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Dysnatremia is an Independent Indicator of Mortality in Hospitalized Patients

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Data Collection B
Statistical Analysis C
Data Interpretation D
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Background: Dysnatremia is a risk factor for poor outcomes. We aimed to describe the prevalence and outcomes of various dysnatremia in hospitalized patients. High-risk patients must be identified to improve the prognosis of dysnatremia.

Material/Methods: This prospective study included all adult patients admitted consecutively to a university hospital between October 1, 2014 and September 30, 2015.

Result: All 90 889 patients were included in this study. According to the serum sodium levels during hospitalization, the incidence of hyponatremia and hypernatremia was 16.8% and 1.9%, respectively. Mixed dysnatremia, which was defined when both hyponatremia and hypernatremia happened in the same patient during hospitalization, took place in 0.3% of patients. The incidence of dysnatremia was different in various underlying diseases. Multiple logistic regression analyses showed that all kinds of dysnatremia were independently associated with hospital mortality. The following dysnatremias were strong predictors of hospital mortality: mixed dysnatremia (OR 22.344, 95% CI 15.709–31.783, *P*=0.000), hypernatremia (OR 13.387, 95% CI 10.642–16.840, *P*=0.000), and especially hospital-acquired (OR 16.216, 95% CI 12.588–20.888, *P*=0.000) and persistent (OR 22.983, 95% CI 17.554–30.092, *P*=0.000) hypernatremia. Hyponatremia was also a risk factor for hospital mortality (OR 2.225, 95% CI 1.857–2.667). However, the OR increased to 56.884 (95% CI 35.098–92.193) if hyponatremia was overcorrected to hypernatremia.

Conclusions: Dysnatremia was independently associated with poor outcomes. Hospital-acquired and persistent hypernatremia were strong risk factors for hospital mortality. Effective prevention and proper correction of dysnatremia in high-risk patients may reduce the hospital mortality.

MeSH Keywords: Acute Kidney Injury • Adolescent, Hospitalized • Hypernatremia • Hyponatremia • Mortality

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Background

Dysnatremia, a disorder of sodium concentration, is common not only in critically ill patients but also hospitalized patients, and it confers increased risk for adverse outcomes [1]. The prevalence of dysnatremia in the intensive care unit (ICU) ranges from 6.9 to 17.7%, and varies according to the time of onset, the threshold for diagnosis, and the population being assessed [2]. Except for hyponatremia in heart failure [3,4] and cirrhosis [5], there have been rare reports of dysnatremia in hospitalized patients. Substantial additional work is still required to determine the actual occurrence of dysnatremia in clinical settings.

Dysnatremia at admission, including hyponatremia [6] and hypernatremia [7], is an independent risk factor for mortality. Even slightly abnormal sodium levels are independently associated with poor outcomes [2,8]. However, hospital-acquired (HA) dysnatremia may be more lethal than community-acquired (CA) dysnatremia [9], and there may be significant differences in the clinical characteristics, outcomes, and economic burdens between them [10,11]. If iatrogenic pathogenic factors are avoided, and high-risk patients are identified and treated properly, the incidence of hospital-acquired dysnatremia can be decreased.

Although a recent study [12] showed that the impact of sodium correction on mortality was not significant in the presence of multiple comorbidities or severe diseases, the correction of dysnatremia is another important factor influencing the prognosis [13]. About 3.6 to 6.4% of ICU patients developed both hypo- and hypernatremia during hospitalization [14]; this mixed dysnatremia may be induced by improper correction and is associated with mortality rates of up to 42% [15]. Persistent hyponatremia was an independent predictor of death in heart failure patients, but whether persistent dysnatremia predicts higher mortality than improved ones has not been investigated in hospitalized patients.

This study aimed to describe the prevalence of dysnatremia in various underlying diseases, to evaluate the impact of different dysnatremia on outcomes, and to identify high-risk patients who may benefit from effective prevention and proper correction.

Material and Methods

Study design and data collection

This study prospectively enrolled all adult patients admitted consecutively to Zhongshan Hospital, Fudan University in Shanghai, China, between October 1, 2014 and September 30, 2015. All the data were collected from the electronic medical record database of this university hospital. The data included demographics, categories of underlying diseases, and laboratory values, including electrolyte status at admission and during hospitalization. The primary outcome was hospital mortality, while the incidence of acute kidney injury (AKI), the length of hospital stay, and hospital costs were also recorded as secondary outcomes. This study was approved by the Institutional Review Board of the Ethics Committee, Zhongshan Hospital, Fudan University, Shanghai China. As an observational survey, the requirement for informed consent was waived. The patient records and information were anonymized and de-identified before analysis.

Definitions and calculation

Hyponatremia and hypernatremia were defined according to the reference range provided by the Central Laboratory (normal range: 137~147mmol/L). Mixed dysnatremia was defined as both hyponatremia and hypernatremia during hospitalization in the same patient [16]. It was defined as "hypo- to hyper-" mixed dysnatremia if hyponatremia occurred before hypernatremia, and "hyper- to hypo-" if not. CA-dysnatremia was diagnosed when dysnatremia happened at admission, HA-dysnatremia was defined when dysnatremia occurred after 24 h of hospitalization [11], persistent dysnatremia was any degree of dysnatremia which persisted until discharge or death, and if not, improved dysnatremia was defined. We defined acute kidney injury (AKI) according to the Kidney Disease: Improving Global Outcomes (KDIGO) criteria [17]: an increase in serum creatinine (SCr) ≥26.5 μmol/L (0.3 mg/dl) within 48 h or an increase in SCr to ≥1.5 times baseline known or presumed to have occurred within the prior 7 days. We did not consider the urine output for unavailable data. All samples were analyzed in our Central Laboratory. The anion gap (AG) was calculated by the standard formula [18]: AG=$[Na^+]$–$[Cl^-]$–$[HCO_3^-]$, with an elevated AG defined as greater than or equal to 16 mmol/L. Calculated osmolality was=2×($[Na^+]$+$[K^+]$)+[glucose]+[urea], with the normal range from 280 to 310 mOsm/L. Hyperkalemia, hypokalemia, hyperchloremia, hypochloremia, hypercalcemia, hypocalcemia, hyperphosphatemia, hypophosphatemia, hypermagnesemia, hypomagnesemia, hyperuricemia, and hypouricemia were defined according to the reference ranges provided by the Central Laboratory.

Statistical methods

The data were analyzed using SPSS version 24.0 software (SPSS, Chicago, IL, USA). Continuous variables are presented as mean ± standard deviation (SD) if they were statistically normally distributed and categorical variables as numbers and percentages. For the continuous variables, data were analyzed using the *t* test, analysis of variance (ANOVA) (post hoc

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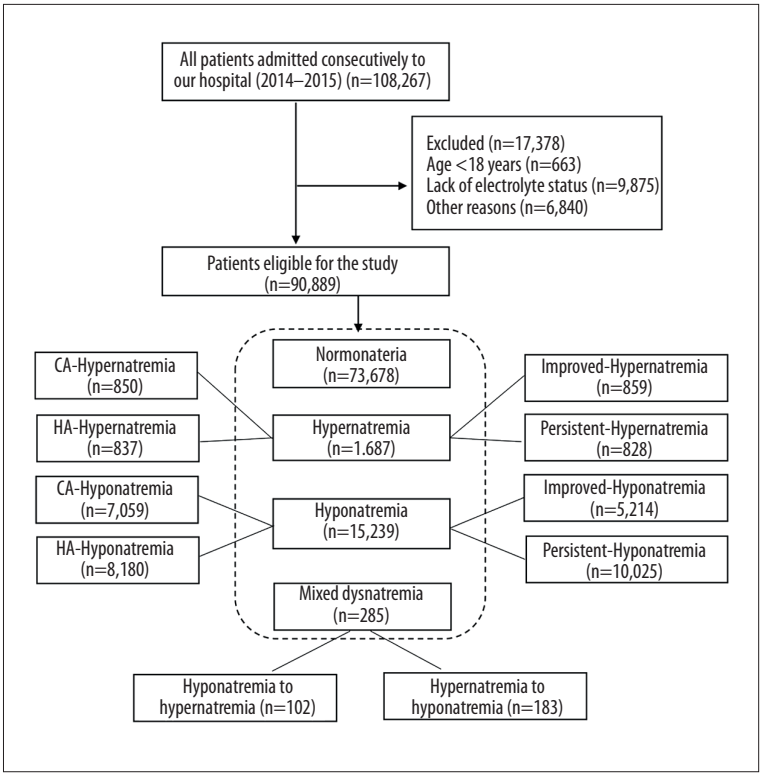

Figure 1. Flowchart of the study. CA – community-acquired; HA – hospital-acquired.

analysis of LSD between 2 groups), Mann-Whitney test, or Kruskal–Wallis test, depending on their distribution and number of variables. The chi-squared (χ^2) test was used to compare categorical variables. Kaplan-Meier survival curves stratified by dysnatremia categories were plotted and compared using a signed log-rank test. Multiple binary logistic regression models with the Wald forward stepwise method were used to assess the independent risk factors for hospital mortality, and the results are presented as odds ratios (ORs) and 95% confidence intervals (CIs). Three multiple logistic regression models were used according to different classification methods of dysnatremia, and further subgroup analyses were conducted. We also used multinomial logistic regression analysis to identify risk factors for developing HA-dysnatremia and persistent dysnatremia. Normonatremia was the reference of HA-dysnatremia and improved dysnatremia as the reference of persistent dysnatremia. A *P*-value <0.05 was deemed to indicate statistical significance.

Results

Demographic and baseline clinical characteristics

The study flowchart is presented in Figure 1. We included 90 889 patients in this study after the screening. The median age was 59 years old (inter-quartile range [IQR]: 49–67), and 60.9% of the included patients were males. The underlying diseases were cardiovascular (17.8%), cancer (14.7%), general surgery (11.9%), digestive (11.1%), urinary and renal (7.6%), cardiothoracic surgery (7.3%), pulmonary (6.8%), orthopedic surgery (3.8%), endocrine (3.0%), hematological (3.0%), neurological (2.9%), obstetrics and gynecology (2.3%), and others (7.9%). According to the serum sodium levels during hospitalization, the included subjects were divided into 4 groups: hyponatremia (16.8%), normonatremia (81.1%), hypernatremia (1.9%), and mixed dysnatremia (0.3%). In the hyponatremia group, 7059 patients (46.3%) developed hyponatremia at admission and 8180 patients (53.7%) after 24 h of hospitalization, while 5214 patients (34.2%) improved and 10 025 patients (65.8%) remained persistent. In the hypernatremia group, 1687 patients were divided into community-acquired (n=850, 50.4%) and hospital-acquired (n=837, 49.6%) hypernatremia, while 859 patients (50.9%) had improved hypernatremia and 828 patients (49.1%) had persistent hypernatremia. Mixed dysnatremia patients were also divided into "hypo- to hyper-" group (n=102) and "hyper- to hypo-" group (n=183) according to the sequence of dysnatremia.

Characteristics of the study subjects are listed in Tables 1–3. As described in Table 1, patients in the 3 dysnatremia groups were older, had higher white blood cell counts (WBC), blood urea nitrogen (BUN), serum uric acid (SUA), and AG, had lower albumin, hemoglobin, and carbon dioxide combining power (CO_2CP), and had more severe liver injury at admission than patients in the normonatremia group. Table 2 shows that

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Table 1. Baseline characteristics of patients according to dysnatremia during hospitalization.

Variable	All (n=90,889)	Normonatremia (n=73,678)	Hyponatremia (n=15,239)	Hypernatremia (n=1,687)	Mixed dysnatremia (n=285)	*P* value
Age, year	59.0 (49.0–67.0)	59.0 (48.0–67.0)	61.0 (51.0–70.0)#	64.0 (54.0–74.0)#	66.0 (56.0–74.0)#	0.000
>65, n (%)	27,680 (30.5)	21,135 (28.7)	5,649 (37.1)	751 (44.5)	145 (50.9)	0.000
Male sex, n (%)	55,383 (60.9)	43,966 (59.7)	10,267 (67.4)	968 (57.4)	182 (63.9)	0.000
BMI, kg/m²	23.2 (20.8–25.6)	23.4 (21.0–25.7)	22.7 (20.5–25.1)#	23.6 (21.4–25.9)	22.5 (20.7–25.5)	0.000
Underlying diseases, n (%)§						0.000
Cancer	13,324 (100.0)	8,926 (67.0)	4,177 (31.3)	188 (1.4)	33 (0.2)	
Pulmonary	6,164 (100.0)	4,890 (79.3)	1,151 (18.7)	108 (1.8)	15 (0.2)	
Cardiovascular	16,139 (100.0)	14,427 (89.4)	1,445 (9.0)	245 (1.5)	22 (0.1)	
Digestive	10,091 (100.0)	8,614 (85.4)	1,363 (13.5)	100 (1.0)	14 (0.1)	
Endocrine	2,707 (100.0)	2,426 (89.6)	215 (7.9)	66 (2.4)	0 (0.0)	
Hematological	2,753 (100.0)	2,319 (84.2)	380 (13.8)	45 (1.6)	9 (0.3)	
Neurological	2,681 (100.0)	2,113 (78.8)	393 (14.7)	149 (5.6)	26 (1.0)	
Urinary and renal	6,934 (100.0)	5,961 (86.0)	810 (11.7)	146 (2.1)	17 (0.2)	
Cardiothoracic surgery	6,633 (100.0)	4,075 (61.4)	2,156 (32.5)	304 (4.6)	98 (1.5)	
General surgery	10,857 (100.0)	8,609 (79.3)	2,045 (18.8)	172 (1.6)	31 (0.3)	
Orthopedic surgery	3,411 (100.0)	3,091 (90.6)	277 (8.1)	39 (1.1)	4 (0.1)	
Gynecological	2,056 (100.0)	1,731 (84.2)	302 (14.7)	23 (1.1)	0 (0.0)	
Others	7,139 (100.0)	6,496 (91.0)	525 (7.4)	102 (1.4)	16 (0.2)	
Clinical data at admission						
SBP, mmHg	122.0 (115.0–135.0)	122.0 (116.0–135.0)	120.0 (110.0–134.0)#	130.0 (119.0–140.0)#	128.0 (110.8–140.0)	0.000
DBP, mmHg	79.0 (70.0–80.0)	80.0 (70.0–80.0)	77.0 (70.0–80.0)#	80.0 (70.0–82.0)	75.0 (66.0–80.0)**	0.000
WBC, 10^9/L	6.0 (4.8–7.5)	5.9 (4.8–7.3)	6.4 (4.9–8.6)#	6.4 (5.0–8.6)#	7.0 (5.2–10.3)#	0.000
Hemoglobin, g/L	129.0 (116.0–141.0)	130.0 (118.0–142.0)	123.0 (106.0–137.0)#	125.0 (108.0–138.0)#	123.0 (100.5–135.5)#	0.000
AST, U/L	20.0 (16.0–28.0)	20.0 (16.0–26.0)	24.0 (17.0–42.0)#	21.0 (16.0–30.0)#	25.0 (18.0–44.0)#	0.000
ALT, U/L	19.0 (13.0–30.0)	18.0 (13.0–29.0)	21.0 (13.0–38.0)#	18.0 (12.0–29.0)	21.0 (13.0–34.0)#	0.000
TBIL, μmol/L	9.2 (6.6–12.9)	9.0 (6.6–12.5)	10.2 (7.0–15.9)#	9.7 (6.8–14.1)#	11.4 (7.5–19.2)#	0.000
Albumin, g/L	40.0 (37.0–43.0)	40.0 (37.0–43.0)	38.0 (33.0–41.0)#	38.0 (34.0–41.0)#	36.0 (30.0–40.0)#	0.000
Glucose, mmol/L	5.2 (4.7–6.2)	5.2 (4.7–6.2)	5.4 (4.8–6.8)#	5.2 (4.7–6.3)	5.5 (4.7–7.7)#	0.000
SCr, μmol/L	72.0 (61.0–86.0)	72.0 (61.0–86.0)	72.0 (60.0–88.0)	80.0 (65.0–105.0)#	78.0 (61.0–101.0)#	0.000
BUN, mmol/L	5.0 (4.0–6.2)	4.9 (4.0–6.1)	5.1 (3.9–6.6)#	5.9 (4.5–8.5)#	6.5 (4.9–10.4)#	0.000
SUA, mmol/L	304.0 (244.0–371.0)	306.0 (249.0–371.0)	286.0 (219.0–364.0)#	326.0 (255.0–415.0)#	317.0 (230.0–406.0)	0.000
Na, mmol/L	141.0 (139.0–143.0)	141.0 (140.0–143.0)	137.0 (135.0–141.0)#	148.0 (143.0–148.0)#	141.0 (138.0–145.0)	0.000
K, mmol/L	4.0 (3.8–4.3)	4.0 (3.8–4.3)	4.1 (3.8–4.4)#	4.0 (3.6–4.3)#	4.0 (3.7–4.4)	0.000
Cl, mmol/L	103.0 (101.0–105.0)	103.0 (101.0–105.0)	100.0 (97.0–103.0)#	107.0 (104.0–110.0)#	103.0 (99.0–107.0)	0.000
Mg, mmol/L	0.91 (0.85–0.97)	0.92 (0.86–0.97)	0.90 (0.83–0.96)#	0.93 (0.86–1.00)#	0.91 (0.83–0.99)	0.000
Ca, mmol/L	2.31 (2.22–2.39)	2.32 (2.23–2.40)	2.26 (2.14–2.36)#	2.27 (2.14–2.36)#	2.24 (2.11–2.34)#	0.000
P, mmol/L	1.13 (0.99–1.26)	1.13 (1.00–1.27)	1.09 (0.93–1.24)#	1.12 (0.93–1.27)#	1.08 (0.88–1.26)#	0.000
Osmolality, mOsm/L	301.6 (297.7–305.4)	302.0 (298.6–305.6)	297.0 (290.2–302.5)#	313.1 (305.1–317.2)#	303.9 (298.6–313.1)#	0.000
CO_2CP, mmol/L	24.0 (23.0–26.0)	25.0 (23.0–26.0)	24.0 (22.0–26.0)#	24.0 (22.0–26.0)**	23.0 (21.0–26.0)#	0.000
AG, mmol/L	14.0 (12.0–15.0)	14.0 (12.0–15.0)	14.0 (12.0–16.0)#	15.0 (13.0–17.0)#	15.0 (13.0–17.0)#	0.000

* $P<0.05$; ** $P<0.01$; # $P<0.001$; § Row N%. The normonatremia group served as the reference when comparing between two groups. BMI – body mass index; SBP – systolic blood pressure; DBP – diastolic blood pressure; WBC – white blood cell; ALT – alanine aminotransferase; AST – aspartate aminotransferase; TBIL – total bilirubin; SCr – serum creatinine; BUN – blood urea nitrogen; SUA – serum uric acid; CO_2CP – carbon dioxide combining power; AG – anion gap.

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Table 2. Characteristics of patients with community-acquired or hospital-acquired dysnatremia.

Variable	Hyponatremia			Hypernatremia		
	CA (n=7,059)	HA (n=8,180)	*P*	CA (n=850)	HA (n=837)	P
Age,year	63.0 (52.0–72.0)	60.0 (50.0–68.0)	0.000	64.0 (54.0–74.3)	63.0 (54.0–73.5)	0.515
>65, n (%)	2,969 (42.1)	2,680 (32.8)	0.000	386 (45.4)	365 (43.6)	0.456
Male sex, n (%)	4,845 (68.6)	5,422 (66.3)	0.002	496 (58.4)	472 (56.4)	0.415
BMI, kg/m2	22.4 (20.0–24.9)	22.8 (20.7–25.3)	0.010	23.4 (20.6–25.7)	23.6 (21.8–26.3)	0.731
Underlying diseases, n(%)[§]			0.000			0.000
Cancer	1,577 (37.8)	2,600 (62.2)	0.000	73 (38.8)	115 (61.2)	0.001
Pulmonary	956 (83.1)	195 (16.9)	0.000	66 (61.1)	42 (38.9)	0.021
Cardiovascular	802 (55.5)	643 (44.5)	0.000	180 (73.5)	65 (26.5)	0.000
Digestive	1,016 (74.5)	347 (25.5)	0.000	71 (71.0)	29 (29.0)	0.000
Endocrine	151 (70.2)	64 (29.8)	0.000	37 (56.1)	29 (43.9)	0.347
Hematological	211 (55.5)	169 (44.5)	0.000	28 (62.2)	17 (37.8)	0.107
Neurological	189 (48.1)	204 (51.9)	0.476	67 (45.0)	82 (55.0)	0.166
Urinary and renal	458 (56.5)	352 (43.5)	0.000	67 (45.9)	79 (54.1)	0.256
Cardiothoracic surgery	299 (13.9)	1,857 (86.1)	0.000	81 (26.6)	223 (73.4)	0.000
General surgery	728 (35.6)	1,317 (64.4)	0.000	74 (43.0)	98 (57.0)	0.042
Orthopedic surgery	137 (49.5)	140 (50.5)	0.291	22 (56.4)	17 (43.6)	0.446
Gynecological	139 (46.0)	163 (54.0)	0.917	13 (56.5)	10 (43.5)	0.553
Others	396 (75.4)	129 (24.6)	0.000	71 (69.6)	31 (30.4)	0.000
Clinical data at admission						
SBP, mmHg	120.0 (110.0–135.0)	120.0 (111.0–132.0)	0.596	130.0 (120.0–140.0)	130.0 (118.0–140.0)	0.825
DBP, mmHg	76.0 (70.0–80.0)	78.0 (70.0–80.0)	0.000	80.0 (70.0–81.0)	80.0 (69.0–82.0)	0.109
WBC, 10^9/L	7.1 (5.2–9.8)	6.0 (4.7–7.6)	0.000	6.3 (4.8–8.2)	6.6 (5.2–8.9)	0.002
Hemoglobin, g/L	117.0 (99.0–132.0)	128.0 (113.0–140.0)	0.000	126.0 (111.0–139.0)	123.0 (106.0–138.0)	0.025
AST, U/L	26.0 (17.0–49.0)	23.0 (17.0–37.0)	0.000	20.0 (16.0–29.0)	21.0 (16.0–31.0)	0.296
ALT, U/L	22.0 (13.0–42.0)	21.0 (13.0–36.0)	0.000	18.0 (13.0–29.0)	18.0 (12.0–30.0)	0.421
TBIL, μmol/L	10.3 (6.6–18.0)	10.1 (7.2–14.7)	0.000	9.4 (6.9–13.1)	10.2 (6.8–15.2)	0.009
Albumin, g/L	36.0 (31.0–40.0)	39.0 (35.0–42.0)	0.000	38.0 (34.0–41.0)	37.0 (33.0–40.0)	0.002
Glucose, mmol/L	5.9 (5.0–7.9)	5.2 (4.7–6.2)	0.000	5.2 (4.7–6.2)	5.2 (4.7–6.4)	0.277
SCr, μmol/L	71.0 (58.0–90.0)	73.0 (61.0–87.0)	0.000	80.0 (65.0–101.0)	79.0 (65.0–109.0)	0.526
BUN, mmol/L	5.0 (3.8–7.0)	5.1 (4.0–6.4)	0.455	5.6 (4.4–8.3)	6.1 (4.6–8.8)	0.081
SUA, mmol/L	267.0 (195.0–356.0)	298.0 (239.0–369.0)	0.000	328.0 (256.0–412.0)	323.5 (255.0–417.3)	0.748
Na, mmol/L	135.0 (133.0–136.0)	140.0 (139.0–142.0)	0.000	148.0 (148.0–150.0)	143.0 (141.0–144.0)	0.000
K, mmol/L	4.1 (3.8–4.4)	4.1 (3.8–4.3)	0.000	4.0 (3.7–4.3)	3.9 (3.6–4.2)	0.018
Cl, mmol/L	97.0 (94.0–99.0)	102.0 (100.0–104.0)	0.000	109.0 (107.0–111.0)	104.0 (102.0–106.0)	0.000
Mg, mmol/L	0.89 (0.82–0.96)	0.90 (0.84–0.97)	0.000	0.94 (0.87–1.01)	0.92 (0.85–0.99)	0.000
Ca, mmol/L	2.23 (2.11–2.35)	2.28 (2.17–2.37)	0.000	2.28 (2.18–2.37)	2.26 (2.11–2.36)	0.001
P, mmol/L	1.05 (0.88–1.22)	1.12 (0.97–1.26)	0.000	1.12 (0.95–1.26)	1.11 (0.92–1.29)	0.880
Osmolality, mOsm/L	289.0 (285.2–293.4)	300.7 (297.0–304.4)	0.000	316.2 (314.1–321.1)	305.2 (301.3–309.7)	0.000
CO_2CP, mmol/L	23.0 (21.0–25.0)	24.0 (22.0–26.0)	0.000	25.0 (23.0–27.0)	24.0 (22.0–26.0)	0.000
AG, mmol/L	14.0 (12.0–16.0)	14.0 (12.0–16.0)	0.000	15.0 (13.0–16.0)	15.0 (13.0–17.0)	0.866

[§] Row N%. CA – community-acquired; HA – hospital-acquired; BMI – body mass index; SBP – systolic blood pressure; DBP – diastolic blood pressure; WBC – white blood cell; ALT – alanine aminotransferase; AST – aspartate aminotransferase; TBIL – total bilirubin; SCr – serum creatinine; BUN – blood urea nitrogen; SUA – serum uric acid; CO_2CP – carbon dioxide combining power; AG – anion gap.

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Table 3. Characteristics of selected patients with improved, persistent and mixed dysnatremia.

Variable	Hyponatremia			Hypernatremia			Mixed dysnatremia		
	Improved (n=5,214)	Persistent (n=10,025)	*P*	Improved (n=859)	Persistent (n=828)	*P*	Hypo to hyper (n=102)	Hyper to hypo (n=183)	*P*
Age,year	61.0 (50.0–70.0)	61.0 (52.0–70.0)	0.028	63.3±15.1	63.4±15.5	0.910	70.4±15.6	61.8±14.8	0.000
>65, n (%)	1,918 (36.8)	3,731 (37.2)	0.601	375 (43.7)	376 (45.4)	0.468	67 (65.7)	78 (42.6)	0.000
Male sex, n (%)	3,348 (64.2)	6,919 (69.0)	0.000	476 (55.4)	492 (59.4)	0.096	65 (63.7)	117 (63.9)	0.972
BMI, kg/m²	22.9±3.7	22.9±3.9	0.743	23.3±4.4	24.1±3.7	0.214	21.8±3.9	23.6±3.5	0.249
Underlying diseases, n (%)[§]			0.000			0.000			0.000
Cancer	1,391 (33.3)	2,786 (66.7)	0.144	124 (66.0)	64 (34.0)	0.000	12 (36.4)	21 (63.6)	0.942
Pulmonary	292 (25.4)	859 (74.6)	0.000	41 (38.0)	67 (62.0)	0.005	6 (40.0)	9 (60.0)	0.727
Cardiovascular	495 (34.3)	950 (65.7)	0.972	99 (40.4)	146 (59.6)	0.000	5 (22.7)	17 (77.3)	0.183
Digestive	324 (23.8)	1039 (76.2)	0.000	27 (27.0)	73 (73.0)	0.000	7 (50.0)	7 (50.0)	0.255
Endocrine	113 (52.6)	102 (47.4)	0.000	38 (57.6)	28 (42.4)	0.270	0	0	–
Hematological	146 (38.4)	234 (61.6)	0.080	14 (31.1)	31 (68.9)	0.007	5 (55.6)	4 (44.4)	0.209
Neurological	165 (42.0)	228 (58.0)	0.001	80 (53.7)	69 (46.3)	0.478	14 (53.8)	12 (46.2)	0.044
Urinary and renal	325 (40.1)	485 (59.9)	0.000	49 (33.6)	97 (66.4)	0.000	11 (64.7)	6 (35.3)	0.010
Cardiothoracic surgery	700 (32.5)	1,456 (67.5)	0.065	222 (73.0)	82 (27.0)	0.000	17 (17.3)	81 (82.7)	0.000
General surgery	885 (43.3)	1,160 (56.7)	0.000	113 (65.7)	59 (34.3)	0.000	11 (35.5)	20 (64.5)	0.970
Orthopedic surgery	101 (36.5)	176 (63.5)	0.426	11 (28.2)	28 (71.8)	0.004	3 (75.0)	1 (25.0)	0.099
Gynecological	84 (27.8)	218 (72.2)	0.018	15 (65.2)	8 (34.8)	0.167	0	0	–
Others	193 (36.8)	332 (63.2)	0.211	26 (25.5)	76 (74.5)	0.000	11 (68.8)	5 (31.2)	0.005
Clinical data at admission									
SBP, mmHg	124.3±17.8	124.2±17.4	0.719	129.0±20.1	129.4±19.5	0.701	127.3±19.3	129.9±25.2	0.503
DBP, mmHg	75.3±11.0	75.9±12.4	0.004	75.7±11.9	78.5±32.7	0.033	74.1±12.1	75.0±13.6	0.624
WBC, 10^9/L	6.5 (5.0–8.9)	6.3 (4.8–8.4)	0.000	8.0±11.1	7.6±4.6	0.325	8.4 (5.8–12.4)	6.4 (5.0–9.1)	0.001
Hemoglobin, g/L	120.6±24.3	120.2±23.8	0.260	121.2±25.1	120.5±26.0	0.553	108.8±27.2	121.4±27.2	0.000
AST, U/L	23.0 (17.0–39.0)	24.0 (17.0–43.0)	0.000	21.0 (16.0–31.0)	20.0 (16.0–29.0)	0.035	118.1±575.9	65.5±241.1	0.283
ALT, U/L	21.0 (13.0–37.3)	22.0 (13.0–39.0)	0.008	47.9±334.6	36.1±84.4	0.321	46.3±83.6	39.8±77.1	0.512
TBIL, μmol/L	10.1 (6.9–15.6)	10.3 (7.0–16.1)	0.045	14.9±27.9	15.3±41.8	0.795	10.5 (6.9–18.9)	11.7 (8.3–19.5)	0.427
Albumin, g/L	38.0 (33.0–41.0)	38.0 (33.0–41.0)	0.204	37.0 (34.0–40.0)	38.0 (34.0–41.0)	0.106	32.9±6.2	36.3±6.1	0.000
Glucose, mmol/L	6.5±3.4	6.5±3.2	0.277	6.1±2.8	6.1±2.7	0.978	7.0±3.3	6.6±3.3	0.418
SCr, μmol/L	73.0 (60.0–89.0)	72.0 (60.0–88.0)	0.006	79.0 (65.0–106.0)	80.0 (65.0–104.0)	0.641	75.5 (58.2–110.3)	79.0 (62.0–100.0)	0.509
BUN, mmol/L	5.0 (3.8–6.7)	5.1 (3.9–6.6)	0.873	5.9 (4.5–8.6)	5.8 (4.5–8.5)	0.629	9.8±9.1	8.6±7.2	0.222
SUA, mmol/L	285.0 (217.0–366.0)	286.0 (220.0–363.0)	0.664	346.1±137.1	351.2±145.5	0.468	307.3±166.1	348.1±147.8	0.034
Na, mmol/L	138.0±4.2	137.1±4.5	0.000	145.5±4.9	146.8±5.0	0.000	135.9±4.6	144.4±4.6	0.000
K, mmol/L	4.1 (3.8–4.3)	4.1 (3.8–4.4)	0.000	3.9±0.6	4.0±0.6	0.028	4.2±0.7	4.0±0.5	0.005
Cl, mmol/L	101.0 (97.0–103.0)	100.0 (96.0–103.0)	0.000	106.4±5.7	107.4±5.7	0.000	98.4±5.4	105.7±5.5	0.000
Mg, mmol/L	0.90 (0.83–0.97)	0.90 (0.83–0.96)	0.354	0.93±0.14	0.95±0.15	0.009	0.92 (0.83–1.00)	0.90 (0.83–0.98)	0.418
Ca, mmol/L	2.24 (2.12–2.35)	2.27 (2.16–2.37)	0.000	2.22±0.20	2.27±0.22	0.000	2.20±0.19	2.22±0.18	0.548
P, mmol/L	1.08 (0.89–1.24)	1.10 (0.94–1.24)	0.000	1.10±0.34	1.15±0.42	0.029	1.07±0.39	1.11±0.38	0.383
Osmolality, mOsm/L	297.5±9.4	295.7±9.6	0.000	312.3±13.4	315.4±13.7	0.000	297.0 (290.9–300.7)	308.0 (302.1–316.9)	0.000
CO_2CP, mmol/L	24.0 (22.0–26.0)	24.0 (22.0–26.0)	0.000	23.1±5.5	22.6±6.2	0.179	22.5±4.3	23.7±4.0	0.019
AG, mmol/L	14.0 (12.0–16.0)	14.0 (12.0–16.0)	0.000	14.9±3.8	15.1±4.1	0.187	15.2±4.1	15.2±3.5	0.995

[§] Row N%. BMI – body mass index; SBP – systolic blood pressure; DBP – diastolic blood pressure; WBC – white blood cell; ALT – alanine aminotransferase; AST – aspartate aminotransferase; TBIL – total bilirubin; SCr – serum creatinine; BUN – blood urea nitrogen; SUA – serum uric acid; CO_2CP – carbon dioxide combining power; AG – anion gap.

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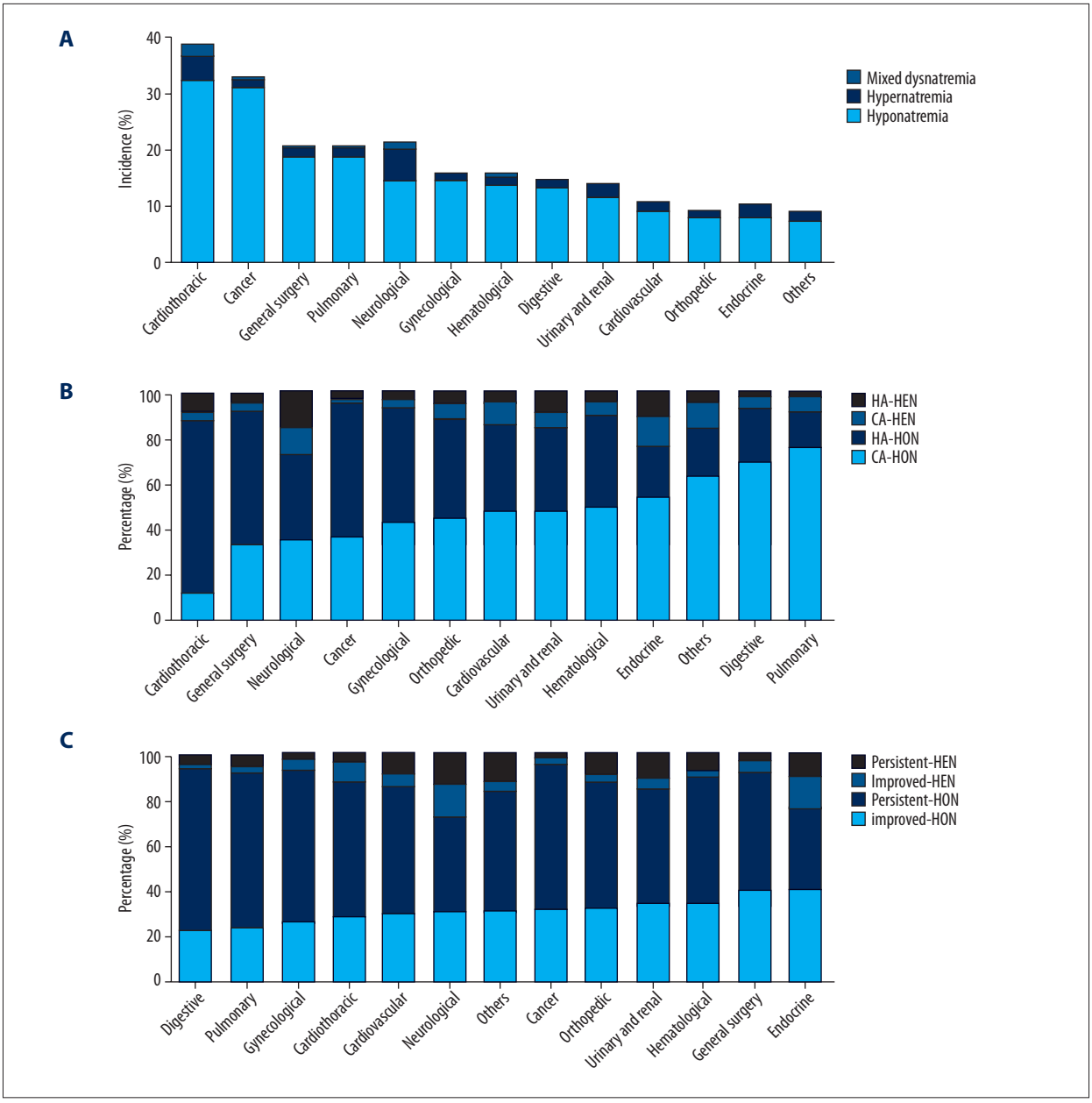

Figure 2. Incidence or percentage of dysnatremia in various underlying diseases. (**A**) The incidence of hyponatremia, hypernatremia, and mixed dysnatremia; (**B**) Percentage of community-acquired or hospital-acquired dysnatremia; (**C**) Percentage of improved or persistent dysnatremia. CA – community-acquired; HA – hospital-acquired; HON – hyponatremia; HEN – hypernatremia.

patients in the HA-hyponatremia were younger, had a higher body mass index (BMI), hemoglobin, albumin, SCr, and SUA, had lower WBC and glucose, and had better liver function than patients in the CA-hyponatremia group. HA-hypernatremia patients were younger, had higher WBC, lower hemoglobin, albumin, and CO_2CP, and had more severe liver injuries at admission than CA-hypernatremia patients. Table 3 shows that the patients with persistent hyponatremia were older, more were males, and more had higher aspartate aminotransferase (AST) and total bilirubin (TBIL) and lower WBC, SCr, serum sodium, and osmolality at admission than the patients with improved hyponatremia. Compared with the improved hypernatremia group, patients in the persistent hypernatremia group had higher serum sodium, chlorine, magnesium, calcium, phosphorus, and osmolality, and had lower AST at admission. Patients in the "hypo- to hyper-" mixed dysnatremia group were older, had higher WBC and K^+, and had lower hemoglobin, albumin, SUA, Na^+, Cl^-, osmolality, and CO_2CP at admission than the patients in the "hyper- to hypo-" group.

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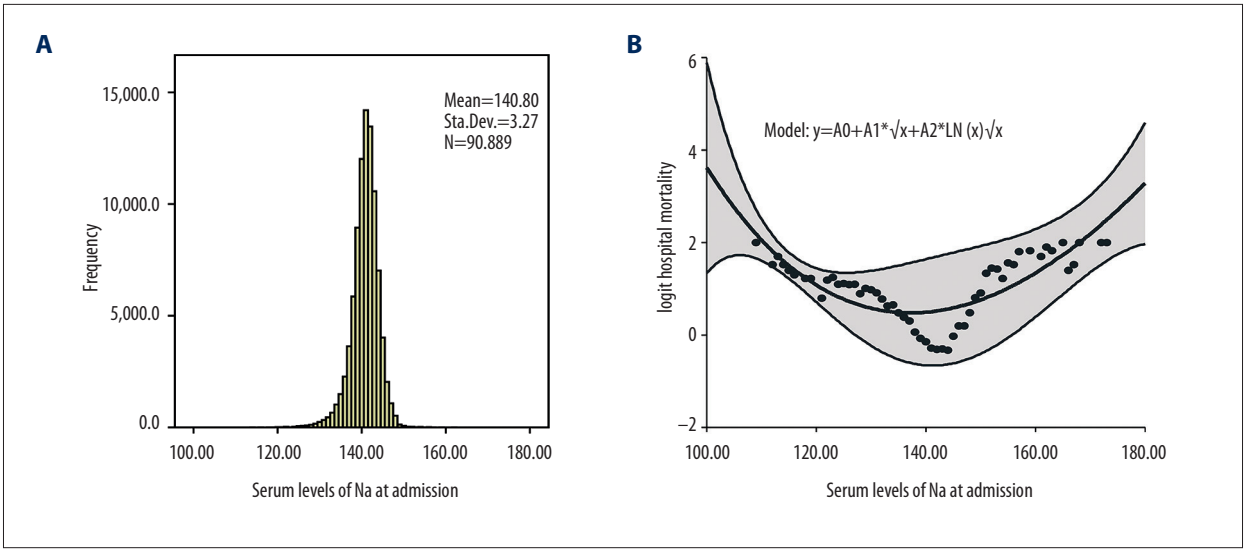

Figure 3. The histogram of the serum sodium levels at admission and its relation to hospital mortality. (**A**) The histogram of serum sodium levels at admission; (**B**) Non-linear relationship between baseline serum sodium levels and the predicted probability of hospital mortality. The range area indicates 95% confidence intervals.

Prevalence of dysnatremia in various underlying diseases

The prevalence of dysnatremia in different underlying diseases is shown in Figure 2, and detailed information is provided in Tables 1–3. The top 4 underlying diseases of hyponatremia were cardiothoracic surgery (32.5%), cancer (31.3%), general surgery (18.8%), and pulmonary diseases (18.7%), while the top 4 ones of hypernatremia were neurological (5.6%), cardiothoracic surgery (4.6%), endocrine (2.4%), and urinary and renal diseases (2.1%). Mixed dysnatremia most often occured in patients with cardiothoracic surgery (1.5%) and neurological diseases (1.0%). The incidence rates of HA-hyponatremia and HA-hypernatremia were higher than the rates of corresponding CA-dysnatremia in patients with cardiothoracic surgery, general surgery, and cancer, while the rates were lower in patients with pulmonary, digestive, and cardiovascular diseases. There were fewer patients with HA-hyponatremia than CA-hyponatremia in endocrine, hematological, and urinary and renal diseases. Hyponatremia was more likely to be persistent than become improved in patients with digestive, pulmonary, gynecological, neurological, general surgery, and urinary and renal diseases, while hypernatremia was more likely to be persistent than become improved in patients with urinary and renal, orthopedic surgery, cardiovascular, hematological, pulmonary, and digestive diseases. All the above differences were statistically significant. "Hypo- to hyper-" mixed dysnatremia was more likely to occur in neurological and urinary and renal diseases than "hyper- to hypo-" mixed dysnatremia, and the reverse was true in cardiothoracic surgery.

Outcomes associated with dysnatremia

The frequency of sodium levels at admission and its relation to hospital mortality are shown in Figure 3. The graph also shows the U-shaped relationship, the fitting curve, and equation. As demonstrated in Figure 4 and Supplementary Table 1, hyponatremia, hypernatremia, and mixed dysnatremia increased hospital mortality, the incidence of AKI, the length of hospital stay, and hospital costs when compared with the normonatremia group. Also, hospital mortalities and AKI were higher, the length of hospital stay was longer, and hospital costs were higher in HA-dysnatremia groups than in the corresponding CA-dysnatremia groups, except that hospital mortality in the HA-hyponatremia group was lower than in the CA-hyponatremia group. Hospital mortalities and AKI were lower, the length of hospital stay was shorter, and hospital costs were lower in persistent dysnatremia groups than in the corresponding improved dysnatremia groups, except that hospital mortality in the persistent hypernatremia group was higher than in the improved hypernatremia group. In addition, the hospital mortality in the "hypo- to hyper-" mixed dysnatremia group was greater than in the "hyper- to hypo-" group (79.7% *vs.* 20.3%, respectively, P=0.000). All differences were statistically significant. Survival analysis (Figure 5) shows the differences in hospital survival.

Multiple logistic regression analyses of risk factors for hospital mortality

We further conducted multiple logistic regression analyses to identify dysnatremia and other independent risk factors for hospital mortality in 3 models, and the results are shown in Tables 4 and 5. In all 3 models, mixed dysnatremia was

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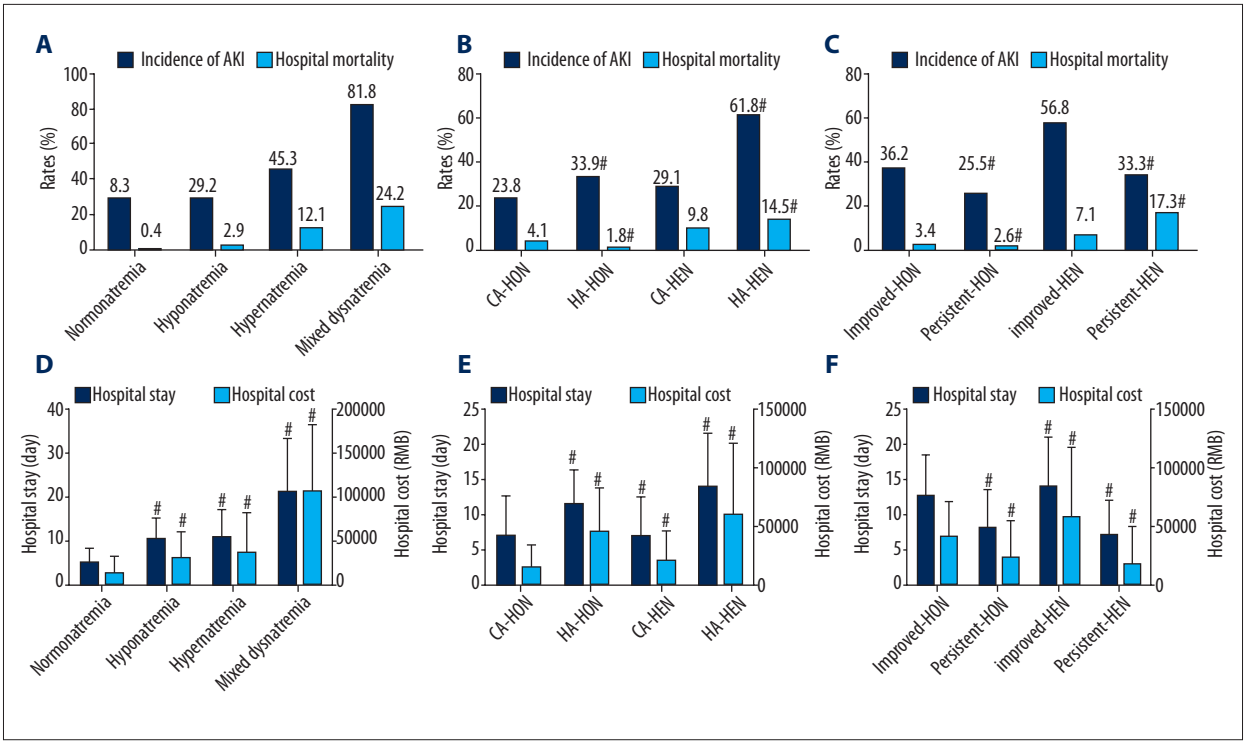

Figure 4. Outcomes of hospitalized patients with dysnatremia. (**A–C**) The incidence of acute kidney injury and hospital mortality; (**D–F**) The length of hospital stay and hospital cost. AKI – acute kidney injury; CA – community-acquired; HA – hospital-acquired; HON – hyponatremia; HEN – hypernatremia; RMB – Ren Min Bi. # $P<0.01$ compared with normonatremia (**D**), CA-dysnatremia (**B, E**) or improved dysnatremia (**C, F**).

identified as the leading independent risk factor for hospital mortality (OR: 22.344 to 22.387, $P=0.000$). The results from Model 1 revealed that hypernatremia was a stronger predictor of hospital mortality than hyponatremia (OR [95% CI]: 13.387 [10.642–16.840] *vs.* 2.225 [1.857–2.667]). The OR of HA-hypernatremia for mortality was nearly twice that of CA-hypernatremia (OR [95% CI]: 16.216 [12.588–20.888] *vs.* 8.827 [6.141–12.689]), while the OR of HA-hyponatremia for mortality was slightly higher than that of CA-hyponatremia (OR [95% CI]: 16.216 [12.588–20.888] *vs.* 8.827 [6.141–12.689]). The OR of persistent hypernatremia for mortality was 3 times higher than that of improved hypernatremia (OR [95% CI]: 22.983 [17.554–30.092] *vs.* 6.830 [4.903–9.516]). However, the OR of persistent hyponatremia for mortality was lower than that of improved hyponatremia (OR [95% CI]: 2.023 [1.653–2.476] *vs.* 2.563 [2.062–3.186]). In addition, the OR of "hypo- to hyper-" mixed dysnatremia for mortality was higher than that of the "hyper- to hypo-" group (OR [95% CI]: 56.884 [35.098–92.193] *vs.* 6.629 [3.499–12.557]).

In addition to dysnatremia, 16 risk factors for hospital mortality were also identified, including older age, male sex, BMI <18.5 kg/m^2, DBP at admission >90 mmHg, and laboratory variables at admission (hypochloremia, CO_2CP >29 mmol/L, AG >16 mmol/L, increased ALT and TBIL, decreased albumin and hemoglobin, WBC>12×10^9/L, increased BUN, lower SCr, hypouricemia, and hyperuricemia).

Subgroup analyses

To identify the high-risk patients with poor outcomes, we also conducted subgroup analyses of dysnatremia as risk factors for hospital mortality. Supplementary Table 2 shows that age ≤65 years, BMI <18.5 kg/m^2, the incidence of AKI, and length of hospital stay ≤30 days increased the ORs of hypernatremia for mortality compared to other subgroups. Different ORs of dysnatremia for mortality were also observed across various underlying diseases. The top 3 ORs of hypernatremia were from cardiothoracic surgery (OR 27.029, 95% CI 12.388–58.976, $P=0.000$), urinary and renal (OR 17.257, 95% CI 8.551–34.826, $P=0.000$), and neurological diseases (OR 16.821, 95%CI 8.191–34.544, $P=0.000$). Supplementary Table 3 shows that the ORs of HA-hypernatremia were higher in these patients with age ≤65 years, male sex, BMI <18.5 kg/m^2, AKI, and length of hospital stay ≤30 days than in other corresponding subgroups. The different ORs of CA- and HA-dysnatremia for mortality across various underlying diseases are also displayed, and both HA-hyponatremia and HA-hypernatremia increased the risk of death in patients with digestive diseases compared to other diseases according to the ORs (21.924 [4.875–98.609]

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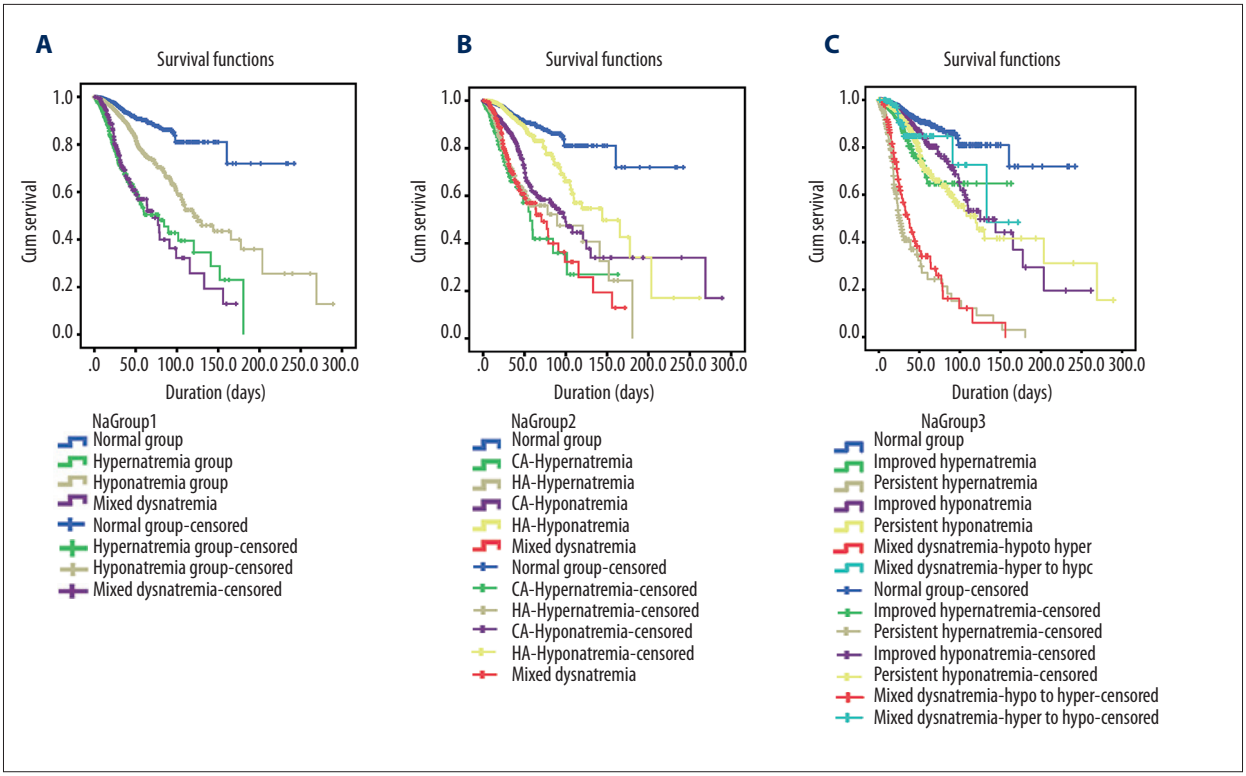

Figure 5. Kaplan-Meier survival curves stratified by dysnatremia categories. (**A**) Survival curve of hyponatremia, normonatremia, hypernatremia and mixed dysnatremia; (**B**) Survival curve of community-acquired *vs.* hospital-acquired dysnatremia; (**C**) Survival curve of improved *vs.* persistent dysnatremia, "hypo to hyper" *vs.* "hyper to hypo" mixed dysnatremia. The vertical lines represent censored subjects. The follow-up duration is different for each subject because it is censored at the end of hospitalization. CA – community-acquired; HA – hospital-acquired.

Table 4. Final multiple logistic regression analysis of dysnatremia as independent risk factors for hospital mortality.

Variable	Multiple logistic analysis		
	OR (95%CI)		*P* value
Model 1§			
Hyponatremia	2.225	(1.857–2.667)	0.000
Hypernatremia	13.387	(10.642–16.840)	0.000
Mixed dysnatremia	22.344	(15.709–31.783)	0.000
Model 2§			
CA-hyponatremia	1.950	(1.552–2.451)	0.000
HA-hyponatremia	2.567	(2.087–3.156)	0.000
CA-hypernatremia	8.827	(6.141–12.689)	0.000
HA-hypernatremia	16.216	(12.588–20.888)	0.000
Mixed dysnatremia	21.387	(14.992–30.510)	0.000
Model 3§			
Improved hyponatremia	2.561	(2.062–3.182)	0.000
Persistent hyponatremia	2.016	(1.649–2.465)	0.000
Improved hypernatremia	6.755	(4.847–9.413)	0.000
Persistent hypernatremia	22.292	(17.041–29.162)	0.000
"Hypo to hyper" mixed dysnatremia	56.884	(35.098–92.193)	0.000
"Hyper to hypo" mixed dysnatremia	6.629	(3.499–12.557)	0.000

§ Normonatremia as the reference. CA – community acquired; HA – hospital acquired; OR – odds ratio; CI – confidence interval.

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Table 5. Final multiple logistic regression analysis of other independent risk factors for hospital mortality.

Variable	Model 1		Model 2		Model 3	
	OR (95%CI)	*P* value	OR (95%CI)	*P* value	OR (95%CI)	*P* value
Age, per year increase	1.048 (1.043–1.054)	0.000	1.049 (1.043–1.054)	0.000	1.048 (1.043–1.054)	0.000
Male sex	1.197 (1.035–1.384)	0.015	1.197 (1.035–1.384)	0.015	1.199 (1.037–1.388)	0.015
BMI <18.5 kg/m^2§	3.155 (1.966–5.063)	0.000	3.076 (1.912–4.949)	0.000	3.240 (2.018–5.201)	0.000
DBP >90 mmHg§	1.470 (1.120–1.930)	0.006	1.473 (1.121–1.934)	0.005	1.468 (1.118–1.927)	0.006
Hypochloridemia§	1.998 (1.668–2.393)	0.000	2.179 (1.785–2.659)	0.000	2.003 (1.671–2.402)	0.000
CO2CP >29 mmol/L§	1.902 (1.452–2.491)	0.000	1.927 (1.467–2.533)	0.000	1.898 (1.447–2.490)	0.000
AG >16 mmol/L§	1.717 (1.430–2.062)	0.000	1.698 (1.412–2.043)	0.000	1.720 (1.432–2.067)	0.000
ALT, per 50U/L increase	1.030 (1.015–1.046)	0.000	1.030 (1.014–1.046)	0.000	1.031 (1.015–1.047)	0.000
TBIL, per 20 μmol/L increase	1.038 (1.015–1.046)	0.001	1.037 (1.014–1.046)	0.001	1.039 (1.016–1.063)	0.001
Albumin, per 5 g/L decrease	1.418 (1.328–1.514)	0.000	1.424 (1.334–1.521)	0.000	1.426 (1.335–1.523)	0.000
Hemoglobin (90–119 g/L)§	1.451 (1.228–1.715)	0.000	1.454 (1.230–1.719)	0.000	1.446 (1.222–1.710)	0.000
Hemoglobin (60–89 g/L)§	1.871 (1.491–2.348)	0.000	1.893 (1.508–2.376)	0.000	1.865 (1.484–2.343)	0.000
Hemoglobin (<60 g/L)§	4.174 (2.961–5.883)	0.000	4.264 (3.027–6.007)	0.000	4.099 (2.902–5.791)	0.000
WBC >12.0×10^9/L§	2.252 (1.874–2.705)	0.000	2.257 (1.878–2.712)	0.000	2.246 (1.868–2.701)	0.000
BUN, per 10 mg/dl increase	1.281 (1.215–1.351)	0.000	1.277 (1.211–1.347)	0.000	1.282 (1.067–1.540)	0.000
SCr, per 0.5 mg/dl increase	0.935 (0.909–0.961)	0.000	0.932 (0.906–0.959)	0.000	0.932 (0.906–0.959)	0.000
Hypouricemia§	1.296 (1.079–1.555)	0.005	1.299 (1.082–1.560)	0.005	1.282 (1.067–1.540)	0.008
Hyperuricemia§	1.536 (1.279–1.846)	0.000	1.523 (1.267–1.830)	0.000	1.546 (1.285–1.859)	0.000

§ Normal range as the reference. BMI – body mass index; DBP – diastolic blood pressure; CO_2CP – carbon dioxide combining power; AG – anion gap; ALT – alanine aminotransferase; TBIL – total bilirubin; WBC – white blood cell; BUN – blood urea nitrogen; SCr – serum creatinine; OR – odds ratio; CI – confidence interval.

vs. 55.185 [13.645–223.184], respectively). Supplementary Table 4 shows that age ≤65 years, BMI <18.5 kg/m^2, presence of AKI, and length of hospital stay ≤30 days elevated the ORs of persistent hyponatremia for mortality compared to the corresponding subgroups. BMI <18.5 kg/m^2, and length of hospital stay ≤30 days also increased the ORs of persistent hypernatremia for mortality. The top 3 ORs of persistent hyponatremia were from hematological diseases, cancer, and cardiothoracic surgery (OR: 29.114, 11.343, and 10.885, respectively), while the top 3 ORs of persistent hypernatremia were from digestive, hematological, and urinary and renal diseases (OR: 50.959, 37.481, and 32.258, respectively).

Risk factors for developing HA-dysnatremia and persistent dysnatremia

As before, if HA-dysnatremia is prevented and dysnatremia is corrected in a timely and appropriate manner, in-hospital mortality can be reduced significantly. Therefore, we further conducted multinomial logistic regression analysis. Patients with cancer, cardiothoracic surgery, general surgery, and neurological diseases were prone to develop both HA-hyponatremia and HA-hypernatremia, while patients with cardiovascular, hematological, and gynecological diseases and orthopedic surgery were more likely to develop HA-hyponatremia, and patients with endocrine diseases were high-risk patients for HA-hypernatremia. Hyponatremia was prone to continue until discharge or death in patients with cardiovascular surgery and pulmonary, digestive, and gynecological diseases. Other risk factors were also identified and are shown in Supplementary Table 5.

Discussion

In this observational study, we found that dysnatremia was common in hospitalized patients and was independently

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associated with poor outcomes, including higher hospital mortality and incidence of AKI, longer length of hospital stay, and higher hospital costs than in patients with normonatremia. Nearly half of dysnatremia happened during hospitalization, while half of hypernatremia and one-third of hyponatremia continued until discharge or death. Multiple logistic regression revealed that all kinds of dysnatremia were independently associated with in-hospital mortality, and mixed dysnatremia (especially "hypo- to hyper-" ones), hypernatremia (especially HA- and persistent hypernatremia), were strong predictors of mortality. Further subgroup analyses proved that the effects of dysnatremia on in-hospital mortality were influenced by age, sex, BMI, AKI, length of hospital stay, and underlying diseases. Patients with cardiothoracic surgery, general surgery, cancer, and neurological diseases were more likely to develop HA-dysnatremia. Other independent risk factors for in-hospital mortality and predictors of HA- and persistent dysnatremia were also identified.

Hyponatremia is the most common electrolyte disorder encountered in clinical practice [19]. The reported prevalence of hyponatremia is determined by various factors, including the definition of hyponatremia, the time of onset, the clinical setting, and the patient population. The incidence of hyponatremia has been reported to be 14.5% on initial measurement in hospitalized patients [20]. Our study found that the total incidence of hyponatremia was 16.8% in hospitalized patients, 46.3% had hyponatremia at admission and 53.7% had it after 24 h of hospitalization, indicating that the incidence of HA-hyponatremia may be underestimated. Timely correction of hyponatremia may be another factor affecting outcomes. Therefore, hyponatremia patients were also divided into improved and persistent groups according to the serum sodium levels before discharge or at death. We found that 34.2% had improved hyponatremia, and 65.8% had persistent hyponatremia. A recent study based on the general population [21] reported that hyponatremia was more common in patients with hypertension, diabetes, coronary artery disease, stroke, chronic obstructive pulmonary disease, and cancer, and was less common in those with none of these comorbidities. In our study, the top 4 underlying conditions associated hyponatremia were cardiothoracic surgery (32.5%), cancer (31.3%), general surgery (18.8%), and pulmonary diseases (18.7%), and the incidence of hyponatremia was 14.7% and 9.0% in cardiovascular and neurological diseases, respectively.

Hypernatremia is another common electrolyte disturbance and is always a reflection of water loss rather than sodium gain. However, it can also be associated with concomitant loss of sodium via hypotonic fluids or adding hypertonic fluids. Research in 2 large Dutch cohorts [22] reported a marked shift in the incidence of dysnatremia from hyponatremia to hypernatremia over 2 decades in ICU patients, which may be related to the increased use of sodium-containing infusions, diuretics, and hydrocortisone. Therefore, iatrogenic factors play a major role in the occurrence and development of hypernatremia. In critically ill patients, the incidence of hypernatremia at admission was 6.9% [2], and 7.7% of the patients with normonatremia at admission developed hypernatremia during ICU hospitalization [23]. Our study found that the total incidence of hypernatremia was 1.9% in hospitalized patients: 50.4% developed hypernatremia at admission and 49.6% after 24 h of hospitalization; 50.9% had improved hypernatremia; and 49.1% had persistent hypernatremia. The top 4 underlying conditions associated with hypernatremia were neurological diseases (5.6%), cardiothoracic surgery (4.6%), endocrine diseases (2.4%), and urinary and renal diseases (2.1%).

Extensive studies have proved the association between dysnatremia and poor outcomes. In this study, we further showed that hypernatremia (OR 13.387, 95% CI 10.642–16.840, P=0.000) and mixed dysnatremia (OR 22.344, 95% CI 15.709–31.783, *P*=0.000) were stronger predictors of mortality than was hyponatremia (OR 2.225, 95% CI 1.857–2.667, *P*=0.000). Improper correction of dysnatremia can lead to mixed dysnatremia. One survey [16] proved that fluctuations in serum sodium levels were independently associated with an increased risk of in-hospital mortality. The mortality rate of patients with mixed dysnatremia in ICU may be up to 42% [15], and we reported that the mortality was 24.2% in hospitalized patients. The OR of mortality was elevated if hyponatremia was over-corrected and changed to hypernatremia (OR 56.884, 95% CI 35.098–92.193, *P*=0.000). However, not only a too quick, but also a too slow correction can increase the risk of death regardless of initial dysnatremia [24]. The ORs of HA- and persistent hypernatremia for in-hospital mortality were obviously higher than the ORs of CA- and improved hypernatremia. These differences of ORs did not exist in hyponatremia. All data indicated that hypernatremia was a strong predictor of in-hospital death, and needed to be corrected in a timely and appropriate manner, while hyponatremia required careful correction.

The effect of dysnatremia on in-hospital mortality may vary substantially across different clinical settings and patient population. Therefore, we further tried to identify the patients at high risk of in-hospital death when dysnatremia occurs. Limited studies have reported the risk factors that increase the ORs of dysnatremia for mortality. Several risk factors were identified in our study. Although older age (>65 years) increased the risk of death in patients with persistent hypernatremia and mixed dysnatremia, the risk of mortality in younger patients was higher in other kinds of dysnatremia than in older patients. This difference have occurred because dysnatremia developed in younger patients only when the underlying diseases were more severe. Low BMI (<18.5 kg/m^2) also increased the risk of mortality in patients with HA-hypernatremia, improved

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and persistent hypernatremia, mixed dysnatremia, and persistent hyponatremia compared to normal and high BMI patients.

Since dysnatremia was independently associated with poor outcomes, we can improve the prognosis of these patients if HA-dysnatremia is prevented and dysnatremia is corrected in a timely and appropriate manner. The main finding in this respect was that there are different risks of dysnatremia in various underlying diseases. Patients with cancer, cardiothoracic surgery, general surgery, and neurological diseases were prone to develop both HA-hyponatremia and HA-hypernatremia. Age, sex, and BMI had not only a great impact on the risk of death, but also on the incidence of dysnatremia. We also identified several risk factors from laboratory data at admission for HA-dysnatremia and persistent dysnatremia.

The present study has several limitations. First, it was designed as an observational and retrospective study and was open to selection bias. Second, we defined persistent dysnatremia when dysnatremia continued until discharge or death, and if not, improved dysnatremia was defined, which had not been reported and needed further evaluation. Although we tried to include many clinical risk factors, some relevant data, including fluid administration, were unavailable in this study.

Conclusions

Dysnatremia was independently associated with poor outcomes. Hospital-acquired and persistent hypernatremia were strong risk factors for in-hospital mortality. Effective prevention and proper correction of dysnatremia in high-risk patients may reduce the in-hospital mortality, but hyponatremia should be carefully corrected.

Competing interests

None of the authors have any financial or non-financial competing interests.

Supplementary Tables

Supplementary Table 1. Outcomes of included patients with dysnatremia.

Group	AKI, n (%)	Death, n (%)	Length of hospital stay, days	Hospital cost, RMB
Model 1				
Normonatremia	6,149 (8.3)	317 (0.4)	5.0 (2.5–8.0)	13,869.1 (7,669.2–32,798.7)
Hyponatremia	4,446 (29.2)	439 (2.9)	10.0 (5.5–15.0)#	29,533.5 (13,362.4–60,616.8)#
Hypernatremia	764 (45.3)	204 (12.1)	10.5 (6.0–17.0)#	37,104.3 (14,016.3–80,466.7)#
Mixed dysnatremia	233 (81.8)	69 (24.2)	21.0 (13.5–32.5)#	106,510.3 (46,623.5–180,214.8)#
P value (χ^2 or ANOVA)	0.000	0.000	0.000	0.000
Model 2				
CA-hyponatremia	1,677 (23.8)	291 (4.1)	7.0 (4.0–12.5)	16,176.1 (9,060.1–33,854.8)
HA-hyponatremia	2,769 (33.9)	148 (1.8)	11.5 (8.0–16.5)	46,061.3 (23,207.6–83,343.8)
P value	0.000	0.000	0.000	0.000
CA-hypernatremia	247 (29.1)	83 (9.8)	7.0 (3.5–12.5)	20,248.1 (9,198.2–46,825.4)
HA-hypernatremia	517 (61.8)	121 (14.5)	14.0 (9.5–21.5)	60,351.1 (29,892.6–121,096.3)
P value	0.000	0.003	0.000	0.000
Model 3				
Improved hyponatremia	1,888 (36.2)	176 (3.4)	12.5 (8.5–18.5)	41,283.8 (20,389.7–71,168.3)
Persistent hyponatremia	2,558 (25.5)	263 (2.6)	8.0 (4.5–13.5)	22,206.9 (11,558.2–54,202.7)
P value	0.000	0.008	0.000	0.000
Improved hypernatremia	488 (56.8)	61 (7.1)	14.0 (9.5–21.0)	57,157.7 (30,575.9–116,872.8)

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Group	AKI, n (%)	Death, n (%)	Length of hospital stay, days	Hospital cost, RMB
Persistent hypernatremia	276 (33.3)	143 (17.3)	7.0 (3.5–12.0)	17,773.6 (8,782.9–49,237.5)
P value	0.000	0.000	0.000	0.000
"Hypo to hyper" mixed dysnatremia	82 (35.2)	55 (79.7)	21.8 (13.4–38.5)	89,939.4 (29,995.7–180,373.3)
"Hyper to hypo" mixed dysnatremia	151 (64.8)	14 (20.3)	20.5 (14.0–30.5)	113,523 (52,375.1–181,003.8)
P value	0.657	0.000	0.603	0.050

[#] *P*<0.001 *vs.* normonatremia group. AKI – acute kidney injury; RMB – Ren Min Bi; CA – community-acquired; HA – hospital-acquired.

Supplementary Table 2. Subgroup multiple logistic regression analysis of dysnatremia as independent risk factors for hospital mortality in model 1.

Subgroup	Hyponatremia[§]		Hypernatremia[§]		Mixed dysnatremia[§]	
	OR (95%CI)	*P* value	OR (95%CI)	*P* value	OR (95%CI)	*P* value
Age, year						
≤65	2.722 (2.034–3.643)	0.000	18.350 (12.853–26.198)	0.000	21.886 (11.753–40.755)	0.000
<65	2.075 (1.653–2.606)	0.000	11.112 (8.440–14.631)	0.000	24.623 (16.162–37.513)	0.000
Gender						
Male	1.963 (1.575–2.447)	0.000	14.659 (11.014–19.512)	0.000	21.475 (13.748–33.544)	0.000
Female	2.860 (2.090–3.913)	0.000	11.952 (8.231–17.353)	0.000	27.276 (15.320–48.564)	0.000
BMI, kg/m²						
<18.5	1.534 (0.453–5.198)	0.492	71.139 (12.345–409.950)	0.000	1233.153 (38.420–39580.284)	0.000
18.5–24.99	2.297 (1.906–2.769)	0.000	13.003 (10.241–16.509)	0.000	20.950 (14.578–30.105)	0.000
≥25	1.689 (0.632–4.513)	0.296	7.195 (2.006–25.806)	0.002	32.104 (2.952–349.133)	0.004
Underlying diseases						
Cancer	1.635 (1.069–2.502)	0.023	11.942 (6.105–23.359)	0.000	26.998 (9.615–75.806)	0.000
Pulmonary	3.062 (2.010–4.633)	0.000	6.266 (3.353–11.710)	0.000	25.139 (7.850–80.503)	0.000
Cardiovascular	4.863 (3.203–7.385)	0.000	9.117 (5.037–16.502)	0.000	9.550 (2.855–31.946)	0.000
Digestive	1.445 (0.726–2.877)	0.295	11.231 (3.914–32.232)	0.000	53.383 (13.800–206.493)	0.000
Hematological	3.398 (2.103–5.490)	0.000	8.980 (3.723–21.660)	0.000	48.642 (8.840–267.664)	0.000
Neurological	2.199 (1.038–4.658)	0.040	16.821 (8.191–34.544)	0.000	23.310 (7.966–68.207)	0.000
Urinary and renal	1.390 (0.746–2.588)	0.300	17.257 (8.551–34.826)	0.000	33.917 (7.819–147.114)	0.000
Cardiothoracic surgery	2.385 (1.065–5.340)	0.035	27.029 (12.388–58.976)	0.000	18.501 (6.336–54.021)	0.000
General surgery	2.282 (1.056–4.931)	0.036	6.568 (2.299–18.763)	0.000	8.285 (1.500–45.761)	0.003
Others	2.321 (10.22–5.273)	0.044	11.917 (4.531–31.341)	0.000	77.078 (16.156–367.723)	0.000
AKI						
Yes	1.810 (1.411–2.322)	0.000	10.784 (8.161–14.252)	0.000	11.053 (7.502–16.285)	0.000
No	1.526 (1.157–2.013)	0.003	4.596 (2.817–7.499)	0.000	16.996 (6.574–43.944)	0.000
Length of hospital stay, day						
≤30	1.627 (1.323–2.001)	0.000	14.168 (11.042–18.179)	0.000	18.563 (11.980–28.763)	0.000
>30	2.928 (1.879–4.561)	0.000	5.233 (2.926–9.360)	0.000	9.789 (5.116–18.730)	0.000

[§] Normonatremia as the reference. BMI – body mass index; AKI – acute kidney injury; OR – odds ratio; CI – confidence interval.

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Supplementary Table 3. Subgroup multiple logistic regression analysis of dysnatremia as independent risk factors for hospital mortality in model 2.

Subgroup	CA-hyponatremia§		HA-hyponatremia§		CA-hypernatremia§		HA-hypernatremia§		Mixed dysnatremia§	
	OR (95%CI)	*P*	OR (95%CI)	*P*	OR (95%CI)	*P*	OR (95%CI)	*P*	OR (95%CI)	*P*
Age, year										
≤65	2.433 (1.694–3.495)	0.000	3.077 (2.216–4.273)	0.000	9.953 (5.545–17.865)	0.000	22.295 (14.862–33.445)	0.000	18.570 (9.827–35.092)	0.000
>65	1.878 (1.414–2.494)	0.000	2.329 (1.786–3.037)	0.000	7.767 (5.146–11.724)	0.000	13.665 (9.957–18.754)	0.000	23.599 (15.462–36.017)	0.000
Gender										
Male	1.755 (1.335–2.308)	0.000	2.219 (1.713–2.875)	0.000	9.094 (5.740–14.406)	0.000	18.348 (13.365–25.190)	0.000	20.081 (12.820–31.454)	0.000
Female	2.307 (1.561–3.410)	0.000	3.387 (2.389–4.803)	0.000	8.502 (4.900–14.752)	0.000	13.847 (9.030–21.232)	0.000	25.346 (14.148–45.406)	0.000
BMI, kg/m²										
<18.5	2.063 (0.531–8.018)	0.296	0.961 (0.168–5.515)	0.965	–	–	74.385 (12.840–430.910)	0.000	1112.828 (35.443–34940.099)	0.000
18.5–24.99	1.951 (1.543–2.4680)	0.000	2.696 (2.182–3.332)	0.000	8.762 (6.066–12.655)	0.000	15.957 (12.260–20769)	0.000	19.960 (13.854–28.758)	0.000
≥25	3.595 (1.223–10.570)	0.020	0.455 (0.058–3.565)	0.454	9.688 (1.099–85.409)	0.041	7.266 (1.712–30.840)	0.007	34.163 (3.095–377.072)	0.004
Underlying diseases										
Cancer	1.368 (0.804–2.328)	0.248	0.036 (0.001–1.2)	0.063	19.477 (9.896–38.334)	0.000	33.15 (12.192–90.129)	0.000	1.368 (0.804–2.328)	0.248
Pulmonary	2.886 (1.546–5.389)	0.001	3.527 (1.571–7.919)	0.002	11.744 (5.31–25.971)	0.000	24.852 (7.745–79.748)	0.000	2.886 (1.546–5.389)	0.001
Cardiovascular	4.514 (2.7–7.548)	0.000	6.997 (3.207–15.263)	0.000	12.403 (5.67–27.133)	0.000	9.718 (2.904–32.513)	0.000	4.514 (2.7–7.548)	0.000
Digestive	1.991 (0.855–4.635)	0.110	21.924 (4.875–98.609)	0.000	7.671 (1.914–30.755)	0.004	55.185 (13.645–223.184)	0.000	1.991 (0.855–4.635)	0.110
Hematological	3.627 (1.909–6.89)	0.000	4.458 (1.212–16.404)	0.025	17.19 (4.915–60.119)	0.000	28.916 (5.208–160.535)	0.000	3.627 (1.909–6.89)	0.000
Neurological	2.671 (1.112–6.42)	0.028	8.124 (2.671–24.713)	0.000	24.574 (11.16–54.11)	0.000	23.028 (7.879–67.307)	0.000	2.671 (1.112–6.42)	0.028
Urinary and renal	2.579 (1.175–5.661)	0.018	13.427 (4.347–41.475)	0.000	20.734 (9.183–46.811)	0.000	36.159 (7.867–166.184)	0.000	2.579 (1.175–5.661)	0.018
Cardiothoracic surgery	2.09 (0.875–4.994)	0.097	20.563 (6.3–67.125)	0.000	29.047 (12.987–64.968)	0.000	18.291 (6.262–53.425)	0.000	2.09 (0.875–4.994)	0.097
General surgery	2.559 (1.084–6.039)	0.032	5.917 (1.332–26.276)	0.019	5.545 (1.547–19.872)	0.009	6.703 (1.179–38.101)	0.032	2.559 (1.084–6.039)	0.032
Others	3.039 (1.109–8.327)	0.031	11.19 (2.581–48.514)	0.001	12.402 (3.918–39.254)	0.000	71.597 (14.877–344.574)	0.000	3.039 (1.109–8.327)	0.031
AKI										
Yes	1.666 (1.224–2.266)	0.001	1.921 (1.455–2.537)	0.000	10.749 (7.000–16.507)	0.000	10.869 (8.026–14.720)	0.000	10.983 (7.443–16.206)	0.000
No	1.558 (1.110–2.188)	0.010	1.541 (1.080–2.199)	0.017	2.844 (1.391–5.817)	0.004	7.200 (3.939–13.163)	0.000	17.113 (6.638–44.117)	0.000
Length of hospital stay, day										
≤30	1.599 (1.241–2.061)	0.000	1.781 (1.381–2.296)	0.000	8.593 (5.808–12.712)	0.000	17.738 (13.487–23.329)	0.000	17.934 (11.561–27.822)	0.000
>30	4.548 (2.809–7.363)	0.000	2.718 (1.701–4.342)	0.000	5.579 (2.488–12.509)	0.000	4.680 (2.461–8.902)	0.000	10866 (5.760–20.499)	0.000

§ Normonatremia as the reference. CA – community-acquired; HA – hospital-acquired; BMI – body mass index; AKI – acute kidney injury; OR – odds ratio; CI – confidence interval.

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Supplementary Table 4. Subgroup multiple logistic regression analysis of dysnatremia as independent risk factors for hospital mortality in model 3.

Subgroup	Improved hyponatremia		Persistent hyponatremia		Improved hypernatremia		Persistent hypernatremia	
	OR(95%CI)	*P*	OR(95%CI)	*P*	OR(95%CI)	*P*	OR(95%CI)	*P*
Age, year								
≤65	2.887 (2.113–3.945)	0.000	12.639 (7.705–20.731)	0.000	25.364 (16.541–38.893)	0.000	21.923 11.773–40.825)	0.000
>65	1.644 (1.264–2.138)	0.000	4.827 (3.166–7.359)	0.000	20.010 (14.552–27.516)	0.000	24.275 (15.899–37.066)	0.000
Gender								
Male	1.779 (1.394–2.271)	0.000	7.318 (4.819–11.113)	0.000	26.151 (18.611–36.745)	0.000	21.742 (13.914–33.974)	0.000
Female	2.555 (1.794–3.639)	0.000	6.448 (3.781–10.996)	0.000	19.409 (12.602–29.891)	0.000	27.078 (15.178–48.307)	0.000
BMI, kg/m²								
<18.5	1.931 (0.472–7.894)	0.360	20.986 (14.599–30.168)	0.000	55.895 (8.888–351.535)	0.000	1209.328 (37.744–38746.89)	0.000
18.5–24.99	2.093 (1.701–2.576)	0.000	6.28 (4.43–8.902)	0.000	22.766 (17.252–30.042)	0.000	20.986 (14.599–30.168)	0.000
≥25	1.777 (0.559–5.648)	0.330	5.025 (0.587–42.991)	0.140	8.816 (1.948–39.891)	0.005	32.095 (2.959–348.159)	0.004
Underlying diseases								
Cancer	1.184 (0.731–1.916)	0.492	11.343 (5.09–25.277)	0.000	13.494 (4.684–38.876)	0.000	25.983 (9.194–73.434)	0.000
Pulmonary	3.416 (2.139–5.456)	0.000	0.962 (0.288–3.214)	0.949	16.5 (8.103–33.597)	0.000	25.592 (7.866–83.263)	0.000
Cardiovascular	4.409 (2.724–7.137)	0.000	5.893 (2.519–13.789)	0.000	13.128 (6.396–26.943)	0.000	9.585 (2.866–32.059)	0.000
Digestive	1.44 (0.699–2.963)	0.323	3.019 (0.329–27.677)	0.328	16.053 (5.374–47.952)	0.000	50.959 (13.174–197.116)	0.000
Hematological	2.78 (1.571–4.918)	0.000	29.114 (7.417–114.275)	0.000	3.738 (1.076–12.978)	0.038	37.481 (7.029–199.851)	0.000
Neurological	1.492 (0.598–3.722)	0.391	8.002 (3.076–20.817)	0.000	47.75 (20.678–110.263)	0.000	28.754 (9.403–87.927)	0.000
Urinary and renal	1.67 (0.829–3.364)	0.152	4.526 (0.977–20.973)	0.054	24.442 (11.571–51.631)	0.000	32.258 (7.501–138.731)	0.000
Cardiothoracic surgery	0.936 (0.304–2.882)	0.909	10.885 (4.104–28.867)	0.000	79.21 (32.91–190.65)	0.000	18.084 (6.162–53.07)	0.000
General surgery	2.279 (0.966–5.377)	0.060	3.499 (0.86–14.233)	0.080	15.866 (4.211–59.776)	0.000	8.242 (1.487–45.693)	0.016
Others	3.978 (1.902–8.317)	0.000	2.31 (0.425–12.545)	0.332	29.003 (10.267–81.93)	0.000	122.536 (27.544–545.138)	0.000
AKI								
Yes	1.915 (1.457–2.518)	0.000	4.893 (3.387–7.068)	0.000	25.307 (18.021–35.538)	0.000	10.927 (7.422–16.087)	0.000
No	1.247 (0.911–1.706)	0.168	1.656 (0.591–4.643)	0.337	7.438 (4.331–12.774)	0.000	17.028 (6.573–44.108)	0.000
Length of hospital stay, day								
≤30	1.507 (1.197–1.898)	0.000	7.109 (4.89–10.337)	0.000	22.685 (16.984–30.299)	0.000	18.657 (12.039–28.914)	0.000
>30	3.514 (2.166–5.703)	0.000	2.823 (1.411–5.651)	0.003	25.407 (10.435–61.859)	0.000	9.913 (5.18–18.973)	0.000

§ Normonatremia as the reference. BMI – body mass index; AKI – acute kidney injury; OR – odds ratio; CI – confidence interval.

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Supplementary Table 5. Multinomial logistic regression analysis of independent risk factors for developing of hospital-acquired and persistent dysnatremia.

Variable	HA-hyponatremia		HA-hypernatremia		Persistent hyponatremia		Persistent hypernatremia	
	OR(95%CI)	*P*	OR(95%CI)	*P*	OR(95%CI)	*P*	OR(95%CI)	*P*
Age, per year increase	1.008 (1.006–1.010)	0.000	1.019 (1.013–1.024)	0.000	1.004 (1.002–1.006)	0.001		
Male sex	1.182 (1.117–1.252)	0.000	0.692 (0.596–0.804)	0.000	1.258 (1.164–1.360)	0.000	1.274 (1.023–1.586)	0.030
BMI <18.5 kg/m^2§	1.811 (1.396–2.350)	0.000						
BMI 25–27.99 kg/m^2§	1.297 (1.102–1.527)	0.002						
BMI 28–32 kg/m^2§	1.269 (0.959–1.680)	0.096						
Cancer	8.344 (7.640–9.113)	0.000	2.768 (2.173–3.525)	0.000				
Pulmonary					1.449 (1.249–1.681)	0.000		
Cardiovascular	1.279 (1.145–1.428)	0.000						
Cardiothoracic surgery	13.330 (12.125–14.654)	0.000	10.989 (9.009–13.403)	0.000	1.416 (1.270–1.580)	0.000		
Digestive					1.651 (1.432–1.903)	0.000		
Endocrine			2.187 (1.465–3.263)	0.000				
General surgery	4.042 (3.670–4.452)	0.000	1.843 (1.429–2.376)	0.000				
Hematological	1.532 (1.280–1.834)	0.000						
Neurological	2.575 (2.185–3.035)	0.000	6.007 (4.586–7.868)	0.000				
Gynecology	3.084 (2.565–3.708)	0.000			1.741 (1.330–2.279)	0.000		
Orthopedic surgery	1.360 (1.128–1.640)	0.001						
SBP>140 mmHg			1.359 (1.111–1.661)	0.003				
DBP <60 mmHg§	1.546 (1.304–1.834)	0.000	2.330 (1.657–3.276)	0.000				
Glucose 5.7–10 mmol/L§	1.133 (1.071–1.198)	0.000						
Glucose >10 mmol/L§	1.319 (1.163–1.496)	0.000						
Hypokalemia			2.169 (1.769–2.659)	0.000				
Hypochloremia§	2.064 (1.874–2.273)	0.000			1.420 (1.308–1.540)	0.000		
Hyperchloremia			1.868 (1.234–2.826)	0.003				
Hypocalcemia	1.460 (1.344–1.586)	0.000	1.650 (1.347–2.021)	0.000				
Hypomagnesemia	1.917 (1.492–2.464)	0.000	1.929 (1.107–3.362)	0.020			1.579 (1.124–2.217)	0.008
Hypermagnesemia			1.504 (1.174–1.928)	0.001				
Hypophosphatemia	1.142 (1.052–1.240)	0.002	1.818 (1.484–2.228)	0.000				
Hyperphosphatemia	1.242 (1.137–1.357)	0.000						
CO2CP <23 mmol/L§	1.230 (1.155–1.310)	0.000						
AG >16 mmol/L§	1.293 (1.199–1.394)	0.000	1.558 (1.298–1.870)	0.000			1.370 (1.069–1.755)	0.013
ALT, per 50 U/L increase	1.015 (1.001–1.030)	0.041						
TBIL, per 20 μmol/L increase	1.087 (1.066–1.108)	0.000	1.102 (1.059–1.147)	0.000	1.031 (1.013–1.050)	0.001		
Albumin, per 5g/L decrease	1.275 (1.234–1.318)	0.000	1.458 (1.347–1.578)	0.000				
Hemoglobin (90–119 g/L)§	1.161 (1.090–1.237)	0.000			1.179 (1.087–1.280)	0.000		
Hemoglobin (60–89 g/L)§	1.471 (1.307–1.656)	0.000			1.277 (1.119–1.457)	0.000		
Hemoglobin (<60 g/L)§	1.713 (1.303–2.252)	0.000			1.233 (0.929–1.638)	0.147		
WBC <4.0×10^9/L§					1.142 (1.025–1.273)	0.016		
WBC >12.0×10^9/L§	1.556 (1.378–1.758)	0.000	2.322 (1.805–2.987)	0.000				
BUN, per 10 mg/dl increase	1.107 (1.066–1.149)	0.000	1.238 (1.149–1.334)	0.000				
SCr, per 0.5 mg/dl increase			0.958 (0.926–0.990)	0.011				
Hypouricemia§	1.084 (1.003–1.170)	0.041						
Hyperuricemia§	1.135 (1.046–1.231)	0.002	1.481 (1.212–1.810)	0.000	1.132 (1.012–1.267)	0.031		

Normonatremia served as the reference for HA-dysnatremia and improved dysnatremia as the reference for corresponding persistent dysnatremia. For underlying diseases, the rest of the other patients served as the references. § Normal range as the reference.
BMI – body mass index; SBP – systolic blood pressure; DBP – diastolic blood pressure; CO_2CP – carbon dioxide combining power; AG – anion gap; ALT – alanine aminotransferase; TBIL – total bilirubin; WBC – white blood cell; BUN – blood urea nitrogen; SCr – serum creatinine; OR – odds ratio; CI – confidence interval.

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