Low serum sodium level during cardiopulmonary bypass predicts increased risk of postoperative stroke after coronary artery bypass graft surgery

Elizandro Munoz III, MD,[a] Holly Briggs, BS,[b] Daniel A. Tolpin, MD,[c] Vei-Vei Lee, MS,[d] Terry Crane, BS,[e] MacArthur A. Elayda, MD, PhD,[d] Charles D. Collard, MD,[c] and Wei Pan, MD[c]

Objective: Rapid decreases in serum sodium levels are associated with altered mental status, seizures, and coma. During cardiac surgery, serum sodium levels decrease rapidly when cardiopulmonary bypass is initiated because cardiopulmonary bypass causes hemodilution. However, whether this decrease influences neurologic outcome after cardiac surgery remains unclear. We investigated whether the average serum sodium level during cardiopulmonary bypass is independently predictive of postoperative stroke or 30-day all-cause mortality in patients who undergo primary coronary artery bypass grafting.

Methods: In a single-institution, retrospective cohort of 2348 consecutive patients who underwent primary, isolated coronary artery bypass grafting, sequential multivariate logistic regression was performed to determine the threshold below which the average serum sodium level during cardiopulmonary bypass independently predicts postoperative stroke or early death. To further test the validity of this threshold and to control for selection bias, stepwise multivariate logistic regression was also performed on propensity score–matched patients (n = 924).

Results: An average serum sodium level less than 130 mEq/L during cardiopulmonary bypass was independently predictive of stroke, both in the entire study cohort (1.44% vs 2.92%; odds ratio, 2.09; 95% confidence interval, 1.1-4.1; $P = .03$) and in the propensity-matched patients (0.9% vs 3.0%; odds ratio, 4.1; 95% confidence interval, 1.3-13.0; $P = .02$). The average serum sodium level during cardiopulmonary bypass was not independently associated with early death, regardless of what threshold value was used.

Conclusions: An average serum sodium level of less than 130 mEq/L during cardiopulmonary bypass is independently associated with an increased risk of postoperative stroke in patients who undergo primary coronary artery bypass grafting. (J Thorac Cardiovasc Surg 2014;147:1351-5)

The incidence of postoperative stroke after coronary artery bypass grafting (CABG) is between 1% and 3%. This complication is associated with significant morbidity and mortality, as well as increased treatment costs.[1-4] Although the cause of neurologic insult after CABG is probably multifactorial, current theories principally attribute it to 3 mechanisms: cerebral emboli (eg, aortic manipulation), hypoperfusion during cardiopulmonary bypass (CPB), and increases in metabolic demand in neural tissue already exposed to relative ischemia.[5-10] In the present study, we hypothesized that an abrupt decrease in sodium levels during CPB may also contribute to the risk of postoperative stroke after CABG.

Rapid decreases in serum sodium levels have been associated with altered mental status, seizures, and coma in nonsurgical patients.[11,12] Likewise, sudden rapid decreases in serum sodium levels may occur secondary to hemodilution when CPB is initiated during cardiac surgery.[13] Warwick and colleagues[13] showed that the degree of change in serum sodium level is linearly related to the size of the patient, the preoperative hemoglobin level, and the circuit prime volume. However, the influence of serum sodium level during CPB on neurologic outcome after cardiac surgery remains unclear. The aim of this study was to investigate whether the average serum sodium level during CPB is independently associated with an increased risk of postoperative stroke or early (30-day all-cause) mortality in patients who undergo primary CABG.

MATERIALS AND METHODS

Patients

After institutional review board approval was obtained, a retrospective cohort study was performed on all patients (N = 2348) who underwent primary, isolated CABG with CPB between January 2004 and December 2007 at the Texas Heart Institute at St Luke's Episcopal Hospital (Houston, Tex).

From the Department of Anesthesiology[a] and the Medical School,[b] Baylor College of Medicine, Houston, Tex; the Divisions of Cardiovascular Anesthesiology[c] and Biostatistics and Epidemiology,[d] Texas Heart Institute, Houston, Tex; and the School of Perfusion Technology,[e] Texas Heart Institute, Houston, Tex.

All support was provided solely by institutional or departmental sources.

Disclosures: Authors have nothing to disclose with regard to commercial support.

Received for publication March 25, 2013; revisions received Aug 29, 2013; accepted for publication Sept 17, 2013; available ahead of print Nov 4, 2013.

Address for reprints: Wei Pan, MD, Division of Cardiovascular Anesthesiology, Texas Heart Institute, 6720 Bertner Ave, Room 0520, Houston, TX 77030 (E-mail: wpan@texasheart.org).

0022-5223/$36.00

http://dx.doi.org/10.1016/j.jtcvs.2013.09.034

PM

Abbreviations and Acronyms
CABG = coronary artery bypass grafting
CI = confidence interval
CPB = cardiopulmonary bypass
OR = odds ratio

Preoperative variables of interest included patient demographics, medical history, preoperative medications, and risk factors.

Data Measurement and Outcome Variables

The CPB machine prime consisted of 1200 to 1400 mL of lactated Ringer's solution with mannitol (25 g). For each patient, the serum sodium level was measured at 15-minute intervals during CPB. The average serum sodium level during CPB was then calculated for each patient.

The incidence of postoperative stroke and early death was abstracted from the Texas Heart Institute cardiac surgical database. A diagnosis of stroke was made if there was clinical evidence of a new focal or global deficit that was confirmed by computed tomography or magnetic resonance imaging. Early death was defined as documented death within 30 days of surgery.

Statistics

All statistical analyses were performed with SAS statistical software (v 9.1, SAS Institute, Inc, Cary, NC) by the Division of Biostatistics and Epidemiology at the Texas Heart Institute. Categoric (frequency) variables were expressed as percentages, and continuous variables were expressed as the mean ± standard deviation. Preoperative demographic variables and risk factors were compared between groups by using univariate (chi-square) analysis for categoric data and multivariate linear regression analysis for continuous numeric data. To determine the threshold at which the average sodium level during CPB independently predicts stroke or early death, sequential multivariable logistic regression analyses were performed in which the threshold for average sodium level was adjusted by 5-mEq/L increments over a range 125 to 145 mEq/L. Odds ratios (ORs) and 95% confidence intervals (CIs) are reported.

To control for selection bias, patients were divided into 2 groups according to whether their serum sodium level was above or below the threshold identified in the serial logistic regression analyses. Then, using data from 27 variables (Table 1), we calculated propensity scores for each patient and matched patients 1:1 between the 2 groups.

RESULTS

A total of 2348 patients were enrolled. Of these, 137 were not included in the analysis because they had missing data in 1 or more of the 45 required perioperative variables. The average sodium level during CPB was then determined for each of the remaining 2211 patients. The distribution of patients by average sodium level during CPB is shown in Figure 1. Sequential multivariable logistic regression analyses were then performed to determine the threshold at which the average sodium level during CPB was independently associated with an increased risk of stroke or early death.

Postoperative stroke occurred in 39 patients (1.9%), and early death occurred in 44 patients (2.0%). An average sodium level less than 130 mEq/L during CPB was independently associated with an increased risk of postoperative stroke (2.92% vs 1.44%; OR, 2.1; 95% CI, 1.1-4.1; $P = .03$). Fourteen of the 480 patients (2.92%) with an average sodium level less than 130 mEq/L during CPB had a postoperative stroke evidenced by computed tomography or magnetic resonance imaging, whereas 25 of the 1731 patients (1.44%) with an average sodium level 130 mEq/L or greater during CPB had such a stroke. Other average sodium levels during CPB were not associated with increased risk of postoperative stroke (Figure 2). In contrast, the average serum sodium level during CPB was not independently associated with early death at any threshold. Of the 14 patients with an average sodium level during CPB less than 130 mEq/L who had a stroke, 10 manifested neurologic deficits within 2 days of surgery, and 2 had early mortality. Other independent predictors of postoperative stroke included age greater than 65 years (OR, 2.8; 95% CI, 1.3-6.0; $P = .01$) and a history of peripheral vascular disease (OR, 3.7; 95% CI, 1.9-7.1; $P < .001$).

To further control for selection bias, stepwise multivariate logistic regression was performed on the propensity score–matched patients (n = 924; Table 1) who were grouped by whether their average sodium level during CPB was above or below the threshold value of 130 mEq/L. There were no significant differences between groups (ie, <130 vs ≥130 mEq/L) with respect to any variable. Moreover, the preoperative serum sodium level before CPB did not significantly differ between groups (141 ± 2.4 mEq/L in Na <130 vs 138 ± 2.8 mEq/L in Na ≥130). After propensity matching, an average serum level less than 130 mEq/L during CPB was still independently associated with an increased risk of postoperative stroke compared with an average sodium level of 130 mEq/L or greater (0.9% vs 3.0%; OR, 4.1; 95% CI, 1.3-13.0; $P = .02$; Figure 3).

DISCUSSION

Previous studies have shown that intraoperative aortic manipulation and hypoperfusion during CPB are associated with increased risk of postoperative stroke after cardiac surgery.[5-8] Our results suggest that an average sodium level during CPB less than 130 mEq/L is also an independent risk factor for postoperative stroke, indicating a greater than 2-fold increase in risk. This was true both in our complete patient cohort and in our propensity-matched subgroups. These data suggest a potential novel mechanism for postoperative stroke after cardiac surgery.

There are several potential mechanisms by which hyponatremia may be associated with postoperative stroke. First, central nervous system osmotic swelling may result from an acute decrease in serum sodium levels during CPB. Acute swelling may disrupt the myelin sheath and cause neuronal rupture.[14] Second, acute swelling may also result in increased intracranial pressure and decreased cerebral perfusion pressure.[14-16] Kvalheim and colleagues[16] noted a net fluid gain of 116 mL/kg and an increase in intracranial

PM