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ORIGINAL RESEARCH

Relation Between Serum Sodium Trajectory and Survival in Septic Patients with Cardiopulmonary Bypass Surgery: Based on Medical Information Mart for Intensive Care-IV Database

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ABSTRACT

Objective: The influence of serum sodium level changes on septic patient survival after cardiopulmonary bypass surgery is not clear. We attempted to figure out the impact of serum sodium trajectory changes on the 30-day mortality rate of such patients.

Methods: The Medical Information Mart for Intensive Care (MIMIC)-IV database was searched to gather patients who developed sepsis after cardiopulmonary bypass surgery. A group-based trajectory model (GBTM) was employed to determine the serum sodium trajectory within 72 h of ICU admission. Patients' survival differences between different trajectory groups were compared using Kaplan–Meier (K–M) survival curves. Cox regression models were further employed to explore the correlation between survival status and serum sodium trajectory.

Results: 1,038 eligible patients were involved in this project. GBTM identified 3 serum sodium trajectories, all showing a trend of initial decrease followed by an increase. K–M curve analysis uncovered a notable difference in 30-day survival status between Class 1 and Class 2 (Log-rank $p = 0.039$), while no obvious differences were observed between other groups. Cox hazard analysis revealed that in the three models adjusting for different covariates, Class 2 was connected with the increased risk of survival (OR > 1, $p < 0.05$).

Conclusion: Higher serum sodium trajectory is linked with elevated 30-day death risk in septic patients following cardiopulmonary bypass surgery. Repressing high levels of serum sodium may be beneficial for patient survival.

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KEYWORDS
Cardiopulmonary bypass surgery; group-based trajectory model; sepsis; serum sodium

Introduction

Cardiovascular disease (CVD) ranks as the most common chronic and life-threatening disease worldwide. The Global Burden of Disease Study in 2020 shows that CVD caused about 18.6 million deaths in 2019, making up 32% of the global total mortality [1]. Medication is one of the main methods for treating CVD [2]. However, in most cases, conditions such as coronary artery disease and valve regurgitation or stenosis, which are associated with CVD, are unlikely to be cured through medication, making surgical treatment an impactful option [3, 4]. Median sternotomy, also known as open-heart surgery, is an impactful and prevalent intervention for heart diseases such as heart valve disease, coronary heart disease, or aortic aneurysm [5]. Among them, coronary artery bypass grafting (CABG) is one of the most commonly utilized procedures in open-heart surgery. According to the American Heart Association's US and Global Data Report in 2024, there were 161,816 surgeries involving isolated CABG in 2019, accounting for over half of all adult cardiac surgeries [6].

Cardiopulmonary bypass (CPB) is a widely applied technique in open-heart surgery, which is the standard technique for cardiac surgery. The machine is connected to the patient through a synthetic circuit and tubes, which transport blood from the heart to the machine for oxygenation and removal of carbon dioxide to maintain systemic perfusion and oxygenation of the patient's body [7, 8]. However, this method may lead to the occurrence of numerous complications due to the changes in normal circulation and perfusion. Infectious complications, particularly sepsis or septic shock after CPB, are critical issues linked with high morbidity and mortality rates. A previous study on pediatric patients who had cardiac surgery for congenital heart disease has demonstrated an increased incidence of sepsis after CPB [9]. However, there is currently limited information available in clinical practice regarding the occurrence and risk factors of sepsis in postoperative patients.

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Sodium primarily exists in the blood and extracellular fluid in the body, working together with potassium to maintain osmotic pressure and water balance inside and outside the cells and contributing to the normal functioning of the nervous, cardiovascular, muscular, and other physiological systems [10]. Sodium disorder has an instrumental impact on patients' prognoses. Numerous clinical researches have manifested that sodium imbalance is a prevalent electrolyte disorder during admission and hospitalization of patients in the ICU, which is linked with elevated mortality rates [11, 12]. Hypernatremia is tied to the severity of sepsis, the occurrence of organ failure, and increased in-hospital mortality rates [13–15]. In a study, among septic patients in the ICU, both hypernatremia at admission and hospital-acquired hypernatremia were linked with greater mortality rates [16]. Freitas et al. [17] also pointed out a positive connection between the presence of sepsis and hypernatremia at admission. In addition, as the most common electrolyte disorder among hospitalized patients, hyponatremia is an adverse predictor of various diseases [18–20]. In the emergency department, both hypernatremia and moderate to severe hyponatremia are independent predictors of mortality in septic patients [21]. Therefore, the different changes in sodium levels are essential factors for the survival of critically ill patients, which possesses good value in predicting septic patients' survival risk. However, analyses of serum sodium in current studies are carried out with measurements at discrete time points. The changes in sodium levels during hospitalization and their correlation with the outcomes of patients who develop sepsis after undergoing open-heart surgery with CPB are unknown.

This investigation attempts to uncover the different patterns of longitudinal changes in sodium levels and conduct population clustering through the establishment of a group-based trajectory model (GBTM), and to determine the association between sodium level changes and death rate in patients who develop sepsis after undergoing open-heart surgery with CPB.

Methods

Data source

The data was available from the Medical Information Mart for Intensive Care IV (MIMIC-IV) database established by Beth Israel Deaconess Medical Center in Boston, Massachusetts, USA [22]. It stores the relevant information of patients admitted to the ICU at Beth Israel Deaconess Medical Center between 2008 and 2019. The information includes medical and health data of multiple patients, including their survival records within 1 year after discharge. Specifically, the database contains demographic information, laboratory test results, medication information, imaging reports, hospital records, and nursing levels of the patients (https://mimic.physionet.org/about/mimic/).

Patient selection

To probe into the relationship between *in vivo* serum sodium changes and survival of septic patients who received cardiopulmonary bypass surgery, we gathered clinical data of 299,712 patients from the MIMIC-IV database between 2008 and 2019. All data in the MIMIC-IV were de-identified, being unable to identify specific patients. This project, therefore, did not need any written informed consent from patients or approval from a research ethics committee or an institutional review board.

The following standards were applied to determine which patients were eligible to maintain the accuracy of the data: (a) age > 18 and <90 years; (b) patients who were admitted to the ICU for the first time and stayed in the ICU for more than 24 h; (c) surgical patients were identified through ICD-9 and ICD-10 codes; (d) sepsis was identified through Sepsis-3 criteria. The standards of selecting sepsis patients who meet the Sepsis-3 diagnostic criteria from the MIMIC database were consistent with what was mentioned in the previously published study [23]. All included patients received no less than 4 measurements of serum sodium levels within 72 h after surgery.

We excluded the following patients: (a) patients who did not have laboratory measurements and baseline data of serum sodium before ICU admission; (b) patients who did not have survival information; (c) patients who died within 24 h of admission. 1,038 eligible participants were finally involved in the investigation. The screening process of participants is presented in Figure 1.

Variable collection

The variables collected in this project included demographic data (age, gender, race, marital status), laboratory measurements (length of stay (LOS), hospital mortality, heart rate, bicarbonate, respiratory rate, mean arterial pressure (MBP), temperature, saturation of peripheral oxygen (SpO_2), hematocrit, chloride, hemoglobin, glucose, lactate, platelets, potassium, international normalized ratio (INR), prothrombin time (PT), sodium, partial thromboplastin time (PTT), blood urea nitrogen (BUN), white blood cell (WBC) count, mean corpuscular hemoglobin (MCH), partial pressure of oxygen (pO_2), partial pressure of carbon dioxide (pCO_2), mean corpuscular volume (MCV), pH, excess base, mean corpuscular hemoglobin concentration (MCHC), vasoactive agents (yes or no), red cell distribution width (RDW), creatinine, mechanical ventilation (yes or no), severity scores (GCS), coma scale, simplified acute physiology score II (SAPSII), sequential organ failure assessment (SOFA), Charlson comorbidity index), microbiological cultures (sputum, urine, blood, and others), and medical history congestive heart failure (yes or no), kidney disease (yes or no), diabetes (yes or no), chronic lung disease (yes or no), and liver disease (yes or no).

Serum sodium was the baseline value before admission to the ICU. Severity scores, laboratory measurements, and vital signs collected multiple times during the ICU period were all determined by the values corresponding to the most severe level measured within the first 24 h after ICU admission.

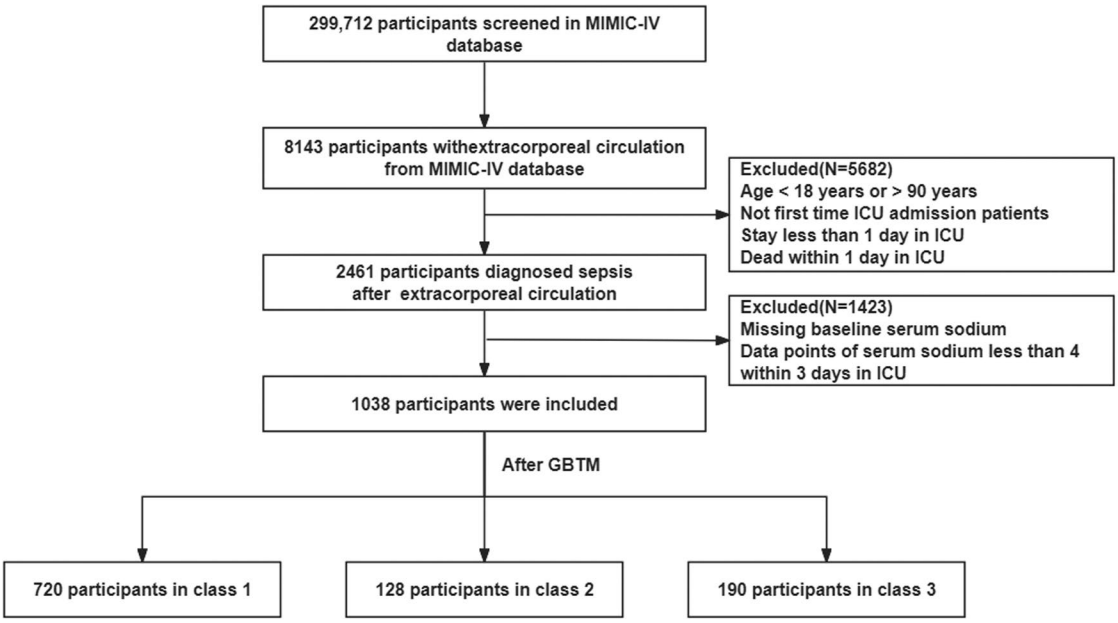

Figure 1. Flow chart of participant population.

Trajectory grouping of serum sodium

We resorted to a GBTM approach to determine serum sodium levels with similar developmental trajectories. Based on the serum sodium levels before ICU admission, patients were clustered into three groups: hypernatremia, normal sodium level, and hyponatremia. The level and shape of the trajectory were determined by the regression parameters of the model, which were estimated by maximum likelihood estimation. After using the GBTM method, based on the serum sodium levels measured within 72 h after ICU admission, we grouped patients into three groups: hyponatremia, normal sodium level, and hypernatremia. Specifically, the number of groups was set by a basic model without covariates and using linear, quadratic, and cubic polynomials to fit GBTM for serum sodium measurement. The grouping of serum sodium trajectories based on the GBTM model was mainly determined by the following indicators: (1) Bayesian information criterion (BIC); (2) Akaike information criterion (AIC); (3) Sample-size adjusted BIC (SABIC); (4) Entropy and the ratio of samples to the total samples in each trajectory group; (5) Average posterior probability (Avepp), which reflects the posterior probability of each being classified into the corresponding trajectory subgroup, usually with a threshold of >0.7 for acceptance; (6) patients >5% were classified in each trajectory.

Statistical analysis

Continuous variables in the statistical analysis were expressed as median (IQR). By the Mann–Whitney *U* test, we made comparisons between groups. Categorical data were presented as percentages (%) and compared using the chi-square test. The baseline serum sodium concentration was divided into three groups to assess the relation between the level of serum sodium and demographic and clinical variables in patients with postoperative sepsis after cardiopulmonary bypass surgery. A bilateral *P* value <0.05 was deemed the statistical significance for between-group comparisons. The baseline characteristics of the serum sodium best-fitting model were constructed by utilizing the GBTM. By graphing Kaplan–Meier (K–M) curves, we compared the survival differences between groups as well as among hypernatremia, normal sodium levels, and hyponatremia samples before ICU admission. The Cox proportional hazards regression model was employed to measure the notable differences in survival status and adverse events after stratifying patients based on different serum sodium trajectories, with covariates adjusted. Data in this project were processed by utilizing R (4.2.3) statistical software, with the following R packages: *tableone*, *mice*, *jskm*, and *survival* employed.

Samples were excluded from the project when they had missing variable proportions greater than 20%. By utilizing the Random Forest (RF) method in the *mice* package, other missing variables were handled.

Results

Baseline characteristics

1,038 septic patients after cardiopulmonary bypass surgery between 2008 and 2019 were included in this work, including 748 males (72.1%) and 290 females (27.9%). The samples were classified into three groups based on the pre-ICU admission serum sodium levels: normal sodium ($n = 976$), hyponatremia ($n = 54$), and hypernatremia ($n = 8$), as shown in Table 1. Baseline characteristics demonstrated that positive microbial blood cultures were relatively common in patients with hyponatremia (3.7%). We detected notable differences in serum chloride levels of patients in the three groups ($p < 0.05$, Table 1).

Table 1. Baseline characteristics of the study population.

Characters	Total (*N* = 1038)	Hyponatremia (<135mEq/L) (*N* = 54)	Normal sodium levels (135–145mEq/L) (*N* = 976)	hypernatremia (>145mEq/L) (*N* = 8)	P-Value
Gender					**0.008**
Female	290 (27.9)	12 (22.2)	272 (27.9)	6 (75.0)	
Male	748 (72.1)	42 (77.8)	704 (72.1)	2 (25.0)	
Age (years)	69.00 [62.00, 76.00]	70.50 [65.00, 75.75]	69.00 [62.00, 76.00]	67.50 [62.00, 76.75]	0.617
Race					0.574
White	712 (68.6)	34 (63.0)	671 (68.8)	7 (87.5)	
Black	33 (3.2)	1 (1.9)	32 (3.3)	0 (0.0)	
Other race	293 (28.2)	19 (35.2)	273 (28.0)	1 (12.5)	
Marital status					0.381
Married	632 (60.9)	32 (59.3)	597 (61.2)	3 (37.5)	
Unmarried	406 (39.1)	22 (40.7)	379 (38.8)	5 (62.5)	
LOS (day)	2.09 [1.26, 3.29]	2.18 [1.30, 4.31]	2.08 [1.26, 3.25]	3.85 [1.93, 5.04]	0.188
Hospital mortality	80 (7.7)	7 (13.0)	73 (7.5)	0 (0.0)	0.242
Vital signs					
Heart rate (times/min)	81.97 [77.11, 87.92]	84.85 [80.72, 89.94]	81.74 [76.99, 87.88]	83.78 [75.98, 86.55]	0.068
MBP (mmHg)	73.55 [69.93, 77.22]	72.07 [67.51, 74.38]	73.73 [70.08, 77.31]	72.49 [67.97, 76.31]	0.053
Breath rate (times/min)	17.49 [16.02, 18.86]	17.64 [15.93, 18.64]	17.48 [16.02, 18.90]	17.15 [15.41, 17.81]	0.68
Temperature (°C)	36.72 [36.51, 36.95]	36.72 [36.56, 36.87]	36.71 [36.50, 36.96]	36.82 [36.55, 36.93]	0.907
SpO2	97.93 [97.05, 98.78]	98.39 [97.47, 98.95]	97.93 [97.04, 98.78]	97.27 [96.64, 98.25]	0.133
Glucose (mg/dL)	128.57 [122.06, 137.58]	130.02 [127.33, 144.77]	128.48 [121.95, 137.10]	129.13 [120.94, 141.68]	0.062
Severity score					
GCS					0.808
≥13	885 (85.3)	47 (87.0)	830 (85.0)	8 (100.0)	
9–12	27 (2.6)	1 (1.9)	26 (2.7)	0 (0.0)	
<9	126 (12.1)	6 (11.1)	120 (12.3)	0 (0.0)	
SAPSII	36.00 [30.00, 43.00]	38.50 [31.00, 45.00]	36.00 [30.00, 43.00]	33.00 [30.00, 43.25]	0.297
SOFA	5.00 [4.00, 7.00]	5.00 [4.00, 8.00]	5.00 [4.00, 7.00]	6.00 [5.00, 7.50]	0.644
Charlson comorbidity index	4.00 [3.00, 6.00]	4.50 [4.00, 6.75]	4.00 [3.00, 5.25]	4.50 [2.75, 7.25]	0.062
Laboratory tests					
Aniongap (mmol/L)	13.00 [11.00, 15.00]	13.00 [12.00, 15.00]	13.00 [11.00, 15.00]	13.00 [11.75, 13.00]	0.48
Bicarbonate (mmol/L)	22.00 [21.00, 24.00]	22.00 [20.00, 23.00]	22.00 [21.00, 24.00]	23.00 [22.00, 25.00]	0.057
Chloride (mmol/L)	109.00 [107.00, 111.00]	106.00 [103.25, 108.00]	109.00 [107.00, 111.00]	108.00 [107.75, 114.25]	**<0.001**
Hematocrit (μmol/L)	26.40 [23.90, 29.60]	25.40 [23.57, 28.40]	26.50 [23.90, 29.70]	24.20 [23.27, 26.83]	0.248
Hemoglobin (g/dL)	9.10 [8.00, 10.10]	8.75 [7.82, 9.90]	9.10 [8.00, 10.10]	8.05 [7.47, 8.83]	0.187
Lactate (mg/dL)	2.50 [2.00, 3.30]	2.45 [1.90, 3.38]	2.50 [2.00, 3.30]	2.65 [1.87, 3.95]	0.958
Platelet (K/μL)	128.00 [104.00, 159.75]	126.00 [99.00, 169.75]	128.00 [104.00, 159.00]	109.00 [85.00, 128.00]	0.201
Potassium (K/μL)	4.60 [4.40, 4.90]	4.60 [4.30, 4.97]	4.60 [4.40, 4.90]	4.60 [4.42, 4.62]	0.825
PTT (s)	34.50 [30.02, 44.20]	34.15 [30.65, 43.48]	34.50 [30.00, 44.20]	33.50 [29.08, 44.28]	0.978
INR	1.40 [1.30, 1.60]	1.50 [1.40, 1.67]	1.40 [1.30, 1.60]	1.35 [1.28, 1.52]	0.124
PT (s)	15.90 [14.60, 17.40]	16.20 [15.20, 17.92]	15.80 [14.60, 17.40]	15.10 [13.73, 16.42]	0.114
Sodium (mEq/L)	139.00 [137.00, 141.00]	134.00 [132.00, 134.00]	139.00 [138.00, 141.00]	146.00 [146.00, 146.50]	**<0.001**
BUN (mg/dL)	17.00 [13.00, 21.00]	17.00 [13.25, 22.75]	17.00 [13.00, 21.00]	16.50 [10.00, 20.75]	0.75
WBC (K/μL)	15.90 [12.70, 19.90]	17.80 [13.38, 21.05]	15.80 [12.70, 19.80]	14.00 [11.15, 19.60]	0.173
pO2 (mmHg)	93.00 [77.00, 117.00]	95.00 [73.00, 125.00]	93.00 [77.75, 117.00]	87.50 [70.25, 105.75]	0.692
pCO2 (mmHg)	48.00 [44.00, 52.00]	47.50 [44.00, 51.00]	48.00 [44.00, 52.00]	49.00 [44.50, 52.75]	0.612
pH	7.32 [7.28, 7.34]	7.31 [7.28, 7.35]	7.32 [7.28, 7.34]	7.32 [7.29, 7.34]	0.961
Base excess (mEq/L)	−3.00 [−5.00, −1.00]	−3.00 [−5.00, −1.25]	−3.00 [−5.00, −1.00]	−3.00 [−5.50, −1.75]	0.693
MCH (pg)	30.20 [28.90, 31.37]	30.55 [28.92, 31.95]	30.20 [28.90, 31.30]	29.35 [28.62, 29.67]	0.205
MCHC (g/L)	33.20 [32.30, 34.00]	33.40 [32.50, 34.30]	33.20 [32.30, 34.00]	32.00 [31.70, 32.25]	0.025
MCV (fL)	89.00 [86.00, 93.00]	89.00 [87.00, 94.00]	89.00 [86.00, 93.00]	90.50 [86.75, 92.00]	0.907
RDW	14.00 [13.20, 14.90]	13.90 [13.20, 15.07]	14.00 [13.20, 14.90]	14.75 [14.08, 14.95]	0.618
Creatinine (mg/dL)	1.00 [0.80, 1.20]	1.00 [0.80, 1.20]	1.00 [0.80, 1.20]	0.80 [0.58, 1.07]	0.396
Treatment measures					
Vasopressor					0.129
No	916 (88.2)	43 (79.6)	866 (88.7)	7 (87.5)	
Yes	122 (11.8)	11 (20.4)	110 (11.3)	1 (12.5)	
Mechanical ventilation					0.396
No	952 (91.7)	47 (87.0)	898 (92.0)	7 (87.5)	
Yes	86 (8.3)	7 (13.0)	78 (8.0)	1 (12.5)	
Culture					
Blood	3 (0.3)	2 (3.7)	1 (0.1)	0 (0.0)	**<0.001**
Urine	55 (5.3)	3 (5.6)	51 (5.2)	1 (12.5)	0.656
Sputum	22 (2.1)	0 (0.0)	22 (2.3)	0 (0.0)	0.49
Other	87 (8.4)	5 (9.3)	81 (8.3)	1 (12.5)	0.887
Comorbidity					
Congestive heart failure					0.3
No	727 (70.0)	33 (61.1)	689 (70.6)	5 (62.5)	
Yes	311 (30.0)	21 (38.9)	287 (29.4)	3 (37.5)	
Chronic pulmonary disease					0.106
No	813 (78.3)	37 (68.5)	771 (79.0)	5 (62.5)	
Yes	225 (21.7)	17 (31.5)	205 (21.0)	3 (37.5)	

(*Continued*)

Table 1. Continued.

Characters	Total (*N* = 1038)	Hyponatremia (<135mEq/L) (*N* = 54)	Normal sodium levels (135–145mEq/L) (*N* = 976)	hypernatremia (>145mEq/L) (*N* = 8)	P-Value
Renal disease					0.651
No	885 (85.3)	45 (83.3)	834 (85.5)	6 (75.0)	
Yes	153 (14.7)	9 (16.7)	142 (14.5)	2 (25.0)	
Liver disease					0.67
No	1001 (96.4)	53 (98.1)	940 (96.3)	8 (100.0)	
Yes	37 (3.6)	1 (1.9)	36 (3.7)	0 (0.0)	
Diabetes					0.517
No	688 (66.3)	32 (59.3)	651 (66.7)	5 (62.5)	
Yes	350 (33.7)	22 (40.7)	325 (33.3)	3 (37.5)	

LOS, length of stay; MBP, mean blood pressure; GCS, Glasgow Coma Scale; SAPSII, Simplified Acute Physiology Score II; SOFA, Sequential Organ Failure Assessment; WBC, white blood cell; RBC, red blood cell; RDW, red cell distribution width; PTT, partial thromboplastin time; PT, prothrombin time; INR, international normalized ratio; BUN, blood urea nitrogen; MCH, mean corpuscular hemoglobin; MCHC, mean corpuscular hemoglobin concentration; MCV, mean corpuscular volume.

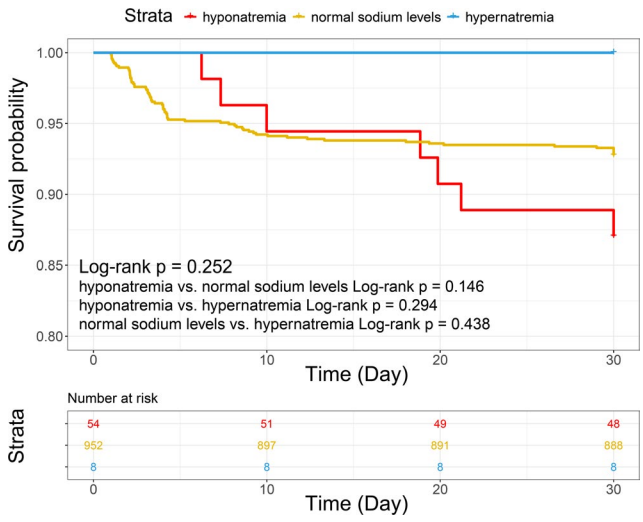

Figure 2. K–M survival curves showing the association between serum sodium and 30-day mortality.

Association between different serum sodium levels and mortality rates

Different serum sodium grouping and K–M curves displaying patients' survival status within 30 days are displayed in Figure 2. The results indicated no obvious difference in initial serum sodium levels of the three groups or overall and inter-group survival status (Log-rank $p > 0.05$).

Characterization of the serum sodium trajectory

In Table S1, AvePP and model-fitting statistics were displayed for determining the changes in serum sodium levels within 72 h after surgery. Lastly, three different trajectory groups met our requirements: Class 1 ($N = 720$, 69.13%), Class 2 ($N = 128$, 12.23%), and Class 3 ($N = 190$, 18.64%) (Table 2). The AvePP of each trajectory group was >0.7, implying a great fit.

We listed clinical and demographic characteristics stratified by serum sodium trajectory group in Table 2. In the three trajectory groups, Class 2 had considerably higher SOFA scores, Charlson comorbidity index, chloride levels, lactate levels, sodium levels, pCO_2, and RDW compared to the other two groups ($p < 0.05$), while hematocrit, hemoglobin, pO_2, and MCHC were considerably lower ($p < 0.05$). Additionally, Class 2 possessed a longer average length of stay of 3.17 days. In terms of INR and PT, the average values in Class 1 were relatively low, at 1.40 and 15.70, respectively. In other aspects, obvious differences ($p < 0.05$) were detected among the three groups in terms of carbonate level, potassium ion level, PH vascular pressure, mechanical ventilation, microbial sputum culture results, and congestive heart failure results.

The trajectory of serum sodium change within 72 h after the surgery is displayed in Figure 3. All three trajectories demonstrated a trend of initially slow decline followed by an increase, with the serum sodium level in Class 2 substantially higher than that in Class 1 and Class 3 ($p < 0.001$).

Serum sodium trajectory and mortality rate

The K–M curves indicated no obvious difference in the survival status of patients with different serum sodium trajectories (Figure 4). Further analysis uncovered no striking difference between any two groups (Log-rank $p > 0.05$) except for Class 1 and Class 2 (Log-rank $p = 0.039$) (Figure 4). The results of landmark analysis unraveled notable differences in survival status between Class 1 and Class 2 after 7 days (Log-rank $p < 0.001$), as well as notable differences in survival status between Class 2 and Class 3 in the first 21 days (Log-rank $p = 0.036$) (Figure S1).

Cox proportional hazards regression analysis of different risk factors and serum sodium trajectories

The Cox proportional hazard model was employed to assess the correlation between the trajectories modeled by GBTM and the 30-day survival status. In all three models, the survival risk of Class 2 was remarkably elevated compared to Class 1 ($p < 0.05$), while no such difference was observed between Class 3 and Class 1 (Table 3).

Discussion

In this project, GBTM was applied in the trajectory analysis to set three serum sodium levels of septic patients after receiving cardiopulmonary bypass surgery. The correlation

Table 2. Participants' characteristics of included patients stratified by trajectory grouping for the GBTM analysis of changes in the 72-h serum sodium.

Characters	Total (*N* = 1038)	Class 1 (*N* = 720)	Class 2 (*N* = 128)	Class 3 (*N* = 190)	*P* value
Gender					0.14
Female	290 (27.9)	196 (27.2)	45 (35.2)	49 (25.8)	
Male	748 (72.1)	524 (72.8)	83 (64.8)	141 (74.2)	
Age (years)	69.00 [62.00, 76.00]	69.00 [62.00, 76.00]	70.00 [61.00, 77.25]	71.00 [63.25, 77.00]	0.229
Race					0.502
White	712 (68.6)	492 (68.3)	90 (70.3)	130 (68.4)	
Black	33 (3.2)	21 (2.9)	7 (5.5)	5 (2.6)	
Other race	293 (28.2)	207 (28.7)	31 (24.2)	55 (28.9)	
Marital status					0.271
Married	632 (60.9)	448 (62.2)	78 (60.9)	106 (55.8)	
Unmarried	406 (39.1)	272 (37.8)	50 (39.1)	84 (44.2)	
LOS (day)	2.09 [1.26, 3.29]	1.97 [1.24, 3.06]	3.17 [1.54, 6.25]	2.14 [1.30, 3.91]	**<0.001**
Hospital mortality	80 (7.7)	51 (7.1)	16 (12.5)	13 (6.8)	0.094
Vital signs					
Heart rate (times/min)	81.97 [77.11, 87.92]	81.59 [76.96, 87.80]	82.25 [77.61, 88.50]	83.00 [77.62, 88.46]	0.499
MBP (mmHg)	73.55 [69.93, 77.22]	73.88 [70.45, 77.29]	72.16 [68.73, 77.25]	72.88 [69.23, 76.49]	0.034
Breath rate (times/min)	17.49 [16.02, 18.86]	17.50 [16.07, 18.89]	17.55 [15.79, 19.13]	17.35 [16.20, 18.76]	0.92
Temperature (°C)	36.72 [36.51, 36.95]	36.72 [36.52, 36.96]	36.69 [36.48, 36.95]	36.71 [36.49, 36.93]	0.546
SpO2	97.93 [97.05, 98.78]	97.89 [97.00, 98.76]	98.09 [97.17, 98.87]	98.10 [97.18, 98.78]	0.204
Glucose (mg/dL)	128.57 [122.06, 137.58]	128.21 [122.03, 136.80]	131.12 [123.26, 139.06]	128.51 [121.71, 138.57]	0.19
Severity score					
GCS					0.741
≥13	885 (85.3)	613 (85.1)	113 (88.3)	159 (83.7)	
9–12	27 (2.6)	20 (2.8)	3 (2.3)	4 (2.1)	
<9	126 (12.1)	87 (12.1)	12 (9.4)	27 (14.2)	
SAPSII	36.00 [30.00, 43.00]	36.00 [30.00, 42.00]	35.50 [31.00, 42.00]	38.00 [31.00, 45.00]	0.23
SOFA	5.00 [4.00, 7.00]	5.00 [4.00, 7.00]	6.00 [5.00, 8.00]	5.00 [4.00, 7.75]	**<0.001**
Charlson comorbidity index	4.00 [3.00, 6.00]	4.00 [3.00, 5.00]	5.00 [3.00, 6.00]	4.00 [3.00, 6.00]	**0.008**
Laboratory tests					
Aniongap (mmol/L)	13.00 [11.00, 15.00]	13.00 [11.00, 15.00]	13.00 [11.00, 14.00]	13.00 [11.00, 15.00]	0.08
Bicarbonate (mmol/L)	22.00 [21.00, 24.00]	22.00 [21.00, 24.00]	22.00 [20.00, 24.00]	22.00 [21.00, 23.00]	**0.021**
Chloride (mmol/L)	109.00 [107.00, 111.00]	109.00 [107.00, 111.00]	110.00 [108.00, 113.25]	107.00 [105.00, 109.00]	**<0.001**
Hematocrit (μmol/L)	26.40 [23.90, 29.60]	26.85 [24.20, 30.00]	25.55 [23.30, 29.02]	25.75 [23.50, 29.00]	**0.005**
Hemoglobin (g/dL)	9.10 [8.00, 10.10]	9.20 [8.10, 10.20]	8.60 [7.70, 9.83]	8.80 [7.80, 9.80]	**0.001**
Lactate (mg/dL)	2.50 [2.00, 3.30]	2.40 [1.98, 3.30]	2.95 [2.10, 4.40]	2.60 [2.00, 3.20]	**0.001**
Platelet (K/μL)	128.00 [104.00, 159.75]	129.00 [105.00, 160.00]	121.00 [98.00, 148.25]	126.00 [102.50, 164.75]	0.083
Potassium (K/μL)	4.60 [4.40, 4.90]	4.60 [4.40, 4.90]	4.60 [4.30, 4.80]	4.60 [4.40, 5.00]	**0.021**
PTT (s)	34.50 [30.02, 44.20]	34.15 [29.80, 44.02]	36.95 [30.08, 50.97]	34.35 [30.52, 42.07]	0.082
INR	1.40 [1.30, 1.60]	1.40 [1.30, 1.60]	1.50 [1.30, 1.60]	1.50 [1.40, 1.67]	**0.007**
PT (s)	15.90 [14.60, 17.40]	15.70 [14.50, 17.20]	16.00 [14.57, 17.60]	16.30 [14.93, 18.00]	**0.009**
Sodium (mEq/L)	139.00 [137.00, 141.00]	137.00 [136.00, 138.00]	140.00 [138.00, 141.00]	134.00 [133.00, 135.00]	**<0.001**
BUN (mg/dL)	17.00 [13.00, 21.00]	17.00 [13.00, 21.00]	17.50 [14.00, 24.00]	17.00 [13.00, 22.00]	0.172
WBC (K/μL)	15.90 [12.70, 19.90]	15.70 [12.57, 19.60]	16.20 [12.88, 20.10]	16.90 [13.10, 20.40]	0.221
pO2 (mmHg)	93.00 [77.00, 117.00]	93.50 [77.75, 117.00]	86.00 [70.75, 107.00]	96.00 [80.00, 125.00]	**0.002**
pCO2 (mmHg)	48.00 [44.00, 52.00]	48.00 [45.00, 52.00]	49.00 [45.00, 55.00]	47.00 [43.00, 51.00]	**<0.001**
pH	7.32 [7.28, 7.34]	7.32 [7.28, 7.34]	7.31 [7.27, 7.33]	7.32 [7.29, 7.35]	**0.003**
Base excess (mEq/L)	−3.00 [−5.00, −1.00]	−3.00 [−5.00, −1.00]	−3.00 [−6.00, −1.00]	−3.00 [−5.00, −1.00]	0.184
MCH (pg)	30.20 [28.90, 31.37]	30.20 [28.90, 31.40]	30.00 [28.80, 31.30]	30.00 [29.00, 31.30]	0.643
MCHC (g/L)	33.20 [32.30, 34.00]	33.30 [32.40, 34.10]	32.90 [32.18, 33.60]	33.20 [32.30, 34.10]	**0.003**
MCV (fL)	89.00 [86.00, 93.00]	89.00 [86.00, 93.00]	89.00 [86.00, 93.25]	89.00 [86.00, 93.00]	0.845
RDW	14.00 [13.20, 14.90]	13.90 [13.20, 14.80]	14.50 [13.40, 15.20]	14.00 [13.20, 15.10]	**0.001**
Creatinine (mg/dL)	1.00 [0.80, 1.20]	0.90 [0.80, 1.10]	1.00 [0.80, 1.30]	1.00 [0.80, 1.20]	0.106
Treatment measures					
Vasopressor					**<0.001**
No	916 (88.2)	656 (91.1)	101 (78.9)	159 (83.7)	
Yes	122 (11.8)	64 (8.9)	27 (21.1)	31 (16.3)	
Mechanical ventilation					**<0.001**
No	952 (91.7)	675 (93.8)	100 (78.1)	177 (93.2)	
Yes	86 (8.3)	45 (6.2)	28 (21.9)	13 (6.8)	
Culture					
Blood	3 (0.3)	3 (0.4)	0 (0.0)	0 (0.0)	0.515
Urine	55 (5.3)	35 (4.9)	9 (7.0)	11 (5.8)	0.568
Sputum	22 (2.1)	11 (1.5)	9 (7.0)	2 (1.1)	**<0.001**
Other	87 (8.4)	55 (7.6)	16 (12.5)	16 (8.4)	0.188
Comorbidity					
Congestive heart failure					0.006
No	727 (70.0)	526 (73.1)	81 (63.3)	120 (63.2)	
Yes	311 (30.0)	194 (26.9)	47 (36.7)	70 (36.8)	
Chronic pulmonary disease					0.07
No	813 (78.3)	578 (80.3)	94 (73.4)	141 (74.2)	
Yes	225 (21.7)	142 (19.7)	34 (26.6)	49 (25.8)	
Renal disease					0.704
No	885 (85.3)	616 (85.6)	106 (82.8)	163 (85.8)	
Yes	153 (14.7)	104 (14.4)	22 (17.2)	27 (14.2)	

(*Continued*)

Table 2. Continued.

Characters	Total (*N* = 1038)	Class 1 (*N* = 720)	Class 2 (*N* = 128)	Class 3 (*N* = 190)	*P* value
Liver disease					0.093
No	1001 (96.4)	700 (97.2)	120 (93.8)	181 (95.3)	
Yes	37 (3.6)	20 (2.8)	8 (6.2)	9 (4.7)	
Diabetes					0.632
No	688 (66.3)	475 (66.0)	82 (64.1)	131 (68.9)	
Yes	350 (33.7)	245 (34.0)	46 (35.9)	59 (31.1)	

LOS, length of stay; MBP, mean blood pressure; GCS, Glasgow Coma Scale; SAPSII, Simplified Acute Physiology Score II; SOFA, Sequential Organ Failure Assessment; WBC, white blood cell; RBC, red blood cell; RDW, red cell distribution width; PTT, partial thromboplastin time; PT, prothrombin time; INR, international normalized ratio; BUN, blood urea nitrogen; MCH, mean corpuscular hemoglobin; MCHC, mean corpuscular hemoglobin concentration; MCV, mean corpuscular volume.

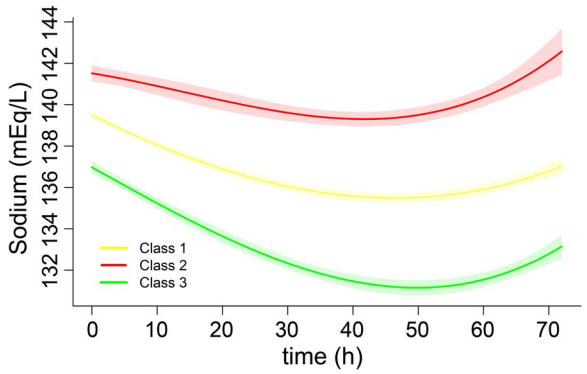

Figure 3. Three trajectories of the serum sodium based on GBTM. Shaded parts represent 95% CI, and the solid lines represent predicted values.

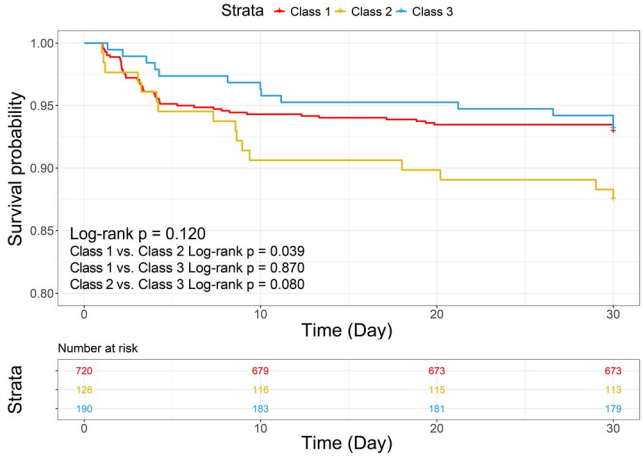

Figure 4. Association between different serum sodium trajectories and 30-day risk of death.

Table 3. Associations between serum sodium and hazard ratios (95% confidence intervals) for 30-day mortality.

Outcomes	Class 1	Class 2	*p*	Class 3	*p*	P_{trend}
Model 1	1.0 (ref.)	1.79 (1.02–3.15)	0.041	0.95 (0.52–1.75)	0.870	0.990
Model 2	1.0 (ref.)	1.78 (1.01–3.14)	0.045	0.94 (0.51–1.72)	0.834	0.880
Model 3	1.0 (ref.)	1.94 (1.02–3.73)	0.044	0.51 (0.26–1.00)	0.052	0.348

Model 1 was unadjusted. Model 2: adjust for age, gender, race. Model 3: model 2 plus adjustment for Glasgow Coma Scale, sodium, glucose, potassium, chloride, white blood cell, hemoglobin, prothrombin time and international normalized ratio.

between trajectory level and mortality risk of patients was determined. Based on the fitting results of the model, we clustered the serum sodium levels of postoperative septic patients into three trajectory groups, among which Class 2 was linked with an elevated risk of 30-day death under no influence of confounding factors.

For critically ill patients, abnormal serum sodium is prevalent during ICU admission [24, 25]. Sodium is mainly metabolized by the kidneys, and its regulatory mechanisms include the renin–angiotensin–aldosterone system and various neurohumoral regulatory systems [26]. The correlation between intensive care clinical prognosis and sodium levels is the theme of multiple studies. In clinical practice, serum sodium is a reliable indicator in ICU clinical testing, highly correlated with clinical symptoms, and easy to measure, effectively reflecting the presence of clinical symptoms and the trend of these symptoms over time [27, 28], which is the reason for all patients admitted to the ICU to be measured. In particular, the trajectory changes of serum sodium concerning the disease have become the focus of clinical research. According to recent research using MIMIC database data, changes in serum sodium levels are linked with elevated heart failure and a 1-year mortality rate [29]. The serum sodium changes in hospitalized patients are significantly correlated with in-hospital mortality and 1-year mortality rate, especially for those with obvious trajectory fluctuations, the impact is the strongest [30]. This project uncovered that a higher level of serum sodium fluctuation trajectory (Class 2) had a bearing on 30-day mortality risk in patients with postoperative sepsis. However, a lower level of serum sodium fluctuation did not seem to have an obvious association with mortality rate, which guides future clinical studies on related diseases.

The research uncovered that although the fluctuation range of serum sodium remained within the normal blood sodium range after the cardiac surgery (138–141 mEq/L), a higher concentration of serum sodium trajectory (Class 2) substantially increased the 30-day mortality risk in patients. Although the mechanism of serum sodium causing increased mortality in patients with postoperative sepsis is elusive, there are possible explanations for this phenomenon. Serum sodium concentration affects cell osmotic pressure and even the function of every cell in the body. In general, patients can usually adapt to chronic changes in serum sodium concentration, but rapid changes in concentration can lead to cerebral edema and osmotic demyelination syndrome [31]. Although the use of CPB technology has facilitated the development of cardiac surgery, intraoperative blood dilution may lead to excessive dilution and significant changes in serum sodium concentration, thereby causing hyponatremia

[32, 33]. Therefore, CPB strategies for patients, including intraoperative ultrafiltration and fluid replacement methods, are applied to reduce the occurrence of associated complications and the risk of mortality [34, 35]. However, these approaches may result in a higher incidence of early hypernatremia. A former investigation on pediatric patients discovered the occurrence of hypernatremia at the end of CPB is significantly linked with more severe electroencephalogram abnormalities, brain damage, and prolonged postoperative mechanical ventilation time [36]. As one of the serious complications after CPB cardiac surgery [9], hypernatremia seems to always accompany the occurrence of sepsis [17]. Based on a secondary analysis of data from three large cohorts of critically ill patients, abnormal changes in serum sodium are revealed to be connected with an elevated risk of 28-day mortality in septic patients [37]. Therefore, we speculated that the presence of sepsis after cardiac surgery may increase patients' sensitivity to changes in serum sodium levels. Therefore, even changes in serum sodium concentration within the normal range may have adverse effects on the prognosis of these patients, thereby increasing their risk of death. This hypothesis emphasized the importance of strict monitoring and management of serum sodium levels after cardiac surgery to reduce potential complications and improve patient survival.

This study contributes to improving the understanding of changes in serum sodium levels in patients after cardiac surgery, as well as the potential impact of these changes on patient prognosis. This may aid in improving patient management and treatment, thus ultimately reducing the risk of death. However, there are certain limitations. Firstly, since the project is a retrospective study on MIMIC-IV, unavoidable biases may affect the validity of the results. Generally, the more key variables included in the model can lead to more accurate predictions. However, due to the limitations of public databases, potential influencing information was not gathered. We cannot adjust all possible confounding factors, such as the specific time point of serum sodium measurement. At the same time, we cannot fully detect the basic health status of patients and cannot effectively obtain data on fluid replacement or the management strategy for serum sodium, or information related to medication treatments that could affect the concentration of serum sodium. Without relevant information, our interpretation of the reasons for patients' serum sodium fluctuations during hospitalization was limited. Future research should consider these unmeasured confounding factors to more accurately assess the relationship between changes in serum sodium levels and patient prognosis. In addition, although this study provides insights into the 30-day mortality risk of sepsis in patients undergoing cardiopulmonary bypass surgery, we acknowledged that the study is limited to short-term outcomes. Due to data limitations, we cannot assess long-term survival and complications that may have a significant impact on the overall prognosis of patients. Future research should be conducted, with more comprehensive databases employed to include long-term follow-up data, thereby providing more comprehensive prognostic information.

Conclusion

We employed GBTM to longitudinally cluster the sodium level data of patients who developed sepsis after cardiopulmonary bypass surgery, unearthing that higher levels of serum sodium fluctuations were aligned with an elevated death risk. The findings of this investigation proffer a reference for the development of prevention and treatment strategies for similar patients in the future.

Disclosure statement

No potential conflict of interest was reported by the author(s).

Ethics approval and consent to participate

Before data from this study were included in the MIMIC-IV public database, all participants signed informed consent forms, adhered to the principles outlined in the Declaration of Helsinki, and were reviewed and approved by the NCHS Ethical Review Board.

Availability of data and materials

The data and materials in the current study are available from the corresponding author on reasonable request.

Consent for publication

Not applicable.

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References

1. Murray CJL, Aravkin AY, Zheng P, et al. Global burden of 87 risk factors in 204 countries and territories, 1990–2019: a systematic analysis for the Global Burden of Disease Study 2019. *Lancet*. 2020;396(10258):1223–1249. doi:10.1016/S0140-6736(20)30752-2.
2. Rudsari HK, Veletic M, Bergsland J, Balasingham I. Targeted drug delivery for cardiovascular disease: modeling of modulated extracellular vesicle release rates. *IEEE Trans Nanobioscience*. 2021;20(4):444–454. doi:10.1109/TNB.2021.3097698.
3. Fagu A, Pingpoh C, Berger T, Siepe M. Bilateral minithoracotomy for mitral valve repair and coronary bypass grafting. *Thorac Cardiovasc Surg Rep*. 2023;12(1):e33–e5. doi:10.1055/s-0043-1768982.
4. Miazza J, Koechlin L, Jeger RV, Reuthebuch OT. First-in-man concomitant mitral valve replacement and coronary artery bypass grafting using a single minimally invasive access. *Eur J Cardiothorac Surg*. 2022;62(1):ezac330. doi:10.1093/ejcts/ezac330.
5. Ren J, Duan S, Wu Y, et al. Multidrug-resistant bacterial infection in adult patients following cardiac surgery: clinical characteristics and risk factors. *BMC Cardiovasc Disord*. 2023;23(1):472. doi:10.1186/s12872-023-03488-1.
6. Martin SS, Aday AW, Almarzooq ZI, et al. 2024 Heart disease and stroke statistics: a report of US and global data from the American Heart Association. *Circulation*. 2024;149(8):e347–e913. doi:10.1161/CIR.0000000000001209.

7. Tan A, Newey C, Falter F. Pulsatile perfusion during cardiopulmonary bypass: a literature review. *J Extra Corpor Technol*. 2022; 54(1):50–60. doi:10.1051/ject/202254050.
8. Holman WL, Timpa J, Kirklin JK. Origins and evolution of extracorporeal circulation: JACC historical breakthroughs in perspective. *J Am Coll Cardiol*. 2022;79(16):1606–1622. doi:10.1016/j.jacc.2022.02.027.
9. Jimenez-Aguilar R, Sanchez-Zauco N, Tiburcio-Felix R, et al. Effects of cardiopulmonary bypass on the development of lymphopenia and sepsis after cardiac surgery in children with congenital cardiopathy. *Exp Ther Med*. 2020;19:435–442.
10. Armstrong CM, Hollingworth S, Na K. Channels: history and structure. *Biophys J*. 2021;120(5):756–763. doi:10.1016/j.bpj.2021.01.013.
11. Huang P, Wang H, Ma D, et al. Serum sodium on admission affects postoperative in-hospital mortality in acute aortic dissection patients. *PLoS One*. 2021;16(12):e0261168. doi:10.1371/journal.pone.0261168.
12. Grim CCA, Termorshuizen F, Bosman RJ, et al. Association between an increase in serum sodium and in-hospital mortality in critically ill patients. *Crit Care Med*. 2021;49(12):2070–2079. doi:10.1097/CCM.0000000000005173.
13. Shirazy M, Omar I, Abduljabbar D, et al. Prevalence and prognostic impact of hypernatremia in sepsis and septic shock patients in the intensive care unit: a single centre experience. *J Crit Care Med (Targu Mures)*. 2020;6(1):52–58. doi:10.2478/jccm-2020-0001.
14. Zhi D, Lin J, Dong L, et al. Risk predictive role of hypernatremia for occurrence of sepsis-induced acute kidney injury. *Ann Palliat Med*. 2021;10(4):4705–4715. doi:10.21037/apm-21-792.
15. Ni H-B, Hu X-X, Huang X-F, et al. Risk factors and outcomes in patients with hypernatremia and sepsis. *Am J Med Sci*. 2016; 351(6):601–605. doi:10.1016/j.amjms.2016.01.027.
16. Lin C-Y, Chen Y-M, Tsai Y-H, et al. Association of hypernatremia with immune profiles and clinical outcomes in adult intensive care unit patients with sepsis. *Biomedicines*. 2022;10(9):10. doi:10.3390/biomedicines10092285.
17. De Freitas G, Gudur A, Vela-Ortiz M, Jodelka J, Livert D, Krishnamurthy M. Where there is sodium there may be sepsis. *J Commun Hosp Intern Med Perspect*. 2019;9(4):296–299. doi:10.1080/20009666.2019.1634407.
18. Kheetan M, Ogu I, Shapiro JI, Khitan ZJ. Acute and chronic hyponatremia. *Front Med (Lausanne)*. 2021;8:693738. doi:10.3389/fmed.2021.693738.
19. Ioannou P, Panagiotakis S, Tsagkaraki E, et al. Increased mortality in elderly patients admitted with hyponatremia: a prospective cohort study. *J Clin Med*. 2021;10(14):10. doi:10.3390/jcm10143059.
20. García-Sanz M-T, Martínez-Gestoso S, Calvo-Álvarez U, et al. Impact of hyponatremia on COPD exacerbation prognosis. *J Clin Med*. 2020;9(2):9. doi:10.3390/jcm9020503.
21. Castello LM, Gavelli F, Baldrighi M, et al. Hypernatremia and moderate-to-severe hyponatremia are independent predictors of mortality in septic patients at emergency department presentation: a sub-group analysis of the need-speed trial. *Eur J Intern Med*. 2021;83:21–27. doi:10.1016/j.ejim.2020.10.003.
22. Johnson AEW, Bulgarelli L, Shen L, et al. MIMIC-IV, a freely accessible electronic health record dataset. *Sci Data*. 2023;10(1):219. doi:10.1038/s41597-022-01899-x.
23. Zheng R, Qian S, Shi Y, Lou C, Xu H, Pan J. Association between triglyceride-glucose index and in-hospital mortality in critically ill patients with sepsis: analysis of the MIMIC-IV database. *Cardiovasc Diabetol*. 2023;22(1):307. doi:10.1186/s12933-023-02041-w.
24. Jin D, Jin S, Liu B, Ding Y, Zhou F, Jin Y. Association between serum sodium and in-hospital mortality among critically ill patients with spontaneous subarachnoid hemorrhage. *Front Neurol*. 2022;13:1025808. doi:10.3389/fneur.2022.1025808.
25. Martino M, Falcioni P, Giancola G, et al. Sodium alterations impair the prognosis of hospitalized patients with COVID-19 pneumonia. *Endocr Connect*. 2021;10(10):1344–1351. doi:10.1530/EC-21-0411.
26. Bie P. Mechanisms of sodium balance: total body sodium, surrogate variables, and renal sodium excretion. *Am J Physiol Regul Integr Comp Physiol*. 2018;315(5):R945–R962. doi:10.1152/ajpregu.00363.2017.
27. Ng PY, Cheung RYT, Ip A, Chan WM, Sin WC, Yap DY. A retrospective cohort study on the clinical outcomes of patients admitted to intensive care units with dysnatremia. *Sci Rep*. 2023; 13(1):21236. doi:10.1038/s41598-023-48399-5.
28. Liu J, Li J, Zhang Q, et al. Association between serum sodium levels within 24 h of admission and all-cause mortality in critically ill patients with non-traumatic subarachnoid hemorrhage: a retrospective analysis of the MIMIC-IV database. *Front Neurol*. 2023;14:1234080. doi:10.3389/fneur.2023.1234080.
29. Xia YM, Wang S, Wu WD, Liang JF. Association between serum sodium level trajectories and survival in patients with heart failure. *ESC Heart Fail*. 2023;10(1):255–263. doi:10.1002/ehf2.14187.
30. Chewcharat A, Thongprayoon C, Cheungpasitporn W, Mao MA, Thirunavukkarasu S, Kashani KB. Trajectories of serum sodium on in-hospital and 1-year survival among hospitalized patients. *Clin J Am Soc Nephrol*. 2020;15(5):600–607. doi:10.2215/CJN.12281019.
31. Danziger J, Zeidel ML. Osmotic homeostasis. *Clin J Am Soc Nephrol*. 2015;10(5):852–862. doi:10.2215/CJN.10741013.
32. Soliman R, Saad D, Abukhudair W, Abdeldayem S. The neurocognitive outcomes of hemodilution in adult patients undergoing coronary artery bypass grafting using cardiopulmonary bypass. *Ann Card Anaesth*. 2022;25(2):133–140. doi:10.4103/aca.aca_206_20.
33. Condello I, Nasso G, Speziale G. Brain and the rapid onset of hyponatremia during cardiopulmonary bypass. *JTCVS Open*. 2023;16:429. doi:10.1016/j.xjon.2022.12.006.
34. Smith BB, Mauermann WJ, Yalamuri SM, et al. Intraoperative fluid balance and perioperative outcomes after aortic valve surgery. *Ann Thorac Surg*. 2020;110(4):1286–1293. doi:10.1016/j.athoracsur.2020.01.081.
35. Mullane R, Fristoe L, Markin NW, et al. Zero balance ultrafiltration using dialysate during nationwide bicarbonate shortage: a retrospective analysis. *J Cardiothorac Surg*. 2019;14(1):163. doi:10.1186/s13019-019-0986-8.
36. Lin R, Du N, Feng J, et al. Postoperative hypernatremia is associated with worse brain injuries on EEG and MRI following pediatric cardiac surgery. *Front Cardiovasc Med*. 2023;10:1320231. doi:10.3389/fcvm.2023.1320231.
37. Li W, Li S, Yuan J, et al. Association between serum sodium and 28-day mortality in sepsis patients: a secondary data analysis from three large critical illness cohorts. *Ther Apher Dial*. 2024; 28(1):96–102. doi:10.1111/1744-9987.14066.