Influence of left ventricular ejection fraction on morbidity and mortality after aortic root replacement

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ABSTRACT

Objective: To better understand morbidity and mortality in patients with a low left ventricular ejection fraction (LVEF) undergoing aortic root replacement.

Methods: All patients who underwent aortic root replacement at our institution between 2005 and 2013 ($n = 595$) were retrospectively reviewed and included in the study. The primary outcome was mortality. Secondary outcomes were in-hospital mortality and perioperative morbidity. Restricted cubic spline analysis showed a relatively linear inverse relationship between LVEF and the hazard ratio for mortality in patients with an LVEF $<50\%$ with no unique cutoff. Therefore, LVEF was treated as a continuous variable. Patients were divided into 3 groups (LVEF $<40\%$, LVEF 40%–49%, and LVEF $\geq 50\%$) in order to illustrate the impact of LVEF on mortality.

Results: LVEF $<40\%$ patients had greater in-hospital mortality (14.0% vs 5.0% vs 1.0%, $P < .001$) and longer median hospital and intensive care unit stays (10.5 vs 8 vs 6 days, $P < .001$ and 4 vs 2 vs 2 days, $P < .001$) than patients with LVEF 40% to 49% or greater than 50%, respectively. Patients with LVEF $<40\%$ had more reoperations for bleeding (18% vs 5.0% vs 5.8%, $P = .004$), postoperative respiratory failure (16% vs 6.7% vs 4.9%, $P = .008$), and need for mechanical circulatory support (8.0% vs 5.0% vs 1.4%, $P = .005$). Using multivariable Cox proportional hazards analysis, we found that reduced LVEF, age, previous, cardiac surgery, and type A dissection were independent predictors of mortality.

Conclusions: Reduced LVEF negatively impacts mortality as well as in-hospital death and perioperative morbidity after aortic root replacement. Careful patient selection and risk discussion are vital in this high-risk population. (J Thorac Cardiovasc Surg 2019;158:984–91)

Kaplan–Meier analysis of survival by left ventricular ejection fraction.

Central Message

Patients with reduced left ventricular ejection fraction have increased morbidity and mortality after aortic root replacement. Careful patient selection and counseling are critical.

Perspective

The impact of reduced left ventricular ejection fraction (LVEF) on outcomes after aortic root replacement is not well defined. This study reports that decreasing LVEF is associated with markedly greater mortality and postoperative morbidity, highlighting the need for careful patient selection and counseling for what is often a prophylactic operation.

See Commentaries on pages 992 and 994.

Aortic root replacement (ARR) is the standard surgical procedure for patients with aortic root aneurysms, as well as select patients with a Stanford type A aortic dissection or endocarditis. Despite the surgical complexity, continued evolution of operative technique and postoperative care

have significantly improved clinical outcomes.^{1–6} Although several studies have identified general risk factors, including emergent surgical indications, reoperation, New York Heart Association functional class, and pre-existing major organ dysfunction, there have been no studies specifically examining the impact of left ventricular ejection fraction (LVEF) on outcomes after aortic root

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Abbreviations and Acronyms

ARR = aortic root replacement
CABG = coronary artery bypass grafting
LVEF = left ventricular ejection fraction

replacement.^{5,7} As the overall cardiac surgery patient population becomes older and sicker, it is important to understand the impact of specific risk factors on the outcomes of specific procedures. Consequently, we reviewed our own institutional experience to better understand early postoperative outcomes in patients with low LVEF undergoing ARR.

MATERIALS AND METHODS

The Columbia University Medical Center institutional review board approved this study and waived the requirement for informed consent.

Patient Selection

All patients who underwent ARR at our institution between 2005 and 2013 were retrospectively reviewed. A total of 595 patients were identified and included in the study.

A restricted cubic spline analysis with 4 knots was conducted to clarify the possible nonlinear association between LVEF and mortality and to see whether any significant hazard changes occur at certain LVEF values. This analysis showed a relatively linear inverse relationship between LVEF and the hazard ratio for death in patients with an LVEF <50% with no unique cutoff ejection fraction at which this association changes (Figure 1). To further illustrate the impact of reduced LVEF on mortality across the population, the patients were then divided into 3 groups by their LVEF (LVEF <40%, LVEF 40%-49%, and LVEF ≥50%). These categories coincide with the 2013 American College of Cardiology Foundation/American Heart Association categorizations of LVEF as reduced, borderline, and preserved.⁸

Clinical, follow-up, and mortality data were collected from our institutional electronic medical record. Mortality data for patients lost to follow-up were collected from the Social Security Death Index through 2014, after which survival data were only available via our institutional medical record. Baseline demographics, echocardiographic data, comorbidities, concomitant procedures, perioperative complications, postoperative complications, length of overall hospital and intensive care unit stay, and survival data were collected for analysis.

Operative Methods

Patients were cannulated for cardiopulmonary bypass using a strategy specifically tailored to the surgical indication, including information from both preoperative computed tomography scans and measurements from the intraoperative transesophageal echocardiogram. The operating surgeon determined whether axillary artery cannulation was used for selective, antegrade cerebral perfusion, as well as whether to spare the aortic valve. For patients undergoing only ARR or aortic root plus ascending aorta replacement, the standard, central cannulation strategy was used. Valve-sparing procedures were performed using the reimplantation technique with a Gelweave Valsalva graft (Vascutek, Renfrewshire, Scotland). Composite bioprosthetics were constructed by sewing a stented biological aortic prosthesis to the skirt of the Valsalva graft (Video 1).^{9,10}

Statistical Analysis

All analyses were performed using STATA 13.1 (StataCorp LP, College Station, Tex) or R v3.5.1 (R Foundation for Statistical Computing, Vienna,

FIGURE 1. Adjusted restricted cubic spline curves with 95% confidence bands for hazard ratios of death with respect to patient left ventricular ejection fraction after aortic root replacement. Reference ejection fraction 50%.

Austria) software. Continuous variables are presented as median and interquartile range and were compared using the Kruskal–Wallis test. Categorical data are presented as number and percentage of the total and compared using the Pearson χ^2 test. Kaplan–Meier analysis was used to assess survival, with the equivalence of the survivor functions of the 3 groups assessed using the log-rank test. In a post-hoc power analysis with a sample size of 47 and sampling ratio of 11 (ie, 520/47), the power to detect a difference in in-hospital mortality (2% vs 12%) was approximately 0.55 with a level of significance of 0.05. Data were complete for preoperative LVEF, as well as perioperative morbidity and mortality. Any other missing data were replaced by multiple imputation methods using predictive mean matching.

To identify preoperative variables associated with mortality, univariable and multivariable Cox proportional hazards regression was performed and hazard ratios for death after root surgery were calculated with their 95% confidence intervals. The model included the following 12 covariates:

VIDEO 1. Intraoperative video showing aortic root replacement using a biological valved conduit. Video available at: [https://www.jtcvs.org/article/S0022-5223\(18\)32971-4/fulltext](https://www.jtcvs.org/article/S0022-5223(18)32971-4/fulltext).

TABLE 1. Patient demographics and baseline characteristics

Patient demographics	LVEF <40% (n = 50)	LVEF 40%-49% (n = 60)	LVEF ≥50% (n = 485)	P
Age, y	64.1 (52.0-71.0)	62.2 (52.2-74.1)	61.0 (50.6-70.0)	.372
Male	41 (82.0)	52 (86.7)	386 (79.6)	.410
Body mass index, kg/m ²	26.2 (23.5-28.7)	26.0 (24.1-28.9)	27.2 (24.5-30.5)	.055
Comorbidities				
Hypertension	30 (60.0)	39 (65.0)	324 (66.8)	.616
Diabetes mellitus	11 (22.0)	5 (8.3)	41 (8.4)	.008
Coronary artery disease	12 (24.0)	17 (28.3)	107 (22.1)	.540
Cerebrovascular disease	4 (8.0)	2 (3.3)	34 (7.0)	.524
Chronic obstructive pulmonary disease	4 (8.0)	4 (6.7)	25 (5.1)	.650
End-stage renal disease	2 (4.0)	0 (0.0)	1 (0.2)	.001
Peripheral vascular disease	0 (0.0)	0 (0.0)	14 (2.9)	.197
Previous myocardial infarction	5 (10.0)	4 (6.7)	21 (4.3)	.182
Atrial fibrillation	12 (24.0)	13 (21.7)	63 (13.0)	.032
Previous cardiac surgery	11 (22.0)	10 (16.7)	69 (14.2)	.324
Aortic dimensions, mm				
Aortic root diameter	44.0 (38.0-52.0)	48.0 (42.0-55.0)	46.0 (40.0-52.0)	.123
Ascending aortic diameter	50.5 (46.0-60.0)	55.0 (49.0-60.0)	51.0 (47.0-57.0)	.080
Echocardiographic data				
LVEF, %	30.0 (25.0-34.0)	44.0 (44.0-44.5)	55.0 (54.0-55.0)	.000
Aortic insufficiency*	2.0 (1.0-3.0)	2.0 (1.0-4.0)	2.0 (0.0-3.0)	.000
Bicuspid aortic valve	19 (38.0)	22 (36.7)	233 (48.0)	.118

Data presented as number (%) or median (interquartile range). LVEF, Left ventricular ejection fraction. *Valve insufficiency scale: 0 (none/trace) to 4 (severe).

age, male sex, body mass index, hypertension, diabetes, coronary artery disease, chronic kidney disease, LVEF, grade of aortic insufficiency, type A aortic dissection, history of previous cardiac surgery, and atrial fibrillation. Potential predictors were identified using a stepwise model building method to minimize the Akaike information criterion. To clarify the possible nonlinear association between LVEF and HRs for mortality, we used a restricted cubic spline model with 4 knots to determine whether there were any significant hazard changes at specific LVEF values. To adjust for baseline profiles, we calculated a generalized propensity score (ie, predicted LVEF) by a linear regression including 11 covariates (same as listed previously, excepting LVEF), by making LVEF a dependent variable. This score was then added to the model to predict survival outcomes. To assess the potential impact of presenting pathology on outcomes, a subgroup analysis was performed in only those patients who presented with an aortic root aneurysm. Two-tailed *P* values of less than .05 were considered to be statistically significant for all tests.

RESULTS

Patient Characteristics

Patient demographics and baseline characteristics are presented in Table 1. There were no differences in age, body mass index, or sex composition between the 2 groups. The prevalence of significant medical comorbidities, including coronary artery disease, history of stroke/transient ischemic attack, and chronic obstructive pulmonary disease, were also similar; however, the rates of diabetes, end-stage renal disease, and atrial fibrillation increased with decreasing LVEF. There was no difference in the proportion of patients in each group with a history of previous cardiac surgery, and the diameter of both the

aortic root and the ascending aorta were similar. The number of patients with a bicuspid aortic valve was also similar across the groups.

Operative Indications and Details

The indications for surgery and details of the performed procedures are listed in Table 2. Significant differences existed in the indications for surgery between the 2 groups. Although the majority of patients in both groups presented with an aortic root aneurysm, aneurysm was less common in patients with LVEF <40% (74% LVEF <40% vs 91.7% LVEF 40%-49% vs 87.6% LVEF ≥50%), and a greater percentage of patients with LVEF <40% presented with Stanford type A aortic dissection (18% LVEF <40% vs 5.0% LVEF 40%-49% vs 10.3% LVEF ≥50%) or infective endocarditis (8.0% LVEF <40% vs 3.3% LVEF 40%-49% vs 1.0% LVEF ≥50%) (overall *P* = .003). The aortic root was replaced using a valve-sparing procedure in 227 (38.1%) patients, a stentless bioprosthesis in 214 (36.0%) patients, a stented bioprosthesis in 137 (23.0%) patients, a mechanical prosthesis in 10 (1.7%) patients, and an aortic homograft in 7 (1.2%) patients. A stented bioprosthesis, stentless bioprosthesis, mechanical prosthesis, or homograft was used more often in patients with lower LVEF, and they likewise underwent fewer valve-sparing procedures (overall *P* < .001).

The rate of concomitant procedures, including ascending aorta, hemiarch, or total arch replacement, as

TABLE 2. Operative details

Operative details	LVEF <40% (n = 50)	LVEF 40%-49% (n = 60)	LVEF ≥50% (n = 485)	P
Indication for surgery				.003
Stanford type A dissection	9 (18)	3 (5.0)	50 (10.3)	
Thoracic aortic aneurysm	37 (74.0)	55 (91.7)	425 (87.6)	
Infective endocarditis	4 (8.0)	2 (3.3)	5 (1.0)	
Other	0 (0.0)	0 (0.0)	5 (1.0)	
Root replacement procedure				.000
Stented bioprosthesis	18 (36.0)	17 (28.3)	102 (21.0)	
Stentless bioprosthesis	17 (34.0)	27 (45.0)	170 (35.0)	
Valve-sparing procedure	10 (20.0)	13 (21.7)	204 (42.1)	
Mechanical bioprosthesis	2 (4.0)	2 (3.3)	6 (1.2)	
Aortic homograft	3 (6.0)	1 (1.7)	3 (0.6)	
Concomitant procedures				
Ascending aorta replacement	30 (60.0)	34 (56.7)	339 (69.9)	.056
Aortic arch replacement	11 (22.0)	10 (16.7)	67 (13.8)	.273
Hemiarch replacement	14 (28.0)	25 (41.2)	169 (34.8)	.324
Coronary artery bypass grafting	8 (16.0)	13 (21.7)	74 (15.3)	.442
Mitral valve repair/replacement	7 (14.0)	10 (16.7)	26 (5.4)	.001
Cardiopulmonary bypass details				
Cardiopulmonary bypass time, min	130.0 (103.0-185.0)	145.0 (118.5-185.0)	128.0 (103.0-159.0)	.009
Aortic crossclamp time, min	94.5 (71.0-122.0)	105.5 (86.5-134.0)	95.0 (77.0-124.0)	.079
Deep hypothermic circulatory arrest/antegrade cerebral perfusion time, min	12.0 (9.0-17.0)	11.5 (10.0-13.0)	11.0 (9.0-15.0)	.716
Cerebral protection				.820
Not needed	21 (42.0)	23 (38.3)	221 (45.6)	
Deep hypothermic circulatory arrest	0 (0.0)	0 (0.0)	1 (0.2)	
Antegrade cerebral perfusion	29 (58.0)	37 (61.7)	263 (54.2)	

Data expressed as number (%) or median (interquartile range). LVEF, Left ventricular ejection fraction.

well as coronary artery bypass grafting (CABG) was similar between the groups. Patients with a LVEF <50% underwent more mitral valve procedures (14.0% LVEF <40% vs 16.7% LVEF 40%-49%, vs 5.4% LVEF ≥50%, $P = .001$). A majority of patients in each group received antegrade selective cerebral perfusion (58.0% LVEF <40% vs 61.7% LVEF 40%-49% vs 54.2% LVEF ≥50%). Only one patient, who had a LVEF ≥50%, required deep hypothermic circulatory arrest. The duration of cardiopulmonary bypass was greatest in patients with a LVEF 40%-49% (130 minutes LVEF <40 vs 145 minutes LVEF 40%-49% vs 128 minutes LVEF ≥50%, $P = .009$). There was no difference in aortic crossclamp or antegrade cerebral perfusion/deep hypothermic circulatory arrest duration between the groups.

Postoperative Outcomes

Postoperative outcomes are presented in Table 3. In-hospital mortality was 14.0% in patients with an LVEF <40% compared with 5.0% in patients whose LVEF was 40% to 49% and 1.0% in patients with an LVEF ≥50% ($P < .001$). Of the 15 patients who died during their index hospitalization, 4 died of cardiogenic shock, 4 of postoperative stroke, 2 of multisystem organ failure, 2 of

malignant arrhythmias, 1 of septic shock, 1 of hypovolemic shock, and 1 from pulmonary embolism.

Significantly more patients with decreased LVEF developed respiratory failure (16.0% LVEF <40% vs 6.7% LVEF 40%-49% vs 4.9% LVEF ≥50%, $P = .008$). Reoperation to control bleeding was also more common in patients with the lowest LVEF (18.0% LVEF <40% vs 5.0% LVEF 40%-49% vs 5.8% LVEF ≥50%, $P = .004$). The postoperative need for mechanical circulatory support was greater in patients with lower LVEF (8.0% LVEF <40% vs 5.0% LVEF 40%-49% vs 1.4% LVEF ≥50%, $P = .005$). There were no differences in the rates of stroke, myocardial infarction, atrial fibrillation, or the need for a new permanent pacemaker. In addition to greater in-hospital death and perioperative morbidity, patients with lower LVEF spent significantly more time both in the hospital and in the intensive care unit.

Using a Cox proportional hazards regression, we identified decreased LVEF, age, a history of previous cardiac surgery, and a surgical indication of type A aortic dissection as independent predictors of mortality (Table 4). Kaplan–Meier survival analysis (Figure 2) demonstrated a difference between the survival curves of the 3 groups at up to 6 years (log-rank $P < .001$).

TABLE 3. Postoperative outcomes

Outcomes	LVEF <40% (n = 50)	LVEF 40%-49% (n = 60)	LVEF ≥50% (n = 485)	P
Intraoperative death	0 (0.0)	1 (1.7)	0 (0.0)	–
In-hospital death	7 (14.0)	3 (5.0)	5 (1.0)	.000
Hospital length of stay, d	10.5 (7.0-19.0)	8.0 (5.0-11.5)	6.0 (5.0-9.0)	<.001
Intensive care unit length of stay, d	4.0 (2.0-8.0)	2.0 (1.0-4.0)	2.0 (1.0-4.0)	<.001
Postoperative complications				
Reoperation for bleeding	9 (18.0)	3 (5.0)	28 (5.8)	.004
Stroke	4 (8.0)	1 (1.7)	19 (3.9)	.233
Respiratory failure	8 (16.0)	4 (6.7)	24 (4.9)	.008
New need for dialysis	4 (8.0)	1 (1.7)	11 (2.3)	.051
Myocardial infarction	0 (0.0)	0 (0.0)	4 (0.8)	.633
Atrial fibrillation	24 (48.0)	21 (35.0)	192 (39.6)	.370
New pacemaker requirement	3 (6.0)	3 (5.0)	26 (5.4)	.973
Aortic reoperation	3 (6.0)	5 (8.3)	25 (5.1)	.591
Need for mechanical circulatory support	4 (8.0)	3 (5.0)	7 (1.4)	.005

Data presented as number (%), median (interquartile range). LVEF, Left ventricular ejection fraction.

A subgroup analysis of only those patients who underwent ARR for aortic root aneurysm found a similar increase in the rates of mortality and major morbidities in patients with lower LVEF (Table E1). The rates of in-hospital death (8.1% LVEF <40% vs 3.6% LVEF 40%-49% vs 0.7% LVEF ≥50%, $P = .001$), reoperation for bleeding (16.2% LVEF <40% vs 3.6% LVEF 40%-49% vs 8.7% LVEF ≥50%, $P = .014$), respiratory failure (13.5% LVEF <40% vs 3.6% LVEF 40%-49% vs 3.3% LVEF ≥50%, $P = .010$), need for new continuous renal-replacement therapy (8.1% LVEF <40% vs 0.0% LVEF 40%-49% vs 1.4% LVEF ≥50%, $P = .007$), and need for postoperative mechanical circulatory support (5.4% LVEF <40% vs 3.6% LVEF 40%-49% vs 0.5% LVEF ≥50%, $P = .005$) were increased in patients with lower LVEF. Hospital and ICU length of stay also were increased.

DISCUSSION

Overall outcomes after ARR procedures are excellent.^{5,11} However, with the population of cardiac surgery patients becoming older and sicker, ever-greater risk cases are being referred for surgical intervention. As aortic surgery is often prophylactic, it is imperative that the risk of a future aortic event, such as dissection or aneurysm rupture, is weighed against the risk of operation when counseling patients. Left ventricular dysfunction is a known risk factor in both CABG and valve surgery.¹²⁻¹⁴ However, to date, there are no studies specifically examining the impact of a low LVEF on outcomes after ARR. Rather, previous series have either examined outcomes in patients deemed to be at overall increased risk, or used functional metrics, such as New York Heart Association class, in their analysis. Consequently, we retrospectively reviewed our institutional experience to better understand the specific

TABLE 4. Cox proportional hazards regression analysis for preoperative characteristics predictive of mortality

Variables	Univariable		Multivariable	
	HR (95% CI)	P value	HR (95% CI)	P value
LVEF	0.94 (0.92-0.97)	<.001	0.96 (0.94-0.99)	.010
Age	1.05 (1.02-1.08)	<.001	1.03 (1.01-1.07)	.010
Male	0.62 (0.29-1.34)	.221	–	–
Body mass index	0.93 (0.85-1.00)	.063	–	–
Diabetes mellitus	1.81 (0.70-4.70)	.223	–	–
Hypertension	1.37 (0.64-2.98)	.416	–	–
CKD (creatinine >2.0)	5.10 (1.22-21.34)	.026	–	–
Coronary artery disease	1.77 (0.85-3.67)	.125	–	–
Atrial fibrillation	2.79 (1.32-5.91)	.007	1.81 (0.83-3.94)	.134
Aortic insufficiency	1.15 (0.90-1.47)	.273	1.22 (0.94-1.59)	.138
Previous cardiac surgery	3.23 (1.56-6.71)	.002	2.93 (1.38-6.19)	.005
Type A dissection	4.90 (2.36-10.19)	<.001	4.02 (1.88-8.59)	<.001

HR, Hazard ratio; CI, confidence interval; LVEF, left ventricular ejection fraction; CKD, chronic kidney disease.

FIGURE 2. Kaplan–Meier analysis of survival by LVEF: LVEF $< 40\%$ (green line), LVEF 40%–49% (red line), LVEF $\geq 50\%$ (blue line). Bars represent 95% confidence intervals. Patients at risk at each time point are presented in the table at bottom. LVEF, Left ventricular ejection fraction.

impact of LVEF on outcomes after ARR, finding that patients with decreased LVEF are at significantly greater risk for mortality and perioperative morbidity, as well as increased hospital and intensive care unit length of stay.

Overall in-hospital mortality in our series was 2.5%, which is consistent with the best outcomes from previously reported series.^{5,11} However, patients with a LVEF $< 40\%$ had a significantly greater early mortality of 14% compared with only 1.0% in patients with a LVEF of at least 50%. Although a low LVEF is known to increase surgical risk in patients undergoing CABG and valve procedures, previous studies have shown that these procedures can be performed safely and with an acceptable increase in mortality.^{15–19} In their large, multicenter study, for example, Topkara and colleagues¹⁶ reported in-hospital mortality of 6.5% for patients with a LVEF $< 20\%$ undergoing CABG compared with 1.4% for those patients with a LVEF $> 40\%$. As a result of such data, CABG and valve procedures are appropriately offered to patients with substantial left ventricular dysfunction. The much greater increase in mortality seen in patients with low LVEF undergoing ARR, however, highlights the complexity of these operations, underscoring the fact that significantly decreased left ventricular function does not impact all patients equally.

In addition to increased mortality, patients with a decreased LVEF also had greater rates of perioperative morbidity. This is consistent with previous studies of patients with low LVEF undergoing cardiac surgery, which

have shown an increased risk of low cardiac output syndrome and need for inotropic support, acute renal failure, prolonged respiratory failure, atrial fibrillation, stroke, sepsis, deep sternal wound infection, and bleeding requiring reoperation.^{16,20–23} In our series, patients with a LVEF $< 40\%$ had a notably greater rate of reoperation for bleeding, as well as increased rates of respiratory failure and postoperative mechanical circulatory support. Furthermore, there was a significant increase in both intensive care unit and overall hospital length of stay. Interestingly, the significant increase in reoperation for bleeding seen in the patients with the lowest LVEF is consistent with studies of patients with reduced LVEF undergoing CABG.¹⁶ However, there is no obvious underlying cause, and this is a potential area for further study.

Williams and colleagues⁵ found that patients who undergo nonelective ascending aorta and arch procedures have significantly worse outcomes when compared with patients whose repairs are performed electively. This is consistent with the known, substantial risk associated with repair of acute aortic syndromes, especially in patients with significant malperfusion syndromes, who have been subclassified and specifically risk stratified by several other groups.^{24,25} In our experience, a significantly greater percentage of patients with a decreased LVEF had a nonelective indication for ARR, specifically Stanford type A dissection or endocarditis, and it is possible that this contributed to the decreased early survival seen in the low LVEF group. However, a subgroup analysis of only those patients who underwent surgery for aneurysmal disease found similarly increased rates of early mortality and significant morbidity. This suggests that although urgent or emergent surgical indications further increase operative risk, they do not account for the marked increase in morbidity and mortality seen in patients with low LVEF.

When considering any patient for ARR, the primary question guiding management should be whether the risk of a future aortic event, such as dissection or rupture, outweighs the risk of surgical repair. Currently, guidelines recommend elective repair of root, ascending, and arch aneurysms measuring > 5.5 cm in patients without a genetic aortopathy or alternative indication for cardiac surgery.²⁶ This recommendation is based on the observation that the risk of aneurysm rupture, dissection, or death exceeds operative mortality at this aneurysm size, assuming an operative mortality of 5%.⁵ However, in this study we found that in patients with aneurysmal disease and a LVEF $< 40\%$, early mortality was 8%, and the rate of major morbidity was 13.9%. Importantly, the restricted spline analysis showed an approximately inversely linear correlation between LVEF and outcomes, so while LVEF categories were used to help illustrate the impact of reduced LVEF across the study population, it is important to realize

that operative risk rises as the ejection fraction falls once the LVEF falls below the normal range. Consequently, size-based guidelines should be considered in the overall context of the patient when there are major risk factors for adverse outcomes, such as significant left ventricular dysfunction. We do not propose that any absolute LVEF valve be used to establish surgical candidacy, but rather that, especially in elective cases, the risk of a prophylactic operation be weighed against its risks. In some cases, continued surveillance may be warranted in patients with aneurysms that meet standard size criteria for intervention.

This study has several important limitations. First, it is necessarily limited by its retrospective, single-institution design, and as a single-center study, it reflects our own institutional treatment biases. Second, the sample size for patients with a LVEF <50% is comparatively small, rendering the study underpowered to detect differences in uncommon clinical events. This was addressed as much as possible by designing the study to focus on mid-term mortality during follow-up rather than aiming to parse out detailed differences between groups with limited patient numbers. For example, the contribution of malperfusion syndromes to outcomes within the subset of patients with an aortic dissection, as well as other potentially interesting subgroup analyses, were outside of the scope of this study.

Left ventricular dysfunction is a complex condition with multiple potential etiologies that do not all respond similarly to medical or surgical therapy. Although the etiology of left ventricular dysfunction in this population is most likely to be severe aortic valve dysfunction, different causes of left ventricular dysfunction could play a role in postoperative outcomes and further study of their specific impact is warranted. Because high-quality, long-term follow-up data were limited, especially by our need to use the Social Security Death Index for patients lost to follow-up, this study was designed to compare mid-term mortality during the period where the most complete follow-up data were available, and therefore we are unable to comment on the long-term results in these patients. Finally, postoperative quality of life is an important consideration when proposing high-risk surgery, and we do not have data on the postoperative quality of life for these patients.

In conclusion, we found that patients with a reduced LVEF who undergo ARR had significantly increased mid-term mortality, as well as in-hospital mortality and major perioperative morbidity when compared with patients with a LVEF >50%. Furthermore, this increased risk is not due to high-risk surgical indications or associated comorbidities but rather likely reflects the inherent risk of performing cardiac surgery in patients with pre-existing left ventricular dysfunction. The significantly higher mid-term mortality, in-hospital mortality, and major morbidity should

be addressed when counseling patients with low LVEF who need aortic root replacement and may be considered when evaluating size-based criteria for elective aneurysm repair in the future.

Conflict of Interest Statement

Dr George is a consultant for Edwards Lifesciences and Medtronic. All other authors have nothing to disclose with regard to commercial support.

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Key Words: aortic root replacement, cardiac surgery, left ventricular ejection fraction, heart failure, outcomes, complications

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FIGURE E1. Patient flow diagram illustrating the study design. *LVEF*, Left ventricular ejection fraction.

TABLE E1. Subgroup analysis of postoperative outcomes in only those patients who underwent aortic root replacement due to aneurysmal disease

Outcomes	LVEF <40% (n = 37)	LVEF 40%-49% (n = 55)	LVEF ≥50% (n = 424)	P
In-hospital death	3 (8.1)	2 (3.6)	3 (0.7)	.001
Hospital length of stay, d	10 (7-15)	7 (5-10)	6 (5-8)	<.001
Intensive care unit length of stay, d	4 (2-7)	2 (1-4)	2 (1-3)	<.001
Postoperative complications				
Reoperation for bleeding	6 (16.2)	2 (3.6)	21 (8.7)	.014
Stroke	3 (8.1)	0 (0.0)	11 (2.6)	.060
Respiratory failure	5 (13.5)	2 (3.6)	14 (3.3)	.010
New need for dialysis	3 (8.1)	0 (0.0)	6 (1.4)	.007
Myocardial infarction	0 (0.0)	0 (0.0)	3 (7.1)	.721
Atrial fibrillation	18 (48.6)	19 (34.5)	168 (39.6)	.397
New pacemaker requirement	2 (5.4)	2 (3.6)	22 (5.2)	.880
Aortic reoperation	2 (5.4)	5 (9.1)	21 (4.9)	.444
Need for mechanical circulatory support	2 (5.4)	2 (3.6)	2 (0.5)	.005

Data presented as number (%) or median (interquartile range). *LVEF*, Left ventricular ejection fraction.