



# Association of Perioperative Serum Sodium Level Fluctuation and Postoperative Complications in Coronary Artery Bypass Graft Surgery

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## Abstract

**Background:** Electrolyte abnormalities are common in coronary artery bypass graft surgery (CABG) using cardiopulmonary bypass (CPB). Changes in serum sodium (Na) concentration more than 15 meq/L in perioperative period ( $\Delta Na > 15$ ) is considered as significant fluctuation. The aim of this study was evaluating the relationship between the significant fluctuation of serum Na level and the complications after coronary artery bypass graft surgery.

**Methods:** In this prospective observational study 59 patients who were candidates for CABG with CPB were enrolled into the study. We recorded patients' demographic data, arterial blood gas analysis (ABG), serum electrolytes including Na levels from anesthesia induction, during and after CPB up to 24 hours after admission in ICU. Postoperative complications until discharge from ICU were compared between patients with significant Na fluctuation and those without it.

**Results:** Thirty-nine patients had serum sodium fluctuation equal and more than 15 mEq/L ( $\Delta Na \geq 15$  group). This group was compared with those who had minor Na variation ( $\Delta Na < 15$ ;  $n = 20$ ). The  $\Delta Na > 15$  mEq/L fluctuation group had higher serum Na and lactate levels, lower base excess in ABG. Patients with at least one postoperative complication, were older and had lower ejection fraction and more sodium fluctuations. Logistic regression analysis showed that serum sodium fluctuation more than 15mEq/L was independently associated with post CABG complications.

**Conclusions:** Perioperative serum sodium fluctuation more than 15mEq/L was independently associated with postoperative complications in patients undergoing CABG.

**Keywords:** Serum Sodium Level, Complications, Coronary Artery Bypass Surgery

## 1. Background

Approximately 63% of the coronary artery bypass graft (CABG) surgeries are carried out on cardiopulmonary bypass (CPB), whereas 27% are CPB free (1). CPB has many advantages, however it could be accompanied by complications like electrolyte and acid-base imbalance, atelectasis, hemolysis, thromboembolism and reduced lung capacity. Cardioplegic solutions and induced hypothermia cause imbalance in the metabolism of serum potassium and PH levels (2). Surgery stress increases catecholamine release thus resulting in antidiuretic hormone (ADH) inducing imbalance in electrolyte and fluids (3). Dilution of the volume in circulation as a result of the volume suctioned from the surgery field and the fluid loss replaced

by crystalloids and colloids all cause hemostatic and electrolyte imbalance (4). One of the important electrolytes in this field is sodium. Sodium is an important electrolyte in blood pressure maintenance in normal ranges and also the proper function of nerves in muscles (5-8).

Moreover sodium plays a crucial role in hemostats and maintaining the physiology of cardiac muscle cells (7, 9). During CPB hypernatremia and hyponatremia with more than 5 meq/L fluctuations may cause complications for patients (10-15). Fluctuations in serum sodium levels are common in patients with heart disease, moreover hyponatremia has been reported as an independent risk factor for morbidity and mortality after cardiac surgery (7). Hyponatremia is induced because of hemodilution during CPB, serums and vasopressors which are applied (15).

Previous studies have shown the influence of hyponatremia on neuron dysfunction after CABG like stroke, encephalopathy and cognitive dysfunction (9). Renal failure and use of mannitol can cause hypernatremia which increases cellular permeability and causes edema (2). Difference in sodium levels is a strong predictor for mortality in patients hospitalized and increase in sodium levels after discharge has been more associated with survival compared to hyponatremia. Fluctuations in sodium levels more than 12 meq/L have been reported to be associated with mortality in ICU (15). Reports have shown that fluctuations more than 15 meq/L have been associated with seizure postoperatively (16).

In previous studies lower levels of sodium have been shown to be associated with nervous complications, however the influence of sodium level fluctuations after CABG and CPB is still not evaluated clearly. The aim of this study was to investigate whether “high serum sodium level variation” during and after CABG is associated with increased postoperative complications.

## 2. Methods

In this prospective observational study 59 adult patients with American society of anesthesiologists (ASA) physical status class II-III undergoing on pump CABG were enrolled. All participants were scheduled for a first time surgery, with cardiopulmonary bypass with no other concomitant surgery such as valve replacement. Patients received detailed information about the surgery and provided written informed consent. The study was approved by the local ethic committee.

Demographic data and intraoperative variables were recorded for all patients. Laboratory data are measured during and after surgery and for the period of ICU stay. Information such as anesthetic drugs and administered solutions, transfusion of blood, diuresis and filtration volume, time of aortic cross clamp, CPB and surgery time, arterial blood gas (ABG), possible complications during and 24 hours after surgery were recorded for all patients. In postoperative period the amount of chest tube drainage, diuresis, ventilation time, minor and major complications (cardiac, renal, respiratory, hepatic neurologic and hematologic) were also documented for all patients.

ABG analyses was done by Techno Medica 602 and 603 apparatus. In this method after the parameters was received from the device they were compared with the guideline book which was considered true if it matched the normal ranges.

All patients underwent on pump CABG and body temperature was kept 30 - 32°C. All patients received 300 U/kg heparin intravenously to prevent clot formation, and if

needed more for keeping the activated clotting time more than 400 seconds. Alpha stat was used to keep acid and base balance. During CPB, hemofiltration was used if needed. Protamine sulfate 1 mg per 100 U used heparin was used for heparin reversal at the end of the CPB and if ACT was abnormal additional doses were used.

The prime solution consisted of 1000 - 500 mL of lactates ringer solution. Also 100 U/kg of heparin was added to the prime. After cardiac arrest, cardioplegic solution in cold crystalloid with 1:1 ratio was administered with a 20 minute interval. All patients received tri-nitroglycerin (TNG) infusion with the dose of 50 - 200  $\mu$ g/h during surgery and ICU stay. Patients Na levels were recorded from the beginning of operation until 24 hours after ICU admission. Maximum and minimum values of the patients' sodium subtracted each other to calculate Delta Na levels (maximum fluctuation). The patients experienced equal or more than 15 meq/L Na fluctuation considered as “ $15 \geq \Delta$  Na Group” and those with fluctuation of serum sodium levels less than 15 meq/L were regarded as “ $15 < \Delta$  Na Group”. All demographic and clinical data and postoperative complications were compared between these two groups.

Statistical analysis was performed with statistical package for social sciences (SPSS) version 22.0 (SPSS Inc., Chicago, IL, USA). Mann-Whitney U-test was served to compare differences in non-parametric data and independent t test evaluated differences in fluctuations between groups. Chi-square test was used to compare categorical parameters between the two groups. P value  $\leq 0.05$  was considered statistically significant.

## 3. Results

Demographic data, Intra-operative and ICU stay information is shown in Table 1, which did not reveal any significant differences between the groups. Additionally, the drugs and solutions administered for participants were compared between groups which did not show any significant differences either (Table 2).

Minor and major complications (neurologic, renal, respiratory, infection and ...) were also compared and did not represent any significant differences (Table 3; P value  $\geq 0.05$ ). Table 4 shows demographic data between patients with complications and without any complications. Intra-operative and ICU stay data were also compared within participants which encountered major complications and those who did not. ICU stay in patients with complications was significantly different (P = 0.003) compared to their counterparts. Although patients did not differ between those with complications and those not, occurrence of at least one major complication showed significant differences among groups. Table 5 shows logistic regression

**Table 1.** Comparison of Demographic, Intraoperative and ICU Values Between the Groups

	15 $\geq$ $\Delta$ Na (n = 20)	15 < $\Delta$ Na (n = 39)	P Value
<b>Gender</b>			
Male	17 (85)	25 (64.1)	0.169
Female	3 (15)	14 (35.9)	
<b>Age, y</b>	60.8 $\pm$ 8.4	63.8 $\pm$ 10	0.264
<b>Body surface area, m<sup>2</sup></b>	1.91 $\pm$ 0.22	1.8 $\pm$ 0.19	0.073
<b>Ejection fraction, %</b>	47.5 $\pm$ 25	45 $\pm$ 10	0.570
<b>Hypertension</b>	13 (65)	18 (46.2)	0.273
<b>Hyperlipidemia</b>	9 (45)	14 (36)	0.692
<b>Diabetes</b>	11 (55)	17 (43.6)	0.579
<b>Thyroid disorders</b>	2 (10)	3 (7.7)	1.000
<b>Myocardial infarction</b>	4 (20)	7 (17.9)	1.000
<b>Addiction</b>	4 (20)	2 (5.1)	0.166
<b>Smoking</b>	4 (20)	8 (20.5)	1.000
<b>Family history of cardiac disease</b>	4 (20)	9 (23.1)	1.000
<b>Aortic clamping, min</b>	41.2 $\pm$ 17.6	35.9 $\pm$ 12.1	0.238
<b>CPB time, min</b>	75.3 $\pm$ 30.2	72.7 $\pm$ 17.7	0.725
<b>Operation time, h</b>	5 $\pm$ 2	4.5 $\pm$ 1	0.076
<b>mechanical ventilation, h</b>	9/5 $\pm$ 6	10 $\pm$ 3	0.785
<b>ICU stay, h</b>	48 $\pm$ 24	48 $\pm$ 25	0.546

for values related to postoperative complications. High sodium level fluctuations were independently related to the occurrence of postoperative complication.

#### 4. Discussion

In this research we evaluated the effect of preoperative serum sodium fluctuation and post-operative CABG complications under CPB. For this purpose the relation between demographic variables, comorbid disease and serum sodium fluctuation was evaluated with postoperative complications. Our study suggests that age, sex, BSA, EF and cardiac risk factors did not have any significant differences between groups. Previous studies are in concordance with our study however some provide information with correlation between serum sodium levels and EF (6, 16). In the present study, the two studied groups revealed no significant differences between intraoperative values

**Table 2.** Comparison of Intraoperative and Postoperative Drugs Received Between Groups<sup>a</sup>

	15 $\geq$ $\Delta$ Na (n = 20)	15 < $\Delta$ Na (n = 39)	P Value
<b>Ringers' solution received in OR, mL</b>	4030 $\pm$ 1592	3748 $\pm$ 979	0.476
<b>Ringers' solution received in ICU, mL</b>	4230 $\pm$ 834	4589 $\pm$ 1385	0.220
<b>Diuresis and filtration in OR, mL</b>	2157 $\pm$ 1342	2098 $\pm$ 1138	0.859
<b>Diuresis and drainage in ICU, mL</b>	5452 $\pm$ 894	5265 $\pm$ 1249	0.556
<b>Pack cell received in OR, mL</b>	1 (4)	0 (0)	0.691
<b>Pack cell received in ICU</b>	0 (187/5)	1 (2.5)	0.574
<b>FFP received in OR</b>	0 (0)	0 (0)	0.765
<b>FFP received in ICU</b>	2 (8)	0 (0)	0.315
<b>PLT received in OR</b>	0 (0)	0 (0)	0.690
<b>PLT received in ICU</b>	1 (4)	0 (0)	0.691
<b>Mannitol received in OR/ICU, mL</b>	400 (137/5)	400 (150)	0.698
<b>Lasix dose in OR, mg</b>	0 (0)	0 (0)	0.393
<b>Lasix dose in ICU, mg</b>	0 (0)	20	0.201
<b>Bicarbonate in OR, mL</b>	87/5 $\pm$ 50	70 $\pm$ 40	0.303
<b>Bicarbonate in ICU (mL)</b>	70 $\pm$ 35	50 $\pm$ 20	0.268
<b>Beta-blocker used before Op.</b>	16 (80)	3 (84.6)	0.721
<b>CCB used before Op.</b>	4 (20)	7 (17.9)	1.000
<b>ACE used before Op.</b>	8 (40)	15 (38.5)	1.000
<b>ARB used before Op.</b>	7 (35)	16 (41)	0.867
<b>Diuretics used before Op.</b>	5 (25)	9 (23.1)	1.000
<b>Vasodilators used before Op.</b>	12 (60)	28 (71.8)	0.533
<b>Epinephrine in OR</b>	8 (40)	15 (38.5)	1.000
<b>TNG used in OR</b>	13 (65)	30 (76.9)	0.506
<b>Inotropes used in OR</b>	7 (35)	6 (15.4)	0.165
<b>Diuretics used in ICU</b>	6 (30)	8 (20.50)	0.626
<b>Vasopressors used in ICU</b>	3 (15)	10 (25.6)	0.511
<b>Vasodilators used in ICU</b>	19 (95)	37 (94.9)	1.000

<sup>a</sup>Values are expressed as mean  $\pm$  SD or median (interquartile ranges).

**Table 3.** Comparison of Complications in Different Organs Between the Groups

Post op. Complications	15 $\geq$ $\Delta$ Na (n = 20)	15 < $\Delta$ Na (n = 39)	P Value
<b>Neurology</b>	2 (10)	9 (23.1)	0.302
<b>Renal</b>	0 (0)	6 (15.4)	0.087
<b>Respiratory</b>	2 (10)	7 (17.9)	0.704
<b>Infection</b>	3 (15)	3 (7.7)	0.398
<b>Bleeding</b>	6 (30)	15 (38.5)	0.722
<b>Cardiac</b>	5 (25)	18 (46.2)	0.195
<b>Cardiac Arrest</b>	0 (0)	2 (5)	0.544

such as CPB, clump, and surgery time, mechanical ventilation, ICU admission and complications during off pump. Homoky et al. (13) also found no significant differences between ICU stay and morbidity. However, Bagheri et al. (2) found significant differences in hospital stay between groups. We also found no difference between groups in

**Table 4.** Comparison of Clinical Variables and Sodium Fluctuation Between Patients with and Without Postoperative Complications

	Without Complication (n = 46)	With Complication (n = 13)	P Value
<b>Gender</b>			
Male	33 (71.7)	9 (69.2)	1.000
Female	13 (28.3)	4 (30.8)	
Age, y	64.22 ± 9.2	57/84 ± 9	0.033
Body surface area, m <sup>2</sup>	1.81 ± 0.21	1.96 ± 0.17	0.026
Ejection fraction, %	45 ± 15	55 ± 5	0.032
Hypertension	22 (47.8)	9 (69.2)	0.294
Hyperlipidemia	18 (39.1)	5 (38.5)	1.000
Diabetes	22 (47.8)	6 (46.2)	1.000
Thyroid dysfunction	3 (6.5)	2 (15.4)	0.302
Myocardial infarction	10 (21.7)	1 (7.7)	0.426
Addiction	4 (8.7)	2 (15.4)	0.605
Smoking	11 (23.9)	1 (7.7)	0.268
Family history of heart disease	10 (21.7)	3 (23.1)	1.000
Aortic cross clamp time, min	38.65 ± 14.22	34.30 ± 14.65	0.338
CPB time, min	75.78 ± 21.20	66.1 ± 26.29	0.169
Operation time, h	4.5 ± 1	4.5 ± 1.75	0.993
Mechanical ventilation time, h	10 ± 4.13	9/5 ± 2.5	0.399
ICU stay time, h	48 ± 26	75 ± 25.4	0.003
Na fluctuation ≥ 15 meq/L	3 (23)	10 (77)	0.001
Na fluctuation < 15 meq/L	36 (78)	10 (22)	

serum and drug intake, blood administration, diuresis and filtration in OR and diuresis and drainage in the ICU.

In our research the maximum complications in patients with high serum sodium levels were bleeding and cardiac complications. In patients with normal sodium levels no renal complications were recorded. Conversely in previous studies the most common comorbid disease with normal sodium levels was high blood pressure (13, 17).

Severe fluctuations in electrolyte level in CABG patients is considered as a complication. In this study, patients with more fluctuations in sodium levels had lower primary creatinine levels. The group with sodium fluctuations had more lactate levels in ICU and lower BE levels. These pa-

tients had higher levels of sodium from the time entering the ICU. In our study one patient with high sodium levels was dead. In Bagheri et al. (2) study, 4 patients died in which 3 were associated with electrolytes fluctuations. Homoky (13) reported 2 deaths which had normal sodium levels. Madan et al. (16) reported correlations between sodium and BUN levels with mortality. However, Hudcova (14) showed higher fluctuation sodium in patients with lower levels of sodium. Madan et al. (16) also found the same results. This discrepancy could be because of the different definition from increased sodium which was more than 2 meq/L in Madan study from 60 - 270 days after the patient was discharged, however in our study this differences was 24 hour after ICU stay.

In our study, patients with at least one complication compared to patients with no complication were older, had lower BSA and EF. In the present study, patients with more complications had overall longer ICU stays. Surgery time, clamp time, CPB time, ventilation and complications did not show any significant differences between groups. Conversely in Kim et al. study (15) there were significant differences between groups with complications and without, in aortic clamp time and CPB time, which may be because of congenital heart diseases studied in the research. In this study sodium bicarbonate administration did not affect serum sodium levels. However in previous studies showed higher levels of serum sodium in patients receiving sodium bicarbonate (14-20).

Our results suggest changes in sodium levels more than 15 meq/L is an independent factor for post-operative complications. Previous studies also found the same results (21-24). Some researchers also reported increased sodium levels after liver transplant is associated with post-operative complications (13-16, 25-29). However another study found this correlation with lower mortality and complications (30).

It is not clear why changes in sodium levels in patients undergoing CABG, which have normal sodium levels, has correlation with post-operative complications. We assume that physiologic changes might have a correlation with serum sodium osmolality changes. Overall changes in serum osmolality affects all cells, however brain is the most sensitive organ. When the serum osmolality increases as a result of increased sodium levels, the osmolality in the brain and other organs also increases (31). Although the electrolyte correction is fast, osmolyte balance is incredibly slow which might affect and harm the body. Although changes in sodium levels in our study did not show any significant differences, patients undergoing CABG might encounter complications in brain and other vital organs which renders information about the mechanism of high level sodium in leading to post-operative complications.

**Table 5.** Logistic Regression for Values Related with Postoperative Complications

Variables	Exp(B)	Sig.	df	Wald	S.E.	B
Age	1.06	0.251	1	1.317	0.051	0.058
Ejection fraction	1.058	0.122	1	2.385	0.036	0.056
Na fluctuation $\geq$ 15 meq/L	11.006	0.003	1	8.813	0.808	2.398
	0.003	0.05	1	3.842	3.018	-5.915

#### 4.1. Limitations

This research had some limitations. One limitation is limited sample size and being a single center study. The exact data may not have been recorded for all patients like transient arrhythmias and other complications like liver disease.

#### 4.2. Conclusions

In conclusion high serum sodium fluctuations may result in post-operative complications. In other words, sodium imbalance irrespective to serum concentration could be independently resulting in post-operative complications. There were no statistically differences between the two study groups regarding each organ (cardiac, respiratory, renal and neurologic) and infectious or bleeding complications.

#### Footnote

**Conflict of Interest:** The authors declare no conflict of interest in this work and there is no financial support in this research.

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