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Small Prosthesis Size in Aortic Valve Replacement Does Not Affect Mortality

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Abstract

Background—Small prosthesis size has been associated with worse postoperative outcomes in aortic valve replacement (AVR). We hypothesized that the use of small AVR prostheses does not independently increase operative mortality following AVR, but rather mortality may be related to co-morbidities.

Methods—From 2003–2008, 4,621 patients underwent primary AVR operations at 13 different statewide centers. Patients were stratified by prosthesis size into small AVR (≤21 mm, n=1,810) and standard AVR (≥23 mm, n=2,811) groups. The effect of prosthesis size on outcomes was evaluated by univariate and multivariable regression analyses.

Results—Operative mortality among primary AVR operations was 3.7%. Among isolated operations, small AVRs included more females (79.9% vs. 21.0%, $p<0.001$), older patients (68.9±12.3 years vs. 63.8±13.9 years, $p<0.001$,) and higher STS predicted risk of mortality (3.1 [3.0] vs. 2.2 [2.0], $p<0.001$) compared to standard AVRs. Small AVRs incurred more major complications (19.5% vs. 15.7%, $p=0.01$), higher mortality (3.9% vs. 2.3%, $p=0.03$), longer postoperative length of stay (6.0 [3.0] vs. 5.0 [3.0] days, $p<0.001$) and higher total costs ($29,738 [18,196] vs. 26,679 [14,890], $p<0.001$) compared to standard AVR. However, using multivariate regression, small AVR prosthesis size and female gender were not independent predictors of mortality while advanced age, bypass time, and aortic annular enlargement were important predictors of operative mortality.

Conclusions—Small aortic valve prosthesis size does not independently increase operative mortality following primary aortic valve replacement. Elevated morbidity and mortality among patients undergoing small AVR is related to the confounding effects of preoperative and operative risk factors. Annular enlargement may not always improve mortality.

Keywords

Aortic Valve Replacement; Prosthesis Size; Mortality

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INTRODUCTION

Aortic valve replacement (AVR) to treat aortic stenosis is one of the most common cardiac operations performed in contemporary cardiac surgery. According to the Society of Thoracic Surgeons (STS), approximately 24,300 isolated aortic valve replacements were performed in 2009, while 18,500 AVR with concomitant coronary artery bypass grafting (CABG) operations were performed in the United States [1]. During the performance of AVR with both mechanical and bioprosthetic valves, implantation of small size prostheses has been an issue of continued debate.

One issue to consider with the implantation of small AV prosthesis is the potential for prosthesis-patient mismatch (PPM) [2–5]. PPM was first described in 1978 by Rahimtoola and defined when “the effective prosthetic valve area, after insertion into the patient, is less than that of a normal human valve” [6]. Several subsequent reports have attempted to objectively define PPM with respect to various prosthetic valve characteristics, including the prosthesis effective orifice area (EOA) and geometric orifice area (GOA) as well as various indexed metrics (iEOA and iGOA) with respect to patient body surface area (BSA) [7–9]. Despite extensive investigation, a universally accepted definition of PPM fails to exist with reported definitions varying from 0.60 cm^2/m^2 to 1.1 cm^2/m^2 [2, 7]. More importantly, the immediate and long-term effects of PPM on patient morbidity and mortality remain unsettled. As a result, various aortic root and annular enlargement techniques have emerged to allow for the implantation of larger AV prosthesis [10–12]. Further complicating the debate is the variance among reported short and long-term outcomes for small AV prosthesis use [2–5, 7–9, 13–16]. In the absence of rigorous prospective evaluation, many reported series are limited by either small patient samples sizes, select single institutional experiences, or very long study periods, which make it difficult to generalize the results to modern day surgical practice.

While the influence of PPM on patient outcomes following AVR remain to be determined, the purpose of this study was to investigate outcomes following AVR prosthesis implantation within a multi-institutional cohort of patients with specific attention to the implications of small AV prosthesis use compared to the use of standard AV prostheses. We hypothesized that operative outcomes following AVR would not be significantly different despite implanted AV prosthesis size.

PATIENTS AND METHODS

Patients

The Virginia Cardiac Surgery Quality Initiative (VCSQI) is a group of 16 different collaborating cardiac surgical centers, both academic and private, within the Commonwealth of Virginia that voluntarily exchange and compare de-identified patient data with the goal of improving cardiac surgical care, quality and costs. Collectively, VCSQI participating centers perform approximately 99% of the Commonwealth’s cardiac operations, and each center contributes patient data to the national STS Adult Cardiac Surgery Database.

Patient level data obtained for this study was extracted from the VCSQI database for the years 2003–2008 and was de-identified with respect to all Health Insurance Portability and Accountability Act (HIPAA) patient identifiers. Included records were those for patients undergoing primary AVR operations without prior sternotomy for CABG, valve, or congenital procedures or any other identifiable cardiovascular reoperation. Patient records were principally stratified by AV prosthesis size into small (≤21 mm) and standard (≥23 mm) prosthesis categories. Subgroup analysis included patients undergoing isolated AVR without concomitant cardiac procedures. The presence of prosthesis patient mismatch was

determined by calculating the indexed effective orifice area (iEOA) with respect to body surface area ≤ 0.85 cm^2/m^2 using referenced estimated values of EOA for individual valve types as reported within the literature [8, 17, 18]. Actual EOA measurements were not available as results of postoperative echocardiograms were not collected within the VSCQI dataset, and the de-identified nature of the dataset precluded any further determination of these parameters. Operative mortality was defined as all patient deaths during hospitalization as well those within 30 days of AVR despite discharge status. A composite incidence of major complications was utilized as a proxy for major morbidity following AVR and included the incidence of deep sternal wound infection, postoperative stroke, renal failure, prolonged ventilation, pneumonia, and need for reoperation. Total hospital costs reflect estimated calculations reported to the VCSQI by participating centers. All other analyzed data reflect the use of established definitions within the STS Adult Cardiac Surgery database [19].

This study was exempt for review by the University of Virginia Institutional Review Board as it was a secondary analysis of the VCSQI data registry, due to the absence of patient identifiers, and because the data is collected for quality analysis and purposes other than research.

Statistical Analysis

Statistical methodology utilized in this study was designed to test the null hypothesis that outcomes following implantation of small AV prostheses are not significantly different from those following implantation of standard AV prostheses. Statistical significance was assessed by an alpha set to 0.05. All study outcomes and data comparisons were established *a priori* before data collection. Primary outcomes of interest were operative mortality and major complication rates as well as risk adjusted operative mortality as a function of valve prosthesis size. Secondary study outcomes included measures of resource utilization and total costs. Missing data for all variables of interest underwent sequential case-wise deletion to obtain a complete dataset for subsequent analysis.

Descriptive statistics for all patient characteristics, risk factors, operative features and postoperative outcomes were obtained using appropriate univariate hypothesis testing. Categorical variables are expressed as group percentages and were compared for independent samples using either Pearson's χ^2 or Fisher's Exact tests. Continuous data are represented as either mean ± standard deviation (SD) for normally distributed variables or median [interquartile range] for non-normally distributed variables. Independent sample analysis of variance (ANOVA) was used for parametric data comparisons, while the Mann Whitney *U* test was used for all non-parametric data comparisons. Calculated test statistics were used to derive reported two-tailed *p*-values.

Multivariable logistic regression analysis was utilized to estimate the independent effect of AV prosthesis size on confounder adjusted mortality. All model covariates (patient age, gender, BSA, AVR prosthesis size, aortic cross clamp time, cardiopulmonary bypass time, STS predicted risk of mortality, performance of annular enlargement, urgent and emergent operative status, NYHA class IV functional status, preoperative renal failure, hemodialysis, hypertension, diabetes, stroke, peripheral arterial disease and performance of concomitant CABG) were considered potential confounders for the effect of AV prosthesis size on mortality and were selected *a priori*. The estimated odds of operative mortality were adjusted for all model covariates. Model performance to discriminate between decedents and survivors was assessed using the area under the Receiver Operating Characteristics curve (AUC), while the Hosmer-Lemeshow test was used to verify model calibration across deciles of observed and predicted risk. In addition, the strength of association between

mortality and all model covariates was assessed by the Wald χ^2 test statistic, which quantifies the relative contribution of each covariate to the performance of the model.

Both unadjusted and confounder adjusted measures of association for the effect of AV prosthesis size and mortality are reported as odds ratios (OR) with a 95% confidence interval. Predictive Analytics SoftWare (PASW) statistics software, version 18.0.0 (IBM Corporation, Somers, NY) was used for all data manipulation and statistical analyses.

RESULTS

Patient Risk Factors and Operative Features for All Primary AVR

Patient characteristics and operative features for all patients undergoing primary AVR with both small and standard AV prostheses are detailed in Table 1. Among preoperative risk factors, patients undergoing small AVR presented with a higher prevalence of co-morbid disease compared to those undergoing standard AVR. Small AVR patients were older and more commonly female with a higher prevalence of preoperative hypertension, peripheral arterial disease, stroke, diabetes, dyslipidemia, and NYHA Class III functional status compared to standard AVR patients. Expectedly, patients undergoing AVR with small prostheses presented with smaller average BSA. Alternatively, patients undergoing standard AVR had a higher prevalence of a preoperative history of infective endocarditis and lower median ejection fractions. Aortic stenosis was by far the most common indication of AVR among both study cohorts. Median STS predicted risk of mortality (PROM) was higher among small AVR patients.

Among operative variables, patients undergoing small AVR underwent a slightly higher percentage of urgent operations compared to those undergoing standard size AVR. Isolated AVR operations occurred in 49.4% of cases, and the performance of AVR with concomitant CABG was similar between small and standard AVR groups. Bioprosthetic valves were the most common type of valve implanted, occurring in 82% of cases in both patient groups. Aortic annular enlargement was performed in 4.3% of small AVR cases compared to 2.7% of standard AVRs (p=0.01). However, despite this disparity, aortic cross clamp and cardiopulmonary bypass perfusion times were longer among those undergoing standard AVR.

Risk Factors Among Isolated AVR Patients

Similar trends in preoperative and operative risk factors were observed for patients undergoing primary, isolated AVRs with both small and standard size AV prostheses (Table 2). Importantly among isolated AVR operations, patients undergoing small AVR presented with elevated STS PROM and preoperative risk compared to patients with standard size AV prosthesis implantation. In this cohort of patients, however, no significant differences in elective, urgent, or emergent operations were observed, and the performance of aortic annular enlargement was not significantly different between small and standard AVR groups (3.7% vs. 3.1%, p=0.33). Median aortic cross clamp and cardiopulmonary bypass times were longer among patients undergoing standard size AVR.

Comparison of Outcomes by Valve Prosthesis Size

The incidence of postoperative complications as well as differences in resource utilization for patients undergoing AVR with small versus standard AV prostheses is presented in Table 3. Overall, few differences in postoperative complications existed among study cohorts. The incidence of PPM among those undergoing small AVR was expectedly higher compared to those undergoing standard AVR (47.3% vs. 18.1%, p<0.001). Further, while small, but statistically significant, differences were observed in the incidence of sepsis and

gastrointestinal complications between study groups, patients undergoing small AVR had a higher rate of prolonged ventilation (11.2% vs. 7.6%, p=0.004) compared to those undergoing standard AVR. As a result, this difference contributed most to the higher composite incidence of major complications observed for the small AVR cohort (19.5% vs. 15.7%, p=0.02). Moreover, patients undergoing small AVR incurred higher operative mortality rates (3.9% vs. 2.3%, p=0.03), longer median postoperative length of stays (p<0.001), and accrued higher median total costs (p<0.001) compared to those undergoing standard size AVR. Among the subset of patients with PPM (iEOA ≤ 0.85 cm^2/m^2), the incidence of mortality was not significantly different compared to those without PPM (iEOA > 0.85 cm^2/m^2): 3.5% vs. 2.6% (p=0.27), while those with PPM had higher rates of prolonged ventilation and a composite incidence of major complications as well as longer postoperative lengths of stay (Table 4).

Unadjusted and risk-adjusted odds ratios for the effect of AV prosthesis size on mortality among all patients (n=4,621) undergoing AVR are presented in Table 5. After accounting for the independent effects of various patient and operation-related risk factors through multivariable logistic regression modeling, AVR prosthesis size was not identified as an independent predictor of operative mortality (p=0.94). Moreover, performance of AVR using either a 19 mm or 21 mm AV prosthesis (compared to 23 mm) was not independently correlated with risk adjusted mortality (both p=0.90). Rather, significant independent multivariate correlates of mortality included: advancing patient age (OR=1.24 [1.01–1.05], p=0.003), preoperative stroke (OR=2.02 [1.26–3.26], p=0.004), preoperative hemodialysis (OR=3.16 [1.45–6.87], p=0.004), urgent (OR=1.68 [1.17–2.42], p=0.01) or emergent (OR=4.56 [1.45–14.38], p=0.01) operative status, increasing cardiopulmonary bypass time (OR=1.02 [1.01–1.03], p<0.001), NYHA Class IV functional status (OR=1.58 [1.03–2.42], p=0.04), and performance of an aortic annular enlargement procedure (OR=2.46 [1.24–4.92], p=0.01). Moreover, the strength of association for the observed relationships between AV prosthesis size and mortality was small relative to those for other risk factors.

The statistical performance of the multivariable logistic regression model achieved adequate discrimination with an AUC of 0.78, and the calibration of the model was adequate across deciles of observed risk as reflected by a Hosmer-Lemeshow p<0.05.

COMMENT

The present study reports contemporary outcomes for aortic valve replacement from a multi-institutional cohort of patients as a function of aortic valve prosthesis size. Considering on going debate regarding whether or not implantation of small AV prostheses results in clinically adverse outcomes, these results contribute to accumulating data and provide generalizable results to expand the discussion beyond single institution or surgeon experiences. The presented data demonstrates that patients undergoing AVR with small AV prostheses often present with higher risk due to advanced age, female gender, smaller BSA, and a higher prevalence of comorbid disease. As a result, these patients incurred higher measures of postoperative morbidity, a higher incidence of mortality, and increased resource utilization and costs. Importantly however, after accounting for the potential influence of confounding variables, AV prosthesis size failed to independently correlate with mortality, and implantation of small (19 mm or 21 mm) prosthesis failed to significantly increase the odds of mortality. Alternatively, the effects of well-established patient- and operation-related risk factors were important determinants of adjusted operative mortality. These data suggest that the implantation of small AV prostheses may serve as a surrogate for the effects of other patient factors on compromised outcomes following AVR.

The implantation of small AV prostheses during replacement remains controversial due to concern for the potential for prosthesis-patient mismatch. Concerns related to the presence of PPM have been documented in several reports [2, 3, 7, 13]. While many of these series report single institution experiences, one recent report analyzed data from the national STS Adult Cardiac Surgery Database (2000–2004) to examine outcomes for 42,310 patients undergoing isolated AVR [8]. This report assessed the effect of BSA, EOA, GOA and their respective derived indices on risk-adjusted mortality, and the authors demonstrated that EOA and GOA inversely correlated with mortality, while BSA was a significant inverse correlate of mortality. Consequently, they concluded that small prosthesis internal orifice area is associated with increased operative mortality following AVR and that increasing BSA may provide a protective effect during AVR. In one of the few prospective evaluations, Hanayama et al, similarly demonstrated significantly higher postoperative mortality (2.6% vs. 0.1%, p=0.001) for patients undergoing small AV prosthesis implantation with subsequent PPM [13]. To the contrary, in the present series, PPM was not associated with either unadjusted or adjusted operative mortality. These results are in agreement with other reports that have failed to demonstrate an association between the implantation of small AV prostheses and compromised operative and long-term survival due to the presence of PPM [3, 7, 14, 20]. In two such studies, both Rao and Blackstone independently documented no significant impact of PPM on intermediate survival following AVR [3, 7]. In the investigation by Rao and colleagues, patient survival as a function of PPM was similar until 7 years postoperative follow-up and then the survival curves diverged. In the series by Blackstone et al, all cause mortality was reported; however, their survival estimates did not consider valve related mortality. Furthermore, Moon and colleagues revealed that the negative effects of PPM may be age-dependent as compromised long-term survival occurred only in patients <70 years of age in their series [9].

In the present series, patients undergoing AVR with small size prostheses incurred higher postoperative morbidity and mortality. This was reflected by the significantly higher unadjusted odds of death associated with patients undergoing AVR with 19 mm (UOR=1.92, p=0.001) and 21 mm (UOR=1.48, p=0.02) valve prostheses compared to the use of 23 mm prostheses. However, other patient- and operation-related factors were also associated with elevated odds of death, including advancing age, preoperative stroke and hemodialysis requirements, urgent/emergent operative status, and advanced NYHA functional status. Consequently, after accounting for the potential effects of these factors, AV prosthesis size did not independently correlate with mortality, while several of these patient factors remained significant predictors of risk-adjusted mortality. This observed loss of effect upon risk adjustment indicates that implantation of small prostheses alone has no effect on patient mortality. Importantly, considered in these results was the observation that patients undergoing small size AVR had lower average body surface areas and represented a higher risk patient population who were older, more commonly female and presented with higher STS PROM. In addition, the inclusion of PPM as a predictor variable in our multivariate model did not significantly affect our model's performance due to colinearity between this factor and valve prosthesis size.

Contrary to other reports, aortic annular enlargement did not improve mortality in this study. In the past, the use of various AV annular enlargement techniques has been purported to confer beneficial effects due to the reduced incidence of PPM. In the presented results, the performance of annular enlargement occurred in a small percentage of patients and was expectedly higher among those undergoing small size AVR. Within the subset of patients undergoing isolated AVR, there were no differences in the performance of annular enlargement between those undergoing small versus standard AVR. These observations suggest the appropriate selection of small valve prostheses among patients undergoing isolated AVR procedures. Even more interesting was that after accounting for AV prosthesis

size, performance of aortic annular enlargement was associated with a 2.5 fold increase in the odds of mortality. While limited in an ability to scrutinize these findings further, they may represent the performance of annular enlargement for reasons other than to avoid PPM, or these results may be confounded by the performance of annular enlargement by inexperienced surgeons. Moreover, due to the low frequency of annular enlargement represented in this study cohort, it is difficult to draw any strong conclusions related to a positive association between annular enlargement and the likelihood of death. Rather, this data appears to suggest that in patients undergoing small AVR, the performance of annular enlargement may not improve survival and that any perceived increased risk from the performance annular enlargement should be considered for each individual patient by their surgeon. Further evaluation of this observation is, thus, justified. Further, several reports have documented the safety and functional advantages of aortic root and annular enlargement at the time of AVR and have highlighted disparities in outcomes as a function of surgeon experience [11, 21–23].

This study has important clinical relevance as it adds to accumulating evidence supporting the safe implantation of small AV prostheses in appropriately selected patients. Based upon these analyses, the increased risk of mortality incurred by patients requiring small AV prostheses may not be a result of a small aortic annulus, and annular enlargement techniques may not necessarily improve outcomes for this select group of patients. Further, these results have direct clinical implications as they suggest that surgical efforts to routinely augment the aortic annulus in order to accommodate the implantation of larger prostheses may subject the patient to unnecessary risk. Thus, careful selection of small AV prostheses for appropriately sized patients should be considered, and focus should be directed toward the optimization of modifiable patient risk factors to improve outcomes for these patients.

The present study has select limitations. First, selection bias must be considered due the retrospective study design and to the influence of surgeon patient selection regarding implantation of small AV prostheses. Second, the analysis of the VCSQI data registry confined all analyses to de-identified data and did not allow for further interrogation of certain data, including actual EOA measurements from postoperative echocardiography, type of annular enlargement technique, surgeon experience with annular enlargement, valve or annulus morphology, degree of valve/annulus calcification, extent of annular debridement, and changes to left ventricular mass and/or function over time. Third, the performed analyses were limited to short-term, operative outcomes and did not allow for the inclusion of intermediate or long-term follow-up, which may be expected to be more largely affected by the long-term consequences of inappropriately sized and implanted valves. Our analyses also did not examine functional status or quality of life following AVR. In addition, alternative definitions for small valve prostheses may be based upon the iEOA or other valve parameters, which may vary depending upon prosthesis type. The disproportionate prevalence of females within the small AVR group may have exerted some effect on the incidence of unadjusted outcomes; however, the confounding influence of this factor was accounted for during multivariate regression. Furthermore, the relatively low incidence of operative mortality following AVR operations constrained modeling efforts for adjusted mortality. Alternative statistical modeling such as propensity matching may result in more balanced cohorts for analysis; however, our logistic regression model performance proved resilient in its ability to adequately discriminate between operative survivors and decedents. Larger study size, possibly utilizing nationwide data, may help to develop model performance in future studies. Future investigation may also help to further define the influence of valve prosthesis size on other endpoints of resource utilization, including ventilation time and intensive care unit or hospital lengths of stay. Finally, cost information reported by the VCSQI was imperfect, and the potential for unrecognized miscoding of data must be considered in any secondary analysis of a data registry.

Conclusions

Continued debate remains regarding the use of small prostheses during aortic valve replacement. However, these data demonstrate that small aortic valve prosthesis size does not independently increase risk-adjusted operative mortality following primary aortic valve replacement. Rather, elevated morbidity and mortality among patients undergoing small size AVR is related to the confounding effects of preoperative and operative risk factors. In addition, annular enlargement may not improve mortality following small AV prosthesis implantation in appropriately selected patients.

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Table 1

Patient demographics, preoperative risk factors and operative features for all patients undergoing small versus standard aortic valve replacements (n=4,621).

Variable	Small AVR (n=1,810)	Standard AVR (n=2,811)	*p*
PREOPERATIVE			
Patient Age*	71.4±11.2	67.1±12.6	**<0.001**
Sex (Female)	73.9%	16.4%	**<0.001**
Height (cm)*	163.00±11.54	174.37±11.23	**<0.001**
Weight (kg)*	75.88±19.02	88.51±19.35	**<0.001**
BSA (m^2)*	1.80±0.24	2.02±0.27	**<0.001**
Hypertension	76.3%	68.7%	**<0.001**
Peripheral Arterial Disease	12.5%	9.5%	**0.002**
Stroke	7.9%	6.3%	**0.04**
Diabetes Mellitus	32.9%	26.4%	**<0.001**
Dyslipidemia	61.3%	58.6%	0.07
Heart Failure	32.0%	30.2%	0.20
NYHA Class			
Class I	7.2%	7.4%	0.91
Class II	24.5%	28.1%	**0.01**
Class III	42.2%	37.6%	**0.02**
Class IV	12.8%	11.6%	0.23
Infective Endocarditis	2.1%	4.1%	**<0.001**
Renal Failure	5.7%	6.3%	0.45
Renal Failure (Hemodialysis)	1.9%	2.4%	0.31
Ejection Fraction (%)†	60.0 [15.0]	55.0 [15.0]	**<0.001**
Aortic Stenosis	91.0%	80.1%	**<0.001**
Aortic Insufficiency	9.0%	19.9%	**<0.001**
STS PROM (%)†	4.5 [4.0]	2.9 [3.0]	**<0.001**
OPERATIVE			
Operative Status			
Elective	70.9%	73.7%	0.04
Urgent	28.2%	25.2%	**0.02**
Emergent	0.8%	0.9%	0.87
Isolated AVR	47.8%	50.5%	0.08
AVR + CABG	52.2%	49.5%	0.08
Prosthesis Type			
Bioprosthetic	82.7%	82.4%	0.87
Mechanical	16.5%	16.1%	0.78
Homograft	0.3%	0.4%	0.80
AVR Prosthesis Implant Size (mm)†	21.0 [2.0]	23.0 [2.0]	**<0.001**

Variable	Small AVR (n=1,810)	Standard AVR (n=2,811)	*p*
Aortic Annular Enlargement	4.3%	2.7%	**0.01**
Cross Clamp Time (min)†	92.0 [47.0]	94.0 [49.0]	**0.02**
Perfusion Time (min)†	121.0 [58.0]	123.0 [61.0]	0.10

*Mean ± standard deviation (SD);

†Median [interquartile range]. AVR=aortic valve replacement; BSA=body surface area; NYHA=New York heart association, STS=Society of Thoracic Surgeons; PROM=predicted risk of mortality; AV=aortic valve.

Table 2

Patient demographics, preoperative risk factors and operative features for all patients undergoing isolated small versus standard aortic valve replacements (n=2,283).

Variable	Small AVR (n=865)	Standard AVR (n=1,418)	*p*
PREOPERATIVE			
Patient Age*	68.93±12.25	63.81±13.93	**<0.001**
Sex (Female)	79.9%	21.0%	**<0.001**
Height (cm)*	161.98±13.13	173.92±11.89	**<0.001**
Weight (kg)*	76.71±19.93	88.86±19.78	**<0.001**
BSA (m^2)*	1.80±0.26	2.02±0.27	**<0.001**
Hypertension	70.1%	62.6%	**<0.001**
Peripheral Arterial Disease	9.7%	5.6%	**<0.001**
Stroke	6.9%	4.9%	**0.04**
Diabetes Mellitus	26.8%	20.5%	**0.001**
Dyslipidemia	51.0%	48.4%	0.24
Heart Failure	32.1%	31.5%	0.75
NYHA Class			
Class I	9.6%	9.4%	0.88
Class II	27.4%	31.1%	0.07
Class III	40.7%	33.4%	**0.001**
Class IV	8.1%	9.7%	0.20
Infective Endocarditis	3.1%	6.1%	**0.001**
Renal Failure	5.5%	5.5%	>0.99
Renal Failure (Hemodialysis)	2.4%	2.2%	0.77
Ejection Fraction (%)†	60.0 [15.0]	55.0 [15.0]	**<0.001**
Aortic Stenosis	89.2%	76.3%	**<0.001**
Aortic Insufficiency	10.7%	23.4%	**<0.001**
STS PROM (%)†	3.1 [3.0]	2.2 [2.0]	**<0.001**
OPERATIVE			
Operative Status			
Elective	78.2%	78.4%	0.88
Urgent	21.2%	20.5%	0.75
Emergent	0.7%	1.0%	0.64
Prosthesis Type			
Bioprosthetic	76.6%	76.2%	0.80
Mechanical	22.2%	22.4%	0.92
Homograft	0.5%	0.6%	>0.99
AVR Prosthesis Implant Size (mm)†	21.0 [2.0]	23.0 [2.0]	**<0.001**
Aortic Annular Enlargement	3.7%	3.1%	0.33
Aortic Cross Clamp Time (min)†	74.0 [31.0]	76.0 [32.0]	**0.02**

Variable	Small AVR (n=865)	Standard AVR (n=1,418)	*p*
Cardiopulmonary Bypass Time (min)†	99.0 [40.0]	102.0 [41.0]	0.08

*Mean ± standard deviation (SD);

†Median [interquartile range]. AVR=aortic valve replacement; BSA=body surface area; NYHA=New York heart association, STS=Society of Thoracic Surgeons; PROM=predicted risk of mortality; AV=aortic valve.

Table 3

Univariate analyses of postoperative outcomes for patients undergoing small versus standard AVR.

Variable	Small AVR (n=865)	Standard AVR (n=1,418)	*P*
Prosthesis-Patient Mismatch (iEOA ≤ 0.85 cm^2/m^2)	47.3%	18.1%	**<0.001**
Sepsis	2.1%	1.0%	**0.04**
Deep Sternal Wound Infection	0.5%	0.2%	0.44
Stroke	1.2%	1.7%	0.37
Perioperative Myocardial Infarction	0.0%	0.2%	0.29
Reoperation (Bleeding/Tamponade)	4.3%	3.7%	0.58
Reoperation (Valve Dysfunction)	0.2%	0.1%	0.64
Atrial Fibrillation	20.8%	21.4%	0.79
Cardiac Arrest	1.8%	1.6%	0.74
Gastrointestinal Event	2.9%	1.6%	0.03
Pneumonia	3.4%	2.5%	0.24
Prolonged Mechanical Ventilation	11.2%	7.6%	**0.004**
New-onset Hemodialysis	1.7%	1.3%	0.37
Renal Failure	4.9%	4.1%	0.40
Major Complications	19.5%	15.7%	**0.02**
Mortality	3.9%	2.3%	**0.03**
Postoperative Length of Stay (Days)†	6.0 [3.0]	5.0 [3.0]	**<0.001**
Total Costs ($)	29,738 [18,196]	26,679 [14,890]	**<0.001**

†Median [interquartile range]. AVR=aortic valve replacement

Table 4

Postoperative outcomes among patients undergoing isolated AVR with and without prosthesis-patient mismatch (iEOA ≤ 0.85 cm^2/m^2).

Variable	PPM (n=667)	No PPM (n=1,616)	*P*
Stroke	1.1%	1.8%	0.27
Prolonged Mechanical Ventilation	13.2%	5.2%	**<0.001**
Renal Failure	5.0%	4.5%	0.36
Major Complications	22.5%	12.7%	**<0.001**
Mortality	3.5%	2.6%	0.27
Postoperative Length of Stay (Days)†	6.0 [4.0]	5.0 [3.0]	**<0.001**

†Median [interquartile range]. PPM=Prosthesis-Patient Mismatch

Table 5

Unadjusted and adjusted associations between patient and operative risk factors and mortality for all patients undergoing AVR (n=4,621).

Risk Factor	Unadjusted		Adjusted			
	UOR (95% CI)	*p*	Wald χ^2	AOR	95% CI	*p*
AVR Prosthesis Size			4.197			0.94
23 mm (Reference)	1.00			1.00	-	
19 mm	1.92 (1.29–2.85)	**0.001**		1.62	0.92–2.88	0.89
21 mm	1.48 (1.07–2.05)	**0.02**		1.43	0.92–2.22	0.90
25 mm	0.58 (0.36–0.92)	**0.02**		0.92	0.52–1.65	0.91
27 mm	0.77 (0.40–1.46)	0.42		1.25	0.53–2.92	0.90
29 mm	0.52 (0.17–2.16)	0.37		0.002	<0.001–>999	0.92
≥31 mm	<0.001 (<0.001–>999)	>0.99		0.001	<0.001–>999	0.94
Female gender	1.57 (1.21–2.05)	**0.001**	0.996	1.24	0.81–1.90	0.32
BSA (mm)	0.49 (0.33–0.72)	**<0.001**	2.535	0.78	0.37–1.70	0.54
Prosthesis-Patient Mismatch (iEOA ≤ 0.85 cm^2/m^2)	1.15 (0.79–1.66)	0.53	1.627	0.68	0.38–1.23	0.20
Patient age (years)	1.03 (1.02–1.05)	**<0.001**	8.670	1.24	1.01–1.05	**0.003**
Preoperative hemodialysis	3.55 (2.15–5.86)	**<0.001**	8.434	3.16	1.45–6.87	**0.004**
Preoperative stroke	1.55 (0.99–2.39)	0.05	8.392	2.02	1.26–3.26	**0.004**
NYHA Class IV	4.36 (3.22–5.65)	**<0.001**	4.413	1.58	1.03–2.42	**0.04**
Urgent status	2.30 (1.77–3.00)	**<0.001**	7.742	1.68	1.17–2.42	**0.01**
Emergent status	7.42 (3.99–13.80)	**<0.001**	6.713	4.56	1.45–14.38	**0.01**
Cardiopulmonary bypass time (min)	1.01 (1.007–1.011)	**<0.001**	37.683	1.02	1.01–1.03	**<0.001**
Aortic Annular Enlargement	1.85 (1.06–3.25)	**0.03**	6.545	2.46	1.24–4.92	**0.01**

Area Under Receiver Operator Curve (AUC)=0.78. Results reported as odds ratios (95% Confidence Interval). UOR=unadjusted odds ratio, AOR=adjusted odds ratio; AVR=aortic valve replacement; BSA=body surface area; NYHA=New York Heart Association, AV=aortic valve.