Does preoperative hyponatremia potentiate the effects of left ventricular dysfunction on mortality after cardiac surgery?

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Objective: Left ventricular dysfunction and preoperative hyponatremia are associated with adverse outcomes after cardiac surgery. However, the interactions between them are unknown. Thus, we evaluated the interaction of low left ventricular ejection fraction (<40%) and preoperative hyponatremia (Na <135 mEq/L) with morbidity and mortality after cardiac surgery.

Methods: The interaction of hyponatremia and ejection fraction with hospital complications, length of stay, and mortality was analyzed using logistic and Cox regression analysis in 2247 patients who underwent cardiac surgery between 2005 and 2008 at The Ohio State University Wexner Medical Center.

Results: Of the patients, 68.5% had normal ejection fraction. Hyponatremia was present in 18% of patients with normal ejection fraction and 35% of patients with low ejection fraction. Hyponatremic patients had higher rates of New York Heart Association class III and IV, more comorbidities, and higher Society of Thoracic Surgeons score and European System for Cardiac Operative Risk Evaluation irrespectively of their ejection fraction. The correlation between preoperative sodium and ejection fraction was weak ($r^2 = 0.04$). Hyponatremia increased the rate of postoperative complications and hospital stay, and decreased 1- and 3-year survivals in patients with both normal and low ejection fraction. Hyponatremia was independently associated with longer hospital stay for normal ejection fraction (multiplier, 1.18; confidence interval, 1.09-1.27; $P < .001$) and low ejection fraction (multiplier, 1.10; confidence interval, 1.0-1.21; $P = .05$), increased need for dialysis for normal ejection fraction (odds ratio, 2.16; confidence interval, 1.08-4.32; $P = .03$), and increased risk of mortality for normal ejection fraction (hazard ratio, 1.56; confidence interval, 1.20-2.05; $P = .001$), but not for patients with low ejection fraction (hazard ratio, 1.21; confidence interval, 0.89-1.65; $P = .21$).

Conclusions: Hyponatremia is more common in patients with low ejection fraction. Although preoperative hyponatremia is independently associated with adverse outcomes in patients with normal ejection fraction, an association with adverse outcomes in patients with low ejection fraction was not demonstrated. (J Thorac Cardiovasc Surg 2013;145:1589-94)

☞ Supplemental material is available online.

Hyponatremia is a common electrolyte abnormality in critically ill patients and adversely affects outcomes.^{1,2} It is particularly common in patients with congestive heart

failure, in whom its prevalence and severity correlate with the prevalence and severity of heart failure and ventricular dysfunction.³⁻⁵ We previously demonstrated that preoperative hyponatremia is common before cardiac surgery and is an independent risk factor for mortality, prolonged hospitalization, and postoperative complications after cardiac surgery.⁶ Left ventricular (LV) dysfunction is also an independent predictor of poor outcomes after cardiac surgery. It has been associated with increased morbidity and mortality after coronary artery bypass surgery, valve surgery, combined bypass and valve surgery, and other cardiac surgery procedures.⁷⁻¹⁰

The interaction between preoperative hyponatremia and LV dysfunction and its effects on outcomes after cardiac surgery have not been evaluated. We hypothesize that hyponatremia may potentiate the adverse effect of LV dysfunction in outcomes after cardiac surgery. We retrospectively studied 2247 patients undergoing cardiac surgery to determine the prevalence of preoperative hyponatremia in patients with LV dysfunction before cardiac surgery and the interaction between preoperative hyponatremia and LV

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Abbreviations and Acronyms

CABG	= coronary artery bypass grafting
CI	= confidence interval
EF	= ejection fraction
LV	= left ventricular
NYHA	= New York Heart Association
STS	= Society of Thoracic Surgeons

dysfunction on hospital complications and on short- and long-term mortality after cardiac surgery.

MATERIALS AND METHODS

From January 2005 to December 2008, 2785 patients underwent cardiac surgery procedures at The Ohio State University Wexner Medical Center. Preoperative serum sodium and LV ejection fraction (EF) determinations were available in 2247 patients. These patients constitute the study population. Hyponatremia was defined as serum sodium less than 135 mEq/L in any of the 3 most recent daily sodium determinations performed within 30 days before surgery. Systolic LV dysfunction was defined as an LV EF less than 40%. LV EF was assessed by ventriculogram in 63.6% of patients, echocardiogram in 35.5% of patients, and other methods in 0.9% of patients. Patients were divided into 4 groups according to EF and hyponatremia status: (1) low EF (EF <40%) and normonatremia (Na $\geq$ 135 mEq/L) group, (2) low EF (EF <40%) and hyponatremia (Na <135 mEq/L) group, (3) normal EF (EF $\geq$ 40%) and normonatremia (Na $\geq$ 135 mEq/L) group, and (4) normal EF (EF $\geq$ 40%) and hyponatremia (Na <135 mEq/L) group.

Data from the institution electronic medical records, the institution Society of Thoracic Surgeons (STS) database, and the Social Security Death Index were analyzed. Outcomes analyzed included early and late mortality, postoperative length of hospital stay, incidence of STS-defined complications,^{11,12} and need for perioperative blood transfusions. Outcomes definitions are listed in [Appendix E1](#). The Ohio State University Wexner Medical Center Institutional Review Board approved this study and granted waiver of Health Insurance Portability and Accountability Act research authorization.

Statistical Analysis

Baseline characteristics are presented as means, standard deviations, medians, and interquartile ranges for continuous variables. Categorical variables are presented as frequencies. Baseline characteristics were compared using Pearson's chi-square test for categorical variables and Kruskal-Wallis for continuous variables. Regression models were developed using a risk factor modeling approach to determine which covariates were included in the model.^{13,14} Covariates that acted as a confounder or an effect modifier were included ([Appendix E2](#)). Logistic regression was used to find the association between hyponatremia and EF status with STS complications. Logistic regression was used when the outcome was early mortality. Linear regression was used when the outcome was log-transformed hospital length of stay. Cox proportional hazard regression was used to find the association of late and overall mortality with hyponatremia and EF status. Serum sodium was treated as both a continuous and a dichotomous variable. Survival was estimated by the Kaplan-Meier method, and differences in survival were compared using the log-rank test. All analyses were conducted using Stata 11.1 (StataCorp LP, College Station, Tex).

RESULTS

Preoperative hyponatremia was present in 527 patients (23.5%) before cardiac surgery. The distribution of preoperative EF is shown in [Figure E1](#). Low EF was present in 707

patients (31.5%). A total of 282 patients (18.3%) in the normal EF group and 245 patients (34.6%) in the low EF group had preoperative hyponatremia. Hyponatremic and normonatremic patients had clinically similar EF within their EF group ([Table 1](#)). The correlation between preoperative serum sodium and preoperative EF was weak ($r^2 = 0.04$).

Demographics, clinical, and surgical characteristics are shown in [Table 1](#). Compared with those with normal EF, patients with low EF were younger and more often male. They more often had congestive heart failure and a higher prevalence of myocardial infarction, chronic obstructive pulmonary disease, stroke, peripheral vascular disease, diabetes, renal dysfunction, and previous cardiac surgery. These comorbidities resulted in higher predicted risk of mortality as determined by European System for Cardiac Operative Risk Evaluation and STS Predicted Risk of Mortality. Hyponatremic patients had a higher rate of New York Heart Association (NYHA) functional class III and IV, higher rate of previous cardiac surgery, and higher European System for Cardiac Operative Risk Evaluation irrespectively of their EF status.

Isolated coronary artery bypass grafting (CABG) and isolated valve surgery were more common in the normal EF group, and combined CABG-valve, ventricular assist device, and other cardiac surgery procedures were more common in the low EF group. Cardiopulmonary bypass time and cross-clamp times were not clinically different among the groups.

[Table 2](#) shows unadjusted clinical outcomes. The rate of postoperative complications (operative, infectious, pulmonary, renal failure, need for dialysis, and other complications) was higher in the low EF group. Hyponatremia increased the incidence of operative, pulmonary, and renal complications compared with normonatremia in both the normal and low EF groups. Low EF was associated with longer hospital stay. Hyponatremia increased the length of hospital stay in both the normal and low EF groups. Early and late mortality were increased in the low EF group compared with the normal EF group (early mortality: 8.5% vs 3.9% in normal EF, $P < .001$; late mortality: 20.4% vs 13.2% in normal EF, $P < .001$). Hyponatremia further increased early and late mortality in both the normal and low EF groups ([Table 2](#)). Kaplan-Meier survival curves by hyponatremia and EF status are shown in [Figure 1](#). Median follow-up was 1.31 years (interquartile range, 0.2-2.58). Hyponatremia decreased the estimated 1- and 3-year survivals in both the normal EF and low EF groups compared with normonatremia.

[Figure E2](#) shows a univariate analysis of the clinical outcomes. Hyponatremia increased the odds of operative, pulmonary, and renal complications; renal failure requiring dialysis; length of hospital stay; and early mortality in both the low and normal EF cohorts. It also increased the hazard of late and overall mortality in both groups. After adjusting for baseline and procedural variables ([Figure 2](#)),

TABLE 1. Patients' clinical characteristics and operative variables stratified according to preoperative left ventricular ejection fraction and serum sodium

	Low EF N = 707			Normal EF N = 1540			P normal vs low EF
	Na ≥135 mEq/L	Na <135 mEq/L	P Na <135 mEq/L vs Na ≥135	Na ≥135 mEq/L	Na <135 mEq/L	P Na <135 mEq/L vs Na ≥135	
			mEq/L			mEq/L	
N	462	245	—	1258	282	—	—
Mean Na ± SD (mEq/L)	138.5 ± 2.2	133.2 ± 3.0	<.001	138.7 ± 1.8	133.9 ± 2.4	<.001	<.001
Age (y)	61 ± 12	59 ± 12	.004	62 ± 13	63 ± 14	.117	.004
Male gender, N (%)	324 (70.1)	175 (71.4)	.718	825 (65.6)	173 (61.4)	.179	.007
White race, N (%)	383 (82.9)	196 (80.0)	.341	1094 (87.0)	236 (83.7)	.147	.006
LV EF (%; mean ± SD)	26 ± 8	24 ± 9	<.001	53 ± 7	53 ± 8	.067	N/A
Mean PA pressure (mm Hg; mean ± SD)	32.3 ± 10.8	32.8 ± 9.6	.380	27.0 ± 9.5	32.0 ± 13.4	<.001	<.001
GFR (mg/min/1.73 m ²)	69 ± 29	64 ± 29	.094	73 ± 26	74 ± 32	.754	.001
NYHA class III-IV (%)	356 (77.1)	204 (83.4)	.050	689 (54.8)	192 (68.2)	<.001	<.001
Diabetes, N (%)	203 (43.9)	115 (46.9)	.446	423 (33.6)	134 (47.5)	<.001	<.001
Hypertension, N (%)	393 (85.1)	196 (80.0)	.086	1035 (82.3)	249 (88.3)	.014	.968
Renal failure on dialysis, N (%)	57 (12.3)	42 (17.0)	.260	86 (6.8)	30 (10.7)	.150	.002
Previous MI, N (%)	286 (61.9)	152 (62.0)	.972	452 (35.9)	116 (41.1)	.102	<.001
COPD, N (%)	147 (31.8)	99 (40.4)	.022	292 (23.2)	84 (29.7)	.020	<.001
Stroke, N (%)	75 (16.2)	42 (17.2)	.864	157 (12.5)	37 (13.2)	.864	.017
PVD, N (%)	94 (20.4)	58 (23.7)	.367	199 (15.8)	59 (20.9)	.038	.009
Previous cardiac surgery, N (%)	59 (12.8)	47 (19.2)	.023	127 (10.1)	45 (16.0)	.005	.011
euroSCORE, % (IQR)	29 (12-54)	46 (23-71)	<.001	10 (4-27)	19 (6-45)	<.001	<.001
STS PROM, % (IQR)	2.68 (1.17-5.99)	2.95 (1.54-6.66)	.337	1.23 (0.62-2.83)	1.53 (0.69-4.69)	.011	<.001
Surgical characteristics							
CPB time, min ± SD	130 ± 53	125 ± 67	.128	117 ± 57	126.0 ± 64	.134	<.001
Crossclamp time, min ± SD	98 ± 39	95 ± 45	.307	91 ± 43	96 ± 49	.485	.001
CABG only, N (%)	179 (38.7)	65 (26.5)	.001	629 (50.0)	130 (46.1)	.236	<.001
Valve surgery only, N (%)	52 (11.3)	23 (9.4)	.443	182 (14.5)	46 (16.3)	.431	.007
CABG valve, N (%)	100 (21.6)	33 (13.5)	.008	125 (9.9)	42 (14.9)	.016	<.001
VAD surgery only, N (%)	11 (2.4)	29 (11.8)	<.001	2 (0.2)	0 (0)	.503	<.001
Other surgery, N (%)	120 (26)	22 (9.0)	<.001	320 (25.4)	64 (22.7)	.33	.013

EF, Ejection fraction; SD, standard deviation; LV, left ventricular; PA, pulmonary artery; GFR, glomerular filtration rate; NYHA, New York Heart Association; MI, myocardial infarction; COPD, chronic obstructive pulmonary disease; PVD, peripheral vascular disease; euroSCORE, European System for Cardiac Operative Risk Evaluation; IQR, inter-quartile range; STS PROM, Society of Thoracic Surgeons Predicted Risk of Mortality; CPB, cardiopulmonary bypass; CABG, coronary artery bypass grafting; VAD, ventricular assist device; N/A, not available.

hyponatremia was associated with increased length of hospital stay for normal EF (multiplier, 1.18; confidence interval [CI], 1.09-1.27; $P < .001$) and low EF (multiplier, 1.10; CI, 1.00-1.21; $P = .05$) cohorts. The odds of dialysis (odds ratio, 2.16; CI, 1.08-4.32; $P = .03$) and early mortality (odds ratio, 1.93; CI, 1.00-3.69; $P = .047$), and the hazard of late (hazard ratio, 1.54; CI, 1.13-2.11; $P = .008$) and overall mortality (hazard ratio, 1.56; CI, 1.20-2.05; $P = .01$) were increased by hyponatremia for patients with normal EF. After adjusting for baseline and operative variables, hyponatremia did not increase early, late, or overall mortality in the low EF cohort.

Figure 3 displays the adjusted overall mortality in function of serum sodium as a continuous variable for low and normal EF cohorts. The adjusted mortality rate increases

with the severity of preoperative hyponatremia in those with normal EF but not in those with low EF.

DISCUSSION

This study demonstrated that (1) preoperative hyponatremia is approximately twice as frequent in patients with low EF than in patients with normal EF, (2) there is not a strong direct correlation between EF and preoperative serum sodium, (3) preoperative hyponatremia increases the unadjusted rate of postoperative complications and mortality and decreases long-term survival for patients with normal EF and patients with low EF, and (4) preoperative hyponatremia increases the hazard of mortality for patients with normal EF. However, preoperative hyponatremia was not

TABLE 2. Unadjusted clinical outcomes stratified by preoperative left ventricular ejection fraction and serum sodium

	Low EF N = 707			Normal EF N = 1540			P normal vs low EF
	Na $\geq$ 135 mEq/L	Na <135 mEq/L	P Na <135 mEq/L vs Na $\geq$ 135 mEq/L	Na $\geq$ 135 mEq/L	Na <135 mEq/L	P Na <135 mEq/L vs Na $\geq$ 135 mEq/L	
N	462	245	—	1258	282	—	—
Complications							
Operative, N (%)	57 (12.3)	55 (22.5)	<.001	103 (8.2)	35 (12.4)	.0250	<.001
Infectious, N (%)	32 (6.9)	20 (8.2)	.549	36 (2.9)	17 (6.0)	.0110	<.001
Pulmonary, N (%)	138 (29.9)	117 (47.8)	<.001	283 (22.5)	92 (32.6)	<.001	<.001
Neurologic, N (%)	12 (2.6)	11 (4.5)	.177	34 (2.7)	8 (2.8)	.9000	.49
Renal failure, N (%)	39 (8.4)	37 (15.1)	.007	73 (5.8)	39 (13.8)	<.001	.006
Dialysis, N (%)	24 (5.2)	24 (9.8)	.021	39 (3.1)	25 (8.9)	<.001	.008
Other, N (%)	134 (29.0)	72 (29.4)	.915	328 (26.1)	90 (31.9)	.0460	.327
Blood transfusion	219 (47.5)	142 (57.9)	.009	513 (40.8)	162 (57.5)	<.001	.002
Hospital LOS, d (IQR)	11.5 (7.61-17.9)	18.2 (10.9-12.8)	<.001	8.28 (6.12-12.8)	11.6 (7.72-19.0)	<.001	<.001
Mortality							
Early mortality, N (%)	30 (6.5)	30 (12.2)	.009	40 (3.2)	20 (7.1)	.0020	<.001
Late mortality, N (%)	84 (18.2)	60 (24.5)	.047	146 (11.6)	57 (20.2)	<.001	<.001

Early mortality: any death during the hospitalization for surgery or after discharge from the hospital, but within 30 days of the procedure. Late mortality: any death after discharge from the hospital and more than 30 days from the operative procedure. For definitions of complications see [Appendix E1](#). EF, Ejection fraction; LOS, length of stay; IQR, interquartile range.

independently associated with an increased hazard of mortality in those with low EF.

Hyponatremia is common in patients with heart failure and patients with LV dysfunction.³⁻⁵ The prevalence of hyponatremia in heart failure ranges from 5% in outpatients to 27% in hospitalized patients.^{1,3-5} The present study reported for the first time the prevalence of preoperative hyponatremia in patients with normal and decreased LV function in need of cardiac surgery. The overall prevalence was similar to that of patients hospitalized with heart failure.^{4,15} However, the

prevalence of hyponatremia in patients with low EF was twice as high as that in patients with normal EF. The high prevalence of preoperative hyponatremia in patients with LV dysfunction waiting for cardiac surgery reflects a more advanced stage of cardiac disease and higher prevalence of associated comorbidities ([Table 1](#)).

Previous studies have demonstrated that hyponatremia is a marker of disease severity in congestive heart failure with and without depressed LV EF.^{1,3,5,16} The current study did not find a strong correlation between serum sodium and LV EF. In addition, EF was similar in patients with and

FIGURE 1. Kaplan-Meier survival curve stratified according to preoperative sodium level and EF. Hyponatremia decreased 1- and 3-year unadjusted survivals for both the low and normal EF cohorts (log-rank $P < .001$). One-year survival for the low EF cohort was 82% (95% CI, 78-86) for Na $\geq$ 135 mEq/L or greater versus 70% (95% CI, 63-75) for Na less than 135 mEq/L. One-year survival for the normal EF cohort was 88% (95% CI, 86-90) for Na $\geq$ 135 mEq/L or greater versus 79% (95% CI, 74-84) for Na less than 135 mEq/L. Three-year survival for the low EF cohort was 64% (95% CI, 58-70) for Na $\geq$ 135 mEq/L or greater versus 56% (95% CI, 48-63) for Na less than 135 mEq/L. Three-year survival for the normal EF cohort was 77% (95% CI, 74-80) for Na $\geq$ 135 mEq/L or greater versus 62% (95% CI, 55-69) for Na less than 135 mEq/L. EF, Ejection fraction; CI, confidence interval.

FIGURE 2. Effect of hyponatremia on clinical outcomes of patients with low and normal ejection fractions by multivariable regression analysis. See Appendix E2 for covariates included in the analysis. EF, Ejection fraction; OR, odds ratio; CI, confidence interval; HR, hazard ratio.

without hyponatremia within each cohort of the current study. These findings are not surprising because the most critical factors in the development of hyponatremia in heart failure is the reduction in cardiac output and the degree of neurohormonal activation.¹⁷ Many patients with decreased EF are capable of maintaining cardiac output secondary to a compensatory increase in LV end-diastolic volume.¹⁸ This study quantified heart failure severity by evaluating NYHA class. Compared with normonatremia, hyponatremic patients had a higher prevalence of NYHA class III and IV symptoms regardless of their EF. Therefore, preoperative hyponatremia correlates more with the overall severity of heart failure than with EF alone.

Hyponatremia has been associated with adverse outcomes in multiple clinical settings.¹⁻⁶ However, the value of preoperative hyponatremia to predict outcomes in patients undergoing cardiac surgery has not been established. Conversely, LV dysfunction is a well-established risk factor associated with adverse outcomes after cardiac surgery procedures.⁷⁻¹⁰ LV dysfunction has been associated with increased risk of early and late mortality after CABG, aortic and mitral valve surgery, and combined valve CABG.⁷⁻¹⁰ The present study demonstrated increased early and late mortality in a large group of patients with low LV EF undergoing a variety of cardiac surgery procedures that are representative of the surgical practice in this country. We expected that the coexistence of preoperative hyponatremia with LV dysfunction may accentuate the adverse effects of LV dysfunction on outcomes. In the OPTIMIZE-HF registry, which included 47,000 patients hospitalized with heart failure, the combination of hyponatremia and LV dysfunction increased the unadjusted rates of in

hospital mortality, length of hospital stay, rehospitalization for heart failure, and long-term mortality compared with hyponatremia alone.³ In addition, hyponatremia was independently associated with an increased risk of mortality in patients with normal EF and patients with low EF. In the present study, preoperative hyponatremia was associated by univariate analysis with postoperative complications, length of hospital stay, and early and late mortality in both low and normal EF cohorts. However, hyponatremia was only independently associated with adverse outcomes in patients with preserved LV systolic function. The failure to observe an independent effect on mortality in patients with low EF is puzzling and led to the generation of 2 hypotheses to explain this finding: (1) The interaction of the therapeutic intervention (cardiac surgery) in outcomes may disrupt that association. Contrary to patients with congestive heart failure treated medically, cardiac surgery procedures may correct or ameliorate heart failure and disrupt the independent effect of hyponatremia in outcomes. (2) Hyponatremia might behave as a marker of disease severity and neurohormonal activation in low EF, whereas in patients with normal EF, it has an independent and direct deleterious effect on myocardial function that predisposes those patients to poor outcomes after surgery. Elucidation of these hypotheses will require additional studies specifically designed to address them.

Study Limitations

First, this was a single-center retrospective study, and the results should be interpreted within such context. Second, despite the overall large population included in the study, there were only 245 patients (10.9%) with hyponatremia and low EF. Third, the preoperative EF was determined by a variety of

FIGURE 3. Association between preoperative serum sodium and adjusted overall mortality for patients with low EF (A) and normal EF (B). The adjusted mortality rate increases with the severity of preoperative hyponatremia in the normal EF cohort (B) but not in the low EF cohort (A). Dashed lines represent 95% CI. See Appendix E2 for covariates included in the model. EF, Ejection fraction; CI, confidence interval.

methods (echocardiogram, ventriculogram, and others) during standard clinical care, which may have resulted in considerable variability in EF measurements. Fourth, low EF was defined as an EF less than 40%. Therefore, patients with moderate and severe LV dysfunction were included in the low EF group. It is possible that preoperative hyponatremia may have different effects on outcomes in those groups. Fifth, serum sodium levels were not adjusted for glucose levels. Hyperglycemia leads to hyponatremia by mechanisms different than those responsible for hyponatremia in heart failure. It is unknown whether hyponatremia secondary to hyperglycemia has any adverse effects on outcomes.¹⁹

CONCLUSIONS

Preoperative hyponatremia is common in patients undergoing cardiac surgery. Eighteen percent of patients with

normal EF and 35% of patients with low EF have preoperative hyponatremia. Although hyponatremia is independently associated with adverse outcomes in patients with normal EF, this study failed to demonstrate an association with adverse outcomes in patients with low EF. Despite this lack of association, preoperative hyponatremia should be addressed before surgery regardless of the patient's EF. Further studies are necessary to elucidate the reasons for this unexpected response to hyponatremia in patients with low EF.

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APPENDIX E1. OUTCOMES DEFINITIONS

Early mortality was defined as any death that occurred during the hospitalization in which the operation was performed or after discharge from the hospital, but within 30 days of the procedure.

Late mortality included any death that occurred both after discharge from the hospital and more than 30 days from the operative procedure.

Complications Defined by the Society of Thoracic Surgeons

Operative complications included (a) perioperative myocardial infarction; (b) reoperation for bleeding, cardiac tamponade, native or prosthetic valve dysfunction, and graft occlusion; (c) other cardiac reoperations; and (d) noncardiac reoperations.

Pulmonary complications included (a) reintubation during hospital stay, (b) ventilatory support for more than 24 hours after surgery, (c) pulmonary embolism, and (d) pneumonia.

Infectious complications included (a) wound infections (sternal, thoracotomy, leg, and arm incisions) and (b) sepsis.

Neurologic complications included (a) stroke, (b) transient ischemic attack, (c) comma, and (d) paralysis or paraplegia.

Renal complications included renal failure defined as a postoperative serum creatinine greater than 2 mg/dL, or twice the preoperative creatinine level, or the need for renal replacement therapy.

Other complications included (a) cardiac arrest, (b) tamponade, (c) multisystem organ failure, and (d) atrial fibrillation.

APPENDIX E2. COVARIATES INCLUDED IN MULTIVARIABLE REGRESSION ANALYSIS MODELS

1. Logistic operative complication model: European System for Cardiac Operative Risk Evaluation (euroSCORE), inotropic medications, previous cardiac surgery, cardiogenic shock, coronary artery bypass grafting (CABG), valve surgery, stroke, surgery status (elective, emergency, or urgent), glomerular filtration rate (GFR), and New York Heart Association (NYHA) class.
2. Logistic infectious complication model: euroSCORE, inotropic medications, cardiogenic shock, intra-aortic balloon pump (IABP), arrhythmia, CABG, valve surgery, other cardiac surgery, stroke, previous myocardial infarction (MI), surgery status (elective, emergency, or urgent), GFR, and NYHA classification.
3. Logistic pulmonary complication model: euroSCORE, inotropic medications, IABP, arrhythmia, cardiogenic shock, CABG, valve, ventricular assist device (VAD), stroke, chronic obstructive pulmonary disease (COPD), surgery status (elective, emergency, or urgent), GFR, and NYHA class.
4. Logistic neurologic complication model: euroSCORE, patient age, gender, previous cardiac surgery, inotropic medications, IABP, diabetes, cardiogenic shock, arrhythmia, CABG, valve surgery, VAD surgery, other cardiac surgery, stroke, peripheral vascular disease (PVD), previous MI, hypertension, surgery status (elective, emergency, or urgent), GFR, and NYHA class.
5. Logistic renal failure requiring dialysis model: euroSCORE, previous cardiac surgery, inotropic medications, cardiogenic shock, arrhythmia, CABG, valve surgery, VAD surgery, stroke, previous MI, surgery status (elective, emergency, or urgent), GFR, and NYHA class.
6. Logistic other complication model: euroSCORE, patient age, gender, previous cardiac surgery, inotropic medication, IABP, diabetes, cardiogenic shock, arrhythmia, CABG, valve surgery, VAD surgery, stroke, PVD, previous MI, COPD, surgery status (elective, emergency, or urgent), prior GFR, and NYHA class.
7. Linear length of hospital stay model: euroSCORE, inotropic medications, cardiogenic shock, arrhythmia, CABG, valve surgery, VAD surgery, stroke, surgery status (elective, emergency, or urgent), GFR, and NYHA class.
8. Logistic early mortality model: patient age, GFR, euroSCORE, preoperative inotropic medications, VAD surgery, other cardiac surgery, cardiogenic shock, and NYHA class.
9. Cox proportional hazard late mortality model: patient age, GFR, euroSCORE, preoperative inotropic medications, VAD surgery, other cardiac surgery, cardiogenic shock, and NYHA classification.
10. Cox proportional hazard overall mortality model: patient age, GFR, euroSCORE, preoperative inotropic medications, VAD surgery, cardiogenic shock, and surgery status (elective, emergency, or urgent).

FIGURE E1. Distribution of preoperative LV EF. Low EF was present in 707 patients (31.5%). A total of 550 patients (24.5%) had moderate reduction of EF (EF, 20%-39%). A total of 157 patients (7.0%) had severe reduction of EF (<20%). *LV*, Left ventricular; *EF*, ejection fraction.

FIGURE E2. Effect of hyponatremia on clinical outcomes of patients with low and normal ejection fractions by univariate analysis. *EF*, Ejection fraction; *OR*, odds ratio; *CI*, confidence interval; *HR*, hazard ratio.