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

Juan A. Crestanello, MD,[a] Gary Phillips, MAS,[b] Michael S. Firstenberg, MD,[a] Chittoor Sai-Sudhakar, MBBS,[a] John Sirak, MD,[a] Robert Higgins, MD,[a] and William T. Abraham, MD[c]

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

From the Division of Cardiac Surgery,[a] Center for Biostatistics,[b] and Division of Cardiovascular Medicine,[c] The Ohio State University, Wexner Medical Center, Columbus, Ohio.

This work was supported by a research grant from Biogen Idec (Weston, Mass).

Disclosures: Dr Crestanello received a research grant from Biogen Idec, and Dr Abraham received a research grant and consulting fees from Biogen Idec. All other authors have nothing to disclose with regard to commercial support.

Presented at the American Heart Association 2011 Scientific Sessions, Orlando, Florida, November 12-16, 2011.

Received for publication Feb 28, 2012; revisions received Nov 15, 2012; accepted for publication Dec 10, 2012; available ahead of print April 8, 2013.

Address for reprints: Juan A. Crestanello, MD, N-816 Doan Hall, 410 West 10th Ave, Columbus, OH 43210 (E-mail: juan.crestanello@osumc.edu).

0022-5223/$36.00

http://dx.doi.org/10.1016/j.jtcvs.2012.12.093

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 ≥135 mEq/L) group, (2) low EF (EF <40%) and hyponatremia (Na <135 mEq/L) group, (3) normal EF (EF ≥40%) and normonatremia (Na ≥135 mEq/L) group, and (4) normal EF (EF ≥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. Categoric variables are presented as frequencies. Baseline characteristics were compared using Pearson's chi-square test for categoric 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),