (1.3%)	17 (1.5%)	-0.015
History of PCI	108 (2.8%)	33 (2.5%)	75 (3.0%)	-0.034	31 (2.7%)	30 (2.6%)	0.005
Non-acute type A aortic dissection	291 (7.6%)	71 (5.3%)	220 (8.8%)	-0.138	66 (5.7%)	66 (5.7%)	0.000
History of CVA	215 (5.6%)	61 (4.5%)	154 (6.2%)	-0.073	55 (4.8%)	61 (5.3%)	-0.024
Carotid artery disease	49 (1.3%)	11 (0.8%)	38 (1.5%)	-0.066	11 (1.0%)	12 (1.0%)	-0.009
PAD	252 (6.6%)	72 (5.4%)	180 (7.2%)	-0.077	65 (5.6%)	74 (6.4%)	-0.033
Marfan syndrome	500 (27.7%)	288 (47.1%)	212 (17.8%)	0.661	179 (36.2%)	152 (30.4%)	0.124
CHF NYHA class							
Class III	171 (4.5%)	28 (2.1%)	143 (5.7%)	-0.189	28 (2.4%)	25 (2.2%)	0.017
Class IV	43 (1.1%)	8 (0.6%)	35 (1.4%)	-0.081	8 (0.7%)	5 (0.4%)	0.035
LVEF							
<60%	1817 (47.3%)	526 (39.1%)	1291 (51.7%)	-0.256	488 (42.3%)	496 (43.0%)	-0.015
<30%	82 (2.1%)	22 (1.6%)	60 (2.4%)	-0.055	21 (1.8%)	20 (1.7%)	0.006
Aortic regurgitation							
Grade III	1368 (35.6%)	400 (29.7%)	968 (38.8%)	-0.192	382 (33.1%)	414 (35.9%)	-0.060
Grade IV	1605 (41.8%)	487 (36.2%)	1118 (44.8%)	-0.176	454 (39.3%)	460 (39.9%)	-0.012
Mitral regurgitation ≥III	286 (7.4%)	75 (5.6%)	211 (8.5%)	-0.113	67 (5.8%)	58 (5.0%)	0.034
Current β-blocker use	983 (26.2%)	368 (28.1%)	615 (25.2%)	0.066	293 (26.2%)	290 (25.7%)	0.010
Use of anticoagulation	38 (1.0%)	4 (0.3%)	34 (1.4%)	-0.119	4 (0.4%)	4 (0.4%)	0.000
Preoperative administration of inotropic agents	24 (1.1%)	1 (0.1%)	23 (1.5%)	-0.155	1 (0.1%)	1 (0.2%)	-0.001

(Continued)

TABLE 1. Continued

Variable	Total	VSRR	CVG		VSRR (matched)	CVG (matched)	SMD
N	3841	1345	2496	SMD	1155	1155	(matched)
N cases VSRR and CVG replacement ≥ 10 per y	613 (16.0%)	323 (24.0%)	290 (11.6%)	0.328	236 (20.4%)	197 (17.1%)	0.087

VSRR, Valve-sparing root replacement; CVG, composite valve graft; SMD, standardized mean difference; BSA, body surface area; BMI, body mass index; CKD, chronic kidney disease; COPD, chronic obstructive pulmonary disease; CCS, Canadian Cardiovascular Society; PCI, percutaneous coronary intervention; CVA, cerebrovascular accident; PAD, peripheral arterial disease; CHF, congestive heart failure; NYHA, New York Heart Association, LVEF, left ventricular ejection fraction. *Current smoker was defined as a patient with a history of smoking within 1 month before surgery. †Chronic kidney disease was defined as either detection of proteinuria or serum creatinine level ≥ 1.3 mg/dL or estimate glomerular filtration rate ≤ 60 mL/min/1.73 m² (Clinical Practice Guidebook for Diagnosis and Treatment of Chronic Kidney Disease 2009 published by the Japanese Society of Nephrology).

significantly greater in the CVG group (73.6%) than the VSRR group (68.7%, $P < .01$), whereas autologous blood transfusion was performed more frequently in the VSRR group (23.8% vs 33.8%, $P < .01$) (Table 2).

Postoperative Outcomes

Before matching, the incidence of re-exploration for bleeding was similar between the groups (VSRR 3.6%, CVG replacement 4.8%, $P = .11$). The rate of postoperative stroke and hemodialysis was significantly greater in the CVG group (2.7%, 2.3%) than the VSRR group (1.0%, 0.9%, respectively, both $P < .01$). The CVG group had a significantly longer mechanical ventilation time than the VSRR group (14 hours vs 11 hours, respectively, $P < .01$), although their distribution was highly skewed. Prolonged

mechanical ventilation >72 hours was significantly more frequent in the CVG group than the VSRR group (7.4% vs 4.3%, respectively, $P < .01$). Both intensive care unit and postoperative hospital stay were significantly longer in the CVG group (3 and 21 days) than the VSRR group (2 and 18 days, respectively, both $P < .01$). In-hospital mortality rates were significantly greater in the CVG group (2.8%) than the VSRR group (0.7%, $P < .01$) (Table 2).

After matching, the incidence of re-exploration for bleeding was also similar between the groups (VSRR 3.5%, CVG replacement 4.6%, $P = .16$). Otherwise, there were no significant differences related to postoperative morbidity between the 2 groups. In-hospital mortality rates were still significantly greater in the CVG group (1.8%) than the VSRR group (0.8%) (Table 2).

FIGURE 2. Consort type diagram of all patients undergoing either VSRR or CVG replacement. JCVSD, Japan Cardiovascular Surgery Database; VSRR, valve-sparing root replacement; CVG, composite valve graft; CVG-M, mechanical composite valve graft.

TABLE 2. Intra- and postoperative variables, per study group

Variable	Total	VSRR	CVG		VSRR	CVG	
N	3841	1345	2496	P value	(matched) 1155	(matched) 1155	P value (matched)
Intraoperative variables							
Aortic arch replacement	519 (25.5%)	156 (19.5%)	363 (29.4%)	<.01	131 (19.6%)	196 (29.5%)	<.01
Concomitant CABG	445 (11.6%)	106 (7.9%)	339 (13.6%)	<.01	93 (8.1%)	155 (13.4%)	<.01
Concomitant mitral surgery	356 (9.3%)	107 (8.0%)	249 (10.0%)	.04	92 (8.0%)	87 (7.5%)	.70
Concomitant mitral valve repair	293 (7.6%)	105 (7.8%)	188 (7.5%)	.76	90 (7.8%)	68 (5.9%)	.07
Concomitant maze procedure	69 (1.8%)	25 (1.9%)	44 (1.8%)	.84	23 (2.0%)	15 (1.3%)	.14
Homologous blood transfusion	2879 (75.0%)	889 (66.1%)	1990 (79.7%)	<.01	794 (68.7%)	850 (73.6%)	<.01
Autologous blood transfusion	1020 (26.6%)	472 (35.1%)	548 (22.0%)	<.01	390 (33.8%)	275 (23.8%)	<.01
Operation time, min	403 (330-500)	411 (345-496)	399 (320-501)	<.01	410 (343-500)	397 (317-496)	.08
CPB time, min	232 (190-285)	245 (206-292)	223 (181-281)	<.01	245 (205-292)	223 (180-275)	<.01
AXC time, min	182 (147-219)	194 (162-231)	172 (141-213)	<.01	193 (160-231)	172 (148-220)	<.01
Postoperative variables							
Postoperative stroke	82 (2.1%)	14 (1.0%)	68 (2.7%)	<.01	13 (1.1%)	21 (1.8%)	.17
Re-exploration for bleeding	168 (4.4%)	49 (3.6%)	119 (4.8%)	.10	40 (3.5%)	53 (4.6%)	.16
Postoperative hemodialysis	70 (1.8%)	12 (0.9%)	58 (2.3%)	<.01	12 (1.0%)	18 (1.6%)	.26
Postoperative heart block	60 (1.6%)	23 (1.7%)	37 (1.5%)	.59	19 (1.6%)	18 (1.6%)	.87
Postoperative atrial fibrillation	997 (26.0%)	301 (22.4%)	696 (27.9%)	<.01	283 (24.5%)	287 (24.9%)	.85
Intubation time, h	14 (6-19)	11 (5-17)	14 (7-20)	<.01	11 (5-17)	14 (6-20)	.17
Prolonged ventilation >72 h	242 (6.3%)	58 (4.3%)	184 (7.4%)	<.01	55 (4.8%)	77 (6.7%)	.05
ICU stay, d	3 (2-4)	2 (2-4)	3 (2-5)	<.01	2 (2-4)	3 (2-5)	<.01
Postoperative hospital stay, d	19 (14-27)	18 (13-24)	21 (15-28)	<.01	18 (13-24)	20 (15-27)	.21
In-hospital mortality	80 (2.1%)	9 (0.7%)	71 (2.8%)	<.01	9 (0.8%)	21 (1.8%)	.02

VSRR, Valve-sparing root replacement; CVG, composite valve graft; CABG, coronary artery bypass grafting; CPB, cardiopulmonary bypass; AXC, aortic cross clamping; ICU, intensive care unit.

Multivariable Logistic Regression Model to Predict In-Hospital Mortality

A propensity score-adjusted multivariable logistic regression model was developed to identify independent predictors of in-hospital mortality (Table 3). CVG group, age equal to or older than 65 years, and chronic kidney disease (serum Cr > 2.0 mg/dL) were identified as independent predictors of in-hospital mortality.

Subgroup Analysis

Despite appropriate propensity score matching, there were still residual differences in preoperative patient characteristics between the 2 groups. This might be due to increased number of CVG-B replacement in the recent series, which tends to be performed on relatively elderly patients (Figure 1). Therefore, we performed subgroup analysis without patients who had CVG-B replacement.

TABLE 3. Odds ratios in a multivariable logistic regression model to predict in-hospital mortality

	Odds ratios			P value
	Estimate	95% CI lower limit	95% CI higher limit	
VSRR*	0.06	0.01	0.31	<.01
Propensity score	0.08	0.00	4.54	.22
Age <50 y†	3.16	0.61	16.39	.17
Age ≥65 y†	14.43	2.90	71.76	<.01
Chronic kidney disease	9.49	1.99	45.24	<.01
CHF NYHA class ≥ III	4.77	0.78	29.22	.09
Aortic regurgitation ≥ III	0.24	0.05	1.25	.09
N cases of VSRR and CVG replacement at hospital ≥10 per y	0.04	0.00	2.24	.12

CI, Confidence interval; VSRR, valve-sparing root replacement; CHF, congestive heart failure; NYHA, New York Heart Association; CVG, composite valve graft. *Reference: CVG. †Reference: 50 y ≤ age < 65 y.

TABLE 4. Clinical characteristics of patients who underwent aortic root replacement except biological composite valve graft, per study group

Variable	Total	VSRR	CVG-M		VSRR	CVG-M	SMD
N	2527	1345	1182	SMD	(matched)	(matched)	(matched)
					924	924	
Year of operation							
2008-2009	303 (12.0%)	121 (9.0%)	182 (15.4%)	−0.197	106 (11.5%)	122 (13.2%)	−0.053
2010-2011	377 (14.9%)	153 (11.4%)	224 (19.0%)	−0.212	125 (13.5%)	137 (14.8%)	−0.037
2012-2013	548 (21.7%)	269 (20.0%)	279 (23.6%)	−0.087	194 (21.0%)	205 (22.2%)	−0.029
2014-2015	553 (21.9%)	324 (24.1%)	229 (19.4%)	0.115	208 (22.5%)	206 (22.3%)	0.005
2016-2017	746 (29.5%)	478 (35.5%)	268 (22.7%)	0.286	291 (31.5%)	254 (27.5%)	0.088
Age, y	56 (43-65)	55 (41-66)	56 (45-64)	−0.089	56 (43-65)	56 (45-64)	−0.091
Sex (male)	2002 (79.2%)	1049 (78.0%)	953 (80.6%)	−0.065	721 (78.0%)	733 (79.3%)	−0.032
BSA, m ²	1.75 (1.62-1.88)	1.75 (1.62-1.88)	1.75 (1.61-1.88)	0.038	1.75 (1.62-1.88)	1.75 (1.61-1.88)	0.017
BMI	22.6 (20.2-25.2)	22.6 (20.0-25.1)	22.6 (20.4-25.3)	−0.093	22.6 (20.1-25.2)	22.8 (20.3-25.3)	−0.085
Current smoker*	311 (12.3%)	118 (8.8%)	193 (16.3%)	−0.230	101 (10.9%)	113 (12.2%)	−0.041
Diabetes mellitus with medication	122 (4.8%)	67 (5.0%)	55 (4.7%)	0.015	46 (5.0%)	44 (4.8%)	0.010
Hypertension	1529 (60.5%)	798 (59.3%)	731 (61.8%)	−0.051	548 (59.3%)	577 (62.4%)	−0.064
Hyperlipidemia	626 (24.8%)	334 (24.8%)	292 (24.7%)	0.003	232 (25.1%)	230 (24.9%)	0.005
CKD†	217 (8.6%)	119 (8.8%)	98 (8.3%)	0.020	79 (8.5%)	80 (8.7%)	−0.004
Hemodialysis	33 (1.3%)	17 (1.3%)	16 (1.4%)	−0.008	13 (1.4%)	12 (1.3%)	0.009
COPD	356 (14.1%)	207 (15.4%)	149 (12.6%)	0.080	124 (13.4%)	128 (13.9%)	−0.013
Atrial fibrillation	192 (7.6%)	86 (6.4%)	106 (9.0%)	−0.097	67 (7.3%)	69 (7.5%)	−0.008
Triple-vessel coronary disease	28 (1.9%)	11 (1.5%)	17 (2.3%)	−0.060	8 (1.5%)	10 (1.7%)	−0.019
Angina pectoris CCS ≥2	47 (1.9%)	15 (1.1%)	32 (2.7%)	−0.116	13 (1.4%)	12 (1.3%)	0.009
History of PCI	56 (2.2%)	33 (2.5%)	23 (1.9%)	0.035	15 (1.6%)	18 (1.9%)	−0.025
Non-acute type A aortic dissection	198 (7.8%)	71 (5.3%)	127 (10.7%)	−0.202	62 (6.7%)	73 (7.9%)	−0.046
History of CVA	115 (4.6%)	61 (4.5%)	54 (4.6%)	−0.002	45 (4.9%)	42 (4.5%)	0.015
Carotid artery disease	29 (1.1%)	11 (0.8%)	18 (1.5%)	−0.066	9 (1.0%)	10 (1.1%)	−0.011
PAD	153 (6.1%)	72 (5.4%)	81 (6.9%)	−0.063	53 (5.7%)	57 (6.2%)	−0.018
Marfan syndrome	455 (35.1%)	288 (47.1%)	167 (24.3%)	0.490	160 (37.0%)	137 (28.8%)	0.173
CHF NYHA class							
Class III	95 (3.8%)	28 (2.1%)	67 (5.7%)	−0.187	28 (3.0%)	26 (2.8%)	0.013
Class IV	25 (1.0%)	8 (0.6%)	17 (1.4%)	−0.084	6 (0.6%)	9 (1.0%)	−0.036
LVEF							
<60%	1107 (43.8%)	526 (39.1%)	581 (49.2%)	−0.203	398 (43.1%)	423 (45.8%)	−0.054
<30%	52 (2.1%)	22 (1.6%)	30 (2.5%)	−0.063	19 (2.1%)	15 (1.6%)	0.032
Aortic regurgitation							
Grade III	841 (33.3%)	400 (29.7%)	441 (37.3%)	−0.161	319 (34.5%)	346 (37.4%)	−0.061
Grade IV	1027 (40.6%)	487 (36.2%)	540 (45.7%)	−0.194	371 (40.2%)	388 (42.0%)	−0.037
Mitral regurgitation ≥III	168 (6.6%)	75 (5.6%)	93 (7.9%)	−0.092	57 (6.2%)	59 (6.4%)	−0.009
Current β-blocker use	664 (27.0%)	368 (28.1%)	296 (25.6%)	0.057	229 (25.3%)	243 (27.0%)	−0.039
Use of anticoagulation	17 (0.7%)	4 (0.3%)	13 (1.1%)	−0.097	4 (0.4%)	5 (0.6%)	−0.016
Preoperative administration of inotropic agents	11 (0.7%)	1 (0.1%)	10 (1.3%)	−0.136	1 (0.2%)	1 (0.2%)	0.001

(Continued)

TABLE 4. Continued

Variable	Total	VSRR	CVG-M		VSRR (matched)	CVG-M (matched)	SMD
N	2527	1345	1182	SMD	924	924	(matched)
N cases VSRR and CVG replacement ≥10 per y	458 (18.1%)	323 (24.0%)	135 (11.4%)	0.334	154 (16.7%)	131 (14.2%)	0.069

VSRR, Valve-sparing root replacement; CVG-M, mechanical composite valve graft; SMD, standardized mean difference; BSA, body surface area; BMI, body mass index; CKD, chronic kidney disease; COPD, chronic obstructive pulmonary disease; CCS, Canadian Cardiovascular Society; PCI, percutaneous coronary intervention; CVA, cerebrovascular accident; PAD, peripheral arterial disease; CHF, congestive heart failure; NYHA, New York Heart Association; LVEF, left ventricular ejection fraction; CVG, composite valve graft. *Current smoker was defined as a patient with a history of smoking within 1 month before surgery. †Chronic kidney disease was defined as either detection of proteinuria or serum creatinine level ≥ 1.3 mg/dL or estimate glomerular filtration rate ≤ 60 mL/min/1.73 m² (*Clinical Practice Guidebook for Diagnosis and Treatment of Chronic Kidney Disease 2009* published by the Japanese Society of Nephrology).

We then matched patients who underwent VSRR with those who underwent CVG-M replacement in the same manner as Cohort A (a caliper width = 0.051425) (Cohort M, n = 924 each) (Table 4). Mirror histograms and a SMD plot are shown in Figures E3 and E4.

After matching, MFS was still more frequent in the VSRR group; however, most importantly, age was quite similar between the groups (both median 56 years old). Although aortic arch replacement was performed more frequently in the CVG-M group, other concomitant operations were performed with similar frequency. The same trends were observed with regard to transfusion and procedure time as Cohort A (Tables 4 and 5).

As results, the incidence of re-exploration for bleeding was also similar between groups (VSRR 3.9%, CVG replacement 4.0%, $P = .91$). The incidence of postoperative stroke and prolonged mechanical ventilation was significantly greater and intensive care unit stay was significantly longer in the CVG-M group than the VSRR group. In-hospital mortality was still significantly greater in the CVG-M group (2.8%) than the VSRR group (0.8%, $P < .01$) (Table 5).

DISCUSSION

The results of the present study indicated that many cardiovascular risk factors were more frequent in the CVG group, resulting in more frequent CABG performed in the CVG group. VSRR might be performed by more experienced surgeons and associated with a lower incidence of coronary anastomotic problems, which might be another reason for more frequent CABG performed in the CVG group. Furthermore, this might also be the reason why VSRR was associated with lower morbidity and mortality rates. Relatively longer duration of hospitalization in both groups, compared with many other countries, might be due to the Japanese insurance system.

After matching, procedure time was still significantly longer in the VSRR group than the CVG group, but postoperative morbidity rates were comparable between the 2 groups. In-hospital mortality rate was still significantly lower in the VSRR group.

In surgical intervention for aortic root aneurysm with or without AR, surgeons should select the most appropriate

procedure according to the patient's background, with weighting for long-term (anticoagulation, durability) and early (bleeding, mortality) risks. VSRR seems an ideal solution to eliminate the need for anticoagulation treatment and to reduce future risks of reoperations compared with CVG-B replacement, although the follow-up periods of previous studies are still not sufficiently long and the mechanical Bentall procedure is still superior in terms of reoperation.⁹

Recent meta-analyses and large nationwide databases have revealed that the postoperative mortality rate after the Bentall procedure is around 6%, which is greater than those after conventional cardiac operations.¹⁰⁻¹² Common risk factors for early mortality were shown to be advanced age, urgent/emergent operation, concomitant mitral/coronary disease, and longer procedure time.¹³⁻¹⁷ In contrast, bicuspid aortic valve and recent operation were identified as protective factors against early mortality.¹³ Therefore, when performed on an elective basis or for patients at low risk, the postoperative mortality rate decreased to 2.7% to 3.6%,^{11,12,18} which was similar to the rate after conventional aortic valve replacement reported in the United States (3.2%).¹⁹ When performed exclusively in young patients with MFS, postoperative mortality rate further decreased to $<1\%$.^{20,21} In addition, operative mortality after aortic root replacement was reported to be better for greater-volume centers (3.4%) than those with a lower volume (5.8%).²²

Operative mortality after VSRR was reported to be as low as 2% in a recent meta-analysis.²³ There is no significant difference in early mortality between 2 major alternatives.²⁴ Operative mortality also declines up to 1.4% to 1.88% on an elective basis or for patients at low risk in a database in the United States.^{7,18} When performed exclusively in patients with MFS in a high-volume center, VSRR could achieve a mortality rate of nearly 0%.^{25,26}

Little evidence is available regarding comparisons of early outcomes of 2 homogeneous cohorts undergoing VSRR or CVG replacement. Table E1 summarizes reported series comparing early outcomes between the 2 approaches with sufficient numbers of patients (>50 each). Although the results of the present study were derived from a

TABLE 5. Intra- and postoperative variables of patients who underwent aortic root replacement except biological composite valve graft, per study group

Variable	Total	VSRR	CVG-M		VSRR (matched)	CVG-M (matched)	P value
N	2527	1345	1182	P value	924	924	(matched)
Intraoperative variables							
Aortic arch replacement	311 (23.9%)	156 (19.5%)	155 (31.2%)	<.01	89 (17.8%)	142 (30.9%)	<.01
Concomitant CABG	241 (9.5%)	106 (7.9%)	135 (11.4%)	<.01	77 (8.3%)	97 (10.5%)	.10
Concomitant mitral surgery	211 (8.3%)	107 (8.0%)	104 (8.8%)	.44	70 (7.6%)	70 (7.6%)	1
Concomitant mitral valve repair	173 (6.8%)	105 (7.8%)	68 (5.8%)	.04	68 (7.4%)	47 (5.1%)	.05
Concomitant maze procedure	43 (1.7%)	25 (1.9%)	18 (1.5%)	.52	20 (2.2%)	15 (1.6%)	.49
Homologous blood transfusion	1761 (69.7%)	889 (66.1%)	872 (73.8%)	<.01	621 (67.2%)	673 (72.8%)	<.01
Autologous blood transfusion	789 (31.2%)	472 (35.1%)	317 (26.8%)	<.01	325 (35.2%)	252 (27.3%)	<.01
Operation time, min	407 (334-500)	411 (345-496)	401 (321-503)	.02	411 (345-505)	400 (319-496)	.26
CPB time, min	238 (196-290)	245 (206-292)	227 (181-287)	<.01	246 (208-293)	226 (180-284)	<.01
AXC time, min	189 (153-229)	194 (162-231)	181 (144-221)	<.01	197 (167-235)	179 (144-220)	<.01
Postoperative variables							
Postoperative stroke	44 (1.7%)	14 (1.0%)	30 (2.5%)	<.01	12 (1.3%)	26 (2.8%)	.02
Re-exploration for bleeding	97 (3.8%)	49 (3.6%)	48 (4.1%)	.59	36 (3.9%)	37 (4.0%)	.91
Postoperative hemodialysis	35 (1.4%)	12 (0.9%)	23 (1.9%)	.02	9 (1.0%)	17 (1.8%)	.10
Postoperative heart block	43 (1.7%)	23 (1.7%)	20 (1.7%)	.97	9 (1.0%)	14 (1.5%)	.30
Postoperative atrial fibrillation	572 (22.6%)	301 (22.4%)	271 (22.9%)	.75	213 (23.1%)	203 (22.0%)	.58
Intubation time, h	12 (6-18)	11 (5-17)	14 (7-20)	<.01	11 (5-17)	14 (6-19)	.10
Prolonged ventilation >72 h	140 (5.5%)	58 (4.3%)	82 (6.9%)	<.01	42 (4.5%)	65 (7.0%)	.02
ICU stay, d	3 (2-4)	2 (2-4)	3 (2-5)	<.01	2 (2-4)	3 (2-5)	<.01
Postoperative hospital stay, d	19 (14-26)	18 (13-24)	20 (15-28)	<.01	18 (13-24)	20 (15-28)	.35
In-hospital mortality	44 (1.7%)	9 (0.7%)	35 (3.0%)	<.01	7 (0.8%)	26 (2.8%)	<.01

VSRR, Valve-sparing root replacement; CVG-M, mechanical composite valve graft; CABG, coronary artery bypass grafting; CPB, cardiopulmonary bypass; AXC, aortic cross clamping; ICU, intensive care unit.

nationwide database accumulating data from more than 500 institutions over 10 years, in-hospital mortality (<2%) rates of the 2 matched groups were excellent compared with experienced centers. Most importantly, VSRR was associated with lower in-hospital mortality compared with CVG replacement regardless of the prosthesis type. One of the reasons might be that VSRR had been performed favorably in the experienced, high-volume centers. Indeed, in low-volume centers (caseload in the year <10), in-hospital mortality was significantly greater in the CVG group (3.2%) than the VSRR group (1.0%, $P < .01$), whereas the difference became less in high-volume centers (caseload in the year ≥ 10) (CVG 0.9%, VSRR 0%). It is unclear, however, in-hospital mortality became greater in selected patients undergoing CVG-M replacement alone, although the rate of cases performed in high-volume centers (11.4%) was similar to that of Cohort A (11.6%). CVG-M replacement for younger patients with low operative risk might favorably be performed by trainees; however, the experience of surgeon was not available in this database. Further study will be mandatory to clarify the impact of caseload.

Postoperative bleeding is another important issue. With the exception of reports including low-risk patients alone, some reports indicated a greater incidence of re-exploration for bleeding after CVG replacement

(3.1%-8.0%) than VSRR (3.1%-5.9%),^{8,18,27-29} whereas another multi-institutional cohort study yielded contradictory findings (CVG replacement: 5.3%, VSRR: 6.9%).³⁰ In the Society of Thoracic Surgeons database eliminating acute aortic dissection and infective endocarditis, the incidence of re-exploration for bleeding was quite similar for both methods (CVG replacement: 6.2%-6.5%, VSRR: 6%),⁷ as well as in experienced high-volume centers in an elective/urgent setting alone (both 4%).³¹ In the present study, both CVG and VSRR groups had lower incidences of postoperative bleeding (4.1% and 3.6%, respectively) compared with reported series, although this is a nationwide database study (Table 2 and Table E1). VSRR was not associated with a greater incidence of re-exploration for bleeding, but the incidence of homologous blood transfusion was lower than the other. This might have been due to the more frequent use of autologous blood in the VSRR group, which is believed to have more coagulability than packed red blood cell. In VSRR, most surgeons speculate that the risk of postoperative bleeding would be greater in remodeling than reimplantation because only one suture line is necessary for the former. However, in experienced institutions with caseloads >100, the incidence of re-exploration for bleeding was less frequent after remodeling (2%) than after reimplantation (3%-9%).³² It

was unclear in our study which VSRR procedure was more likely to be responsible for postoperative bleeding. However, exclusively in 2017, reimplantation was associated with lower incidence of re-exploration for bleeding (3.6%) than remodeling (6.4%), although difference was not significant ($P = .38$).

Prolonged procedure time is one of the disadvantages of VSRR, although that of CVG replacement in this study was considerably longer than in reported series. In general, reimplantation requires a longer myocardial ischemia time than remodeling.³² According to our original nationwide survey, reimplantation was selected in two thirds of VSRR cases performed in Japan in 2014,³³ as well in the current study during 2017, which may explain the longer procedure time of VSRR in the present study. Indeed, cases of elective, isolated, and first-time remodeling with external suture annuloplasty require only 111 ± 15 minutes aortic crossclamping time ($n = 15$) in the first author's institution (data presented at the 70th Annual Scientific Meeting of the Japanese Association for Thoracic Surgery; September 27, 2017; Sapporo, Japan) (Video 1).

Limitations

The major limitation of this study was the lack of long-term follow-up data due to the inherent nature of this database. In general, CVG replacement is associated with lower risk of proximal reoperation but greater risk of other valve-related complications compared with VSRR.⁹ However, long-term valve durability after VSRR has been improving due to technical refinements over time.^{34,35} When long-term freedom from reoperation and survival become comparable between the groups, VSRR will be selected more often because early outcomes are better.

The second limitation was that only limited information in terms of operative procedure was available to us—details regarding the VSRR procedure, use of annuloplasty, use of cusp repair, and type of coronary re-attachment, etc, were unclear. This kind of information is essential to estimate the actual benefits of one approach over the other.

VIDEO 1. Aortic root remodeling procedure with external suture annuloplasty. Video available at: [https://www.jtcvs.org/article/S0022-5223\(19\)30357-5/fulltext](https://www.jtcvs.org/article/S0022-5223(19)30357-5/fulltext).

In addition, some of patient-specific echocardiographic and radiologic findings were either not collected or available only in recent years. Therefore, we were unable to perform subanalyses with regard to valve etiology, left ventricular dilatation, and proximal aortic dimension, etc. Some of these data are currently available in the latest version, so that further study must be made to clarify the impact of these factors.

The last limitation was residual small inhomogeneity between the groups even after subgroup analysis. We performed matching using baseline characteristics alone; therefore, there were still significant differences in concomitant procedures, which might have impact on the outcomes. Another subgroup analysis with isolated aortic root replacement alone should be performed to clarify this concern.

Despite these limitations, this study in which we analyzed data from more than 1000 propensity-matched patients enrolled in a Japanese nationwide database is clinically informative and will stimulate further clinical research. We hope that a prospective randomized trial for selected candidates will be launched in the near future to confirm the findings of the present study.

CONCLUSIONS

In overall Japanese institutions, VSRR was performed at a greater rate in patients at low risk and was thus associated with better morbidity and mortality rates compared with CVG replacement. After matching, both VSRR and CVG replacement were associated with excellent early postoperative mortality/morbidity rates in current Japanese centers for selected candidates, although VSRR was associated with lower morbidity and mortality rates despite longer procedure time.

Conflict of Interest Statement

Authors have nothing to disclose with regard to commercial support.

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Key Words: valve-sparing root replacement, composite valve graft replacement, database survey, postoperative outcome, aortic regurgitation, in-hospital mortality

APPENDIX E1. FACTORS ENTERED INTO THE PROPENSITY SCORE MATCHING ANALYSIS TO ASSIGN PATIENTS TO UNDERGO VALVE-SPARING ROOT REPLACEMENT OVER COMPOSITE VALVE GRAFT REPLACEMENT

Age
 Year of operation performed
 Sex (male)
 Body surface area
 Body mass index
 Current smoker
 Chronic obstructive pulmonary disease
 Diabetes mellitus with medication
 Hypertension
 Hyperlipidemia
 Chronic kidney disease and hemodialysis
 History of cerebrovascular accident
 Carotid artery disease
 Peripheral arterial disease
 Marfan syndrome
 Atrial fibrillation
 Triple vessel coronary arterial disease

Congestive heart failure New York Heart Association class 0-II, III, IV
 Canadian Cardiovascular Society angina class $\geq$ II
 Left ventricular ejection fraction
 Current β -blocker use
 Current use of an anticoagulant drug
 Preoperative administration of inotropic agents
 Aortic regurgitation grade 0-II, III, IV
 Mitral regurgitation $\geq$ III
 Non-acute type A aortic dissection
 N cases valve-sparing root replacement and composite valve graft replacement $\geq$ 10 per year
 History of percutaneous coronary intervention
 An interaction term between Marfan syndrome and age

E-References

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- E2. Ueki C, Miyata H, Motomura N, Sakata R, Sakaguchi G, Akimoto T, et al. Off-pump technique reduces surgical mortality after elective coronary artery bypass grafting in patients with preoperative renal failure. *J Thorac Cardiovasc Surg*. 2018;156:976-83.

FIGURE E1. Mirror histogram showing the distribution of propensity scores for patients undergoing VSRR (*bars above the zero line*) or CVG replacement (*bars below the zero line*) before and after matching. *Blue areas* represent matched patient pairs, showing that they covered the complete spectrum of cases. VSRR, Valve-sparing root replacement; CVG, composite valve graft.

FIGURE E2. Covariate balance plot before (red squares) and after (blue diamonds) propensity score matching on selected covariates showing the bias reduction after matching. Symbols depict standardized differences for covariates between patients undergoing VSRR and CVG replacement. *CKD was defined as either detection of proteinuria or serum creatinine level ≥ 1.3 mg/dL or estimate glomerular filtration rate ≤ 60 mL/min/1.73 m² (*Clinical Practice Guidebook for Diagnosis and Treatment of Chronic Kidney Disease 2009* published by the Japanese Society of Nephrology). †Current smoker was defined as a patient with a history of smoking within 1 month before surgery. VSRR, Valve-sparing root replacement; CVG, composite valve graft; BSA, body surface area; COPD, chronic obstructive pulmonary disease; PCI, percutaneous coronary intervention; BMI, body mass index; CVA, cerebrovascular accident; PAD, peripheral arterial disease; CCS, Canadian Cardiovascular Society; CKD, chronic kidney disease; CHF, congestive heart failure; NYHA, New York Heart Association; LVEF, left ventricular ejection fraction.

FIGURE E3. Mirror histogram showing the distribution of propensity scores for patients undergoing VSRR (*bars above the zero line*) or CVG-M replacement (*bars below the zero line*) before and after matching. *Blue areas* represent matched patient pairs, showing that they covered the complete spectrum of cases. VSRR, Valve-sparing root replacement; CVG-M, mechanical composite valve graft.

FIGURE E4. Covariate balance plot before (red squares) and after (blue diamonds) propensity score matching on selected covariates showing the bias reduction after matching. Symbols depict standardized differences for covariates between patients undergoing VSRR and CVG-M replacement. *CKD disease was defined as either detection of proteinuria or serum creatinine level ≥ 1.3 mg/dL or estimate glomerular filtration rate ≤ 60 mL/min/1.73 m² (*Clinical Practice Guidebook for Diagnosis and Treatment of Chronic Kidney Disease 2009* published by the Japanese Society of Nephrology). †Current smoker was defined as a patient with a history of smoking within 1 month before surgery. VSRR, Valve-sparing root replacement; CVG, composite valve graft; COPD, chronic obstructive pulmonary disease; BSA, body surface area; PCI, percutaneous coronary intervention; CKD, chronic kidney disease; CVA, cerebrovascular accident; PAD, peripheral arterial disease; BMI, body mass index; CCS, Canadian Cardiovascular Society; LVEF, left ventricular ejection fraction; CHF, congestive heart failure; NYHA, New York Heart Association; CVG-M, mechanical composite valve graft.

TABLE E1. Reported series comparing early outcomes between 2 approaches of aortic root replacement

Study	Number of patients		Mortality				Re-exploration for bleeding		Selection of patients	Source of patients	Definition of mortality
	VSRR (reimplantation)	CVG (biological)	All patients		Elective cases alone		VSRR	CVG			
			VSRR	CVG	VSRR	CVG					
Zehr et al, 2004 ³¹	54 (46)	149 (21)			3.7%	4.0%	4.0%	4.0%	Elective/urgent cases alone	Single institution	Operative
Franke et al, 2010 ¹⁷	76 (76)	67	2.6%	10.4%						Three institutions	In-hospital
Kallenbach et al, 2013 ²⁷	96 (83)	298	1.0%	4.8%			3.1%	6.0%		Single institution	30-day
Caceres et al, 2014 ¹⁸	3585	28,162	4.5%	8.9%	1.4%*	3.1%*	5.2%	7.6%		STS database	Operative
Coselli et al, 2014 ²⁰	239 (238)	77	0.4%	1.0%			5.0%	9.0%	Marfan syndrome international registry	Single institution	30-day
Toeg et al, 2014 ³⁵	68 (68)	96 (34†)			1.5%	5.2%				Single institution	In-hospital
Stamou et al, 2015 ⁷	1918	4718			1.9%	3.8%‡ or 5.7%§	6.0%	6.2%‡ or 6.5%§	No acute aortic dissection, no infective endocarditis	STS database	Operative
Gaudino et al, 2015 ⁸	180 (158)	710 (421)	0.0%	0.3%‡ or 0.2%§			3.9%	3.1%‡ or 3.6%§		Single institution	In-hospital
Lansac et al, 2015 ³⁰	130 (0)	131			3.8%	3.8%	6.9%	5.3%	CAVIAAR registry (elective alone)	20 institutions	30-day
Price et al, 2016 ²⁵	98 (69)	67	0.0%	0.0%			2.0%	1.5%	Marfan syndrome alone	19 institutions	In-hospital
Ouzounian et al, 2016 ³⁴	253 (200)	363 (180)			0.4%	0.5%‡ or 0%§	5.9%	7.1%‡ or 6.1%§		Single institution	In-hospital
Esaki et al, 2017 ²⁸	282 (282)	425 (425)	2.8%	9.6%			5.7%	8.0%		Single institution	Operative
Lee et al, 2018 ²⁹	82 (82)	134	0.0%	1.5%			3.7%	6.7%		Single institution	Operative

Previous reports from the same institution or reports that did not show separate mortality rates were excluded. Operative mortality is defined as death during index hospitalization or within 30 days of the procedure (see Caceres and colleagues¹⁸). VSRR, Valve-sparing root replacement; CVG, composite valve graft; STS, Society of Thoracic Surgeons. *Low-risk cases alone; †including homograft (n=13). Outcomes of CVG are in part presented according to the prosthesis type: ‡mechanical CVG or §biological CVG.