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Original Article

Investigation of the Prognostic Potential of Chloride on Short- and Long-Term Mortality in Heart Failure Patients Admitted to Intensive Care Unit

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SUMMARY

Background: In recent years, chloride has been suggested as a potential prognostic marker for predicting mortality in heart failure (HF). However, the prognostic effect on longer-term mortality has rarely been evaluated in chronic HF with acute conditions. The current study aims to investigate the prognostic role of chloride simultaneously in the short- and long-term mortality in patients admitted to the intensive care unit (ICU).

Methods: Medical Information Mart for Intensive Care IV version 2.2 was applied, with 3,068 subjects included in the study. ICU mortality, in-hospital mortality, and total mortality were evaluated. Logistic regression models and Kaplan-Meier survival curves were used to explore the relationship between chloride levels or hypochloremia/normal group and mortalities.

Results: Chloride level exhibited negative associations with ICU mortality, in-hospital mortality, and total mortality. Correspondingly, hypochloremia exhibited positive associations with ICU mortality, in-hospital mortality, and total mortality. When further adjusted for multiple demographic and clinical characteristics, the aforementioned results remained significant.

Conclusion: Chloride serves as a prognostic marker for predicting mortality for HF patients admitted to ICU. The prognostic effect was revealed simultaneously in short-term mortality and long-term mortality. The add-on of chloride monitoring will be beneficial to the future prevention of mortality of HF.

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1. Introduction

Heart failure (HF) is a major contributor to the global burden of disease. The lifetime risk has been estimated to be 20–45% between the ages of 45 and 95,¹ and approximately 64.3 million people suffer worldwide.² Despite the diagnosis and treatment have been improved over the past 20 years^{3,4} the current survival rates are only 86.5%, 56.7%, and 34.9% for 1, 5, and 10-years, respectively.⁵ Given the challenge posed by HF, improving the prognosis has served as another entry point.

Several prognostic markers have been proposed for HF, such as hyponatremia, B-type natriuretic peptide (BNP), and the N-terminal fragment of proBNP (NT-proBNP).^{6,7} In recent years, chloride has been suggested as another potential prognostic marker for predicting mortality in HF. Similar to sodium, chloride serves as the major potent ion in the extracellular fluid, and potentially alters the plasma volume, vasopressin secretion, and renin-angiotensin-aldosterone (RAAS) system during HF worsening status.⁸ It also reveals an independent and even stronger prognostic effect, when compared to

serum sodium levels.^{9–11}

The previous literature on the relationship between chloride and mortality rate was evaluated in various conditions of HF. For studies focusing on chronic HF (CHF), hypochloremia was associated with an increased risk of 5-year mortality.^{9,12} In those studies further engaged in acute decompensated HF or CHF who admitted to the intensive care unit (ICU), hypochloremia revealed the association with increased 30-day, and 1-year mortality.^{10,13,14} However, the prognostic effect on longer-term mortality has rarely been evaluated in CHF with acute conditions as has been evaluated in the CHF. Additionally, studies that have simultaneously evaluated short- and long-term mortalities were limited. Hence, the current study aims to investigate the prognostic role of chloride in the short- and long-term mortality in patients admitted to the ICU.

2. Methods

2.1. Data source

We applied data from the Medical Information Mart for Intensive Care IV (MIMIC-IV version 2.2) with formal approval of usage. The record ID for the permission to access and utilize was 42188048.

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MIMIC-IV is a publicly available database managed by Beth Israel Deaconess Medical Center. The database includes records from more than 200,000 emergency department admissions and more than 60,000 ICU admissions from 2008 to 2019.¹⁵ The procedural framework for data extraction is openly available on GitHub via the following link (<https://github.com/MIT-LCP/mimic-iv>).

2.2. Definition of clinical outcomes

Chloride is a vital anion essential for maintaining homeostasis. In adults, the normal serum chloride concentration ranges from 96 to 106 milliequivalents per liter (mEq/L). We defined serum chloride levels below 96 mEq/L as hypochloremia. Three main outcomes were specifically evaluated, including ICU mortality, in-hospital mortality, and total mortality. The mortalities were further calculated from official state death records, while survival information was extracted from the MIMIC-IV database.

2.3. Subject selection process

Initially, the MIMIC-IV 2.2 database contained 73,181 patients admitted to ICU. After identifying HF via the International Classification of Diseases Tenth Revision (ICD-10) diagnostic codes (I50.1, I50.2, I50.3, I50.4, I50.8, I50.9, I11.0, I13.0, I13.2), 17,011 patients remained. We further restricted to patients aged ≥ 18 years, ICU care unit without Neuro Intermediate and Neuro Step down, and with data available within 24 hours of admission. To ensure the engagement of patients was clinically significant, we focused on patients with ICU durations greater than 6 hours. For those patients with multiple ICU admissions, only the first ICU stay record will be included. Eventually, 3,068 subjects were included in the study (Figure 1).

2.4. Statistical analysis

Continuous variables were presented as mean and standard deviation (SD), while categorical variables were presented as counts and percentages (%). The chi-squared test or Fisher's exact test was used to compare categorical variables between groups, and the t-test was used to compare continuous variables when appropriate. Logistic regression models were used to explore the relationship between chloride levels or hypochloremia/normal group and mortalities, with results reported as odds ratio (OR) and corresponding 95% confidence interval (95% CI). A purposeful selection approach was used to build the multivariate models. Significant variables from the univariate analysis were included. However, to control for potential confounding factors, age, gender and BMI were retained in the final

model. This method aligns with established practices for building robust regression models and ensures the independent effect of chloride on prognosis. Kaplan-Meier survival curves were also constructed for ICU mortality, in-hospital mortality, and total mortality. All statistical analyses were performed using R (version 4.2.3) and SPSS (version 20). A significance threshold of p-value < 0.05 (two-tailed) was applied.

3. Results

3.1. Baseline demographic and clinical characteristics

Overall, the database consists of 3,068 subjects with a mean age of 74.22 and 42.41% of females. For the clinical assessments, higher mean BMI (30.17 ± 8.53 Kg/m²), creatinine (1.91 ± 1.75 mg/dL), white blood cell levels (12.54 ± 10.14 K/uL), and lower mean hemoglobin (10.08 ± 2.23 gm/dL), were observed in the subjects. For the comorbidity, 13.56% of the patients were combined with cerebrovascular disease, 33.34% with chronic pulmonary disease, 47.88% with renal disease, and 49.09% with DM. Regarding mortality, 9.13% of patients died during their stay in ICU and 44.92% died at the end of follow-up (Table 1).

Comparing patients with hypochloremia and those without (Table 2), we observed significantly younger age (73.26 ± 12.36 vs. 74.42 ± 12.31), higher BMI (31.11 ± 9.61 vs. 29.98 ± 8.27 Kg/m²) in baseline demographic characteristics. Meanwhile, patients with hypochloremia showed significantly higher respiratory rate (20.98 ± 5.81 vs. 20.25 ± 6.21 beats/min), creatinine (2.75 ± 2.37 vs. 1.73 ± 1.54 mg/dL), platelet level (216.31 ± 105.9 vs. 195.64 ± 92.87 K/uL), SAPS II score (41.53 ± 12.49 vs. 39.63 ± 12.72), and LODS score (6.17 ± 3.21 vs. 5.36 ± 3.11). The comorbidity among patients with hypochloremia has a lower percentage of cerebrovascular disease (9% vs. 14%) but a higher percentage of chronic pulmonary disease (40% vs.

Table 1

Baseline demographic characteristics and clinical features of the study population.

Variable	N/Mean	%/SD
Age (years)	74.22	12.32
Female	1301	42.41
BMI (Kg/m ²)	30.17	8.53
Heart rate (bpm)	87.71	20.85
MBP (mmHg)	84.30	18.91
Respiratory rate (beats/min)	20.37	6.15
Cl level (mEq/L)	101.24	6.79
Creatinine (mg/dL)	1.91	1.75
Hemoglobin (gm/dL)	10.08	2.23
Platelet (k/uL)	199.19	95.53
White blood cell (K/uL)	12.54	10.14
Urine output (mL)	226.05	218.37
SAPS II score	39.96	12.70
LODS score	5.50	3.14
Cerebrovascular disease	416	13.56
Chronic pulmonary disease	1023	33.34
Renal disease	1469	47.88
Diabetes mellitus	1506	49.09
Followed up (day)	160.06	253.73
ICU length of stay	3.94	4.82
Duration of hospital stay	12.43	11.75
ICU mortality	280	9.13
In-hospital mortality	450	14.67
Total mortality	1378	44.92
Death within 30 days	425	13.85

BMI, body mass index; Cl, chloride; LODS, Logistic Organ Dysfunction Score; MBP, mean blood pressure; SAPS II, Simplified Acute Physiology Score II.

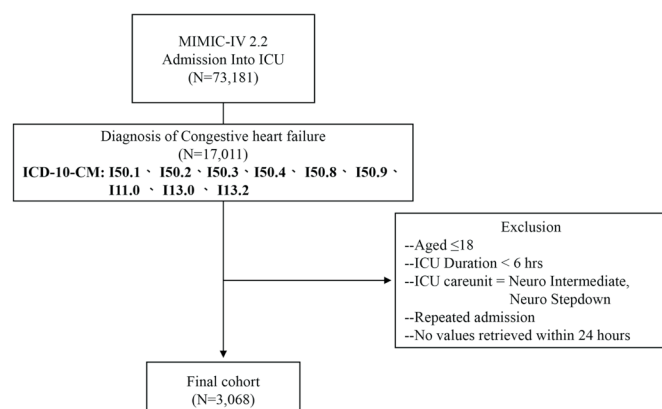


Figure 1. The selection process for subjects diagnosed with HF and submitted to the ICU in the MIMIC-IV 2.2 database.

32%) and renal disease (61% vs. 45%).

3.2. ICU mortality

We then examined the short-term ICU mortality rate via continuous Cl level and hypochloremia/normal group (Table 3). In the univariate model, we discover a higher Cl level showing an inverse association with ICU mortality rate (OR = 0.971, p -value = 0.001). Correspondingly, the hypochloremia group compared to the normal group revealed higher ICU mortality (OR = 1.976, p -value < 0.001). The result from Kaplan-Meier also indicated there were significantly more death

events in the hypochloremia group compared to the normal group (p -value < 0.001, Figure 2). Other clinical features also exhibited negative association with the ICU mortality rate (e.g., higher MBP and urine output) whereas various demographic and clinical features showed positive association with ICU mortality rate (e.g., older and higher heart rate, respiratory rate, creatinine, WBC, SAPS II score, LODS score, rate of cerebrovascular disease, and renal disease). In the multivariate models, when further adjusted for the covariates that revealed associations with ICU mortality, the significances were consistently shown in the Cl level (aOR = 0.958, p -value < 0.001) and hypochloremia group (aOR = 1.912, p -value < 0.001).

Table 2

The baseline demographic characteristics and clinical features comparing patients with normal Cl level (Cl $\geq$ 96 mEq/L) and hyperchloremia (Cl < 96 mEq/L).

Variables	Cl group (mEq/L)		p-value
	Cl < 96 mEq/L (N = 526)	Cl ≥ 96 mEq/L (N = 2542)	
Continuous variables, mean (SD)			
Age (years)	73.26 (12.36)	74.42 (12.31)	0.049*
Gender (female)	240 (0.46)	1061 (0.42)	0.056
BMI (Kg/m ²)	31.11 (9.61)	29.98 (8.27)	0.012*
Heart rate (bpm)	88.97 (20.19)	87.45 (20.98)	0.126
MBP (mmHg)	82.95 (19.78)	84.58 (18.72)	0.072
Respiratory rate (beats/min)	20.98 (5.81)	20.25 (6.21)	0.014*
Creatinine (mg/dL)	2.75 (2.37)	1.73 (1.54)	< 0.001***
Hemoglobin (gm/dL)	9.97 (2.25)	10.1 (2.22)	0.200
Platelet (k/uL)	216.31 (105.9)	195.64 (92.87)	< 0.001***
WBC (K/uL)	12.62 (10.42)	12.52 (10.08)	0.834
Urine output (mL)	229.77 (229.72)	225.28 (215.98)	0.668
SAPS II score	41.53 (12.49)	39.63 (12.72)	0.002**
LODS score	6.17 (3.21)	5.36 (3.11)	< 0.001***
Cerebrovascular disease	49 (0.09)	367 (0.14)	0.002**
Chronic pulmonary disease	208 (0.40)	815 (0.32)	0.001**
Renal disease	323 (0.61)	1146 (0.45)	< 0.001***
Diabetes mellitus	278 (0.53)	1228 (0.48)	0.062

BMI, body mass index; Cl, chloride; LODS, Logistic Organ Dysfunction Score; MBP, mean blood pressure; SAPS II, Simplified Acute Physiology Score II; WBC, white blood cell.

* p < 0.05. ** p < 0.01. *** p < 0.001.

Table 3

The association between ICU mortality and chloride via comparing Cl level (mEq/L) and hypochloremia/normal group.

	Univariate analysis				Multivariate analysis (continuous Cl)				Multivariate analysis			
	OR	95% CI		p-value	aOR	95% CI		p-value	aOR	95% CI		p-value
		Lower	Upper			Lower	Upper			Lower	Upper	
ICU mortality												
Cl level (mEq/L)	0.971	0.955	0.988	0.001**	0.958	0.939	0.978	< 0.001***				
Cl group (Cl < 96 vs. Cl ≥ 96)	1.976	1.492	2.617	< 0.001***					1.912	1.349	2.709	< 0.001***
Female	0.988	0.769	1.266	0.926	1.155	0.851	1.566	0.355	1.157	0.853	1.569	0.347
Age (years)	1.026	1.015	1.037	< 0.001***	1.026	1.011	1.041	0.001***	1.026	1.010	1.041	0.001***
BMI (Kg/m ²)	1.004	0.989	1.017	0.613	1.015	0.998	1.033	0.089	1.016	0.999	1.034	0.067
Heart rate (bpm)	1.012	1.007	1.018	< 0.001***	1.004	0.998	1.011	0.202	1.004	0.998	1.011	0.199
MBP (mmHg)	0.990	0.983	0.997	0.004**	1.000	0.992	1.007	0.902	1.000	0.992	1.007	0.935
Respiratory rate (beats/min)	1.034	1.015	1.053	< 0.001***	1.019	0.996	1.043	0.106	1.020	0.996	1.044	0.100
Creatinine (mg/dL)	1.153	1.092	1.215	< 0.001***	0.997	0.911	1.091	0.950	1.005	0.919	1.098	0.918
Hemoglobin (gm/dL)	1.032	0.977	1.089	0.257								
Platelet (k/uL)	1.000	0.999	1.001	0.811								
WBC (K/uL)	1.013	1.004	1.022	0.003**	1.009	0.998	1.019	0.120	1.009	0.998	1.019	0.109
Urine output (mL)	0.998	0.998	0.999	< 0.001***	1.000	0.999	1.001	0.867	1.000	0.999	1.001	0.830
SAPS II score	1.093	1.082	1.104	< 0.001***	1.027	1.012	1.043	< 0.001***	1.026	1.011	1.041	0.001***
LODS score	1.546	1.480	1.618	< 0.001***	1.445	1.360	1.536	< 0.001***	1.440	1.355	1.531	< 0.001***
Cerebrovascular disease	1.909	1.398	2.574	< 0.001***	1.952	1.339	2.846	0.001***	1.926	1.322	2.806	0.001***
Chronic pulmonary disease	0.813	0.618	1.060	0.131	0.757	0.548	1.044	0.090	0.770	0.558	1.062	0.111
Renal disease	1.506	1.177	1.934	0.001**	0.951	0.689	1.312	0.758	0.936	0.679	1.291	0.688
Diabetes mellitus	0.962	0.752	1.230	0.759								

aOR, adjusted odds ratio; BMI, body mass index; Cl, chloride; LODS, Logistic Organ Dysfunction Score; MBP, mean blood pressure; OR, crude odds ratio; SAPS II, Simplified Acute Physiology Score II; WBC, white blood cell.

* p < 0.05. ** p < 0.01. *** p < 0.001.

3.3. In-hospital mortality

We also examined the in-hospital mortality (Table 4). The results were similar to ICU mortality where higher CI levels exhibited

negative association (OR = 0.965, p -value < 0.001), and the hypochloremia group compared to the normal group exhibited positive association (OR = 1.872, p -value < 0.001). The result from Kaplan-Meier also indicated there were significantly more death events in

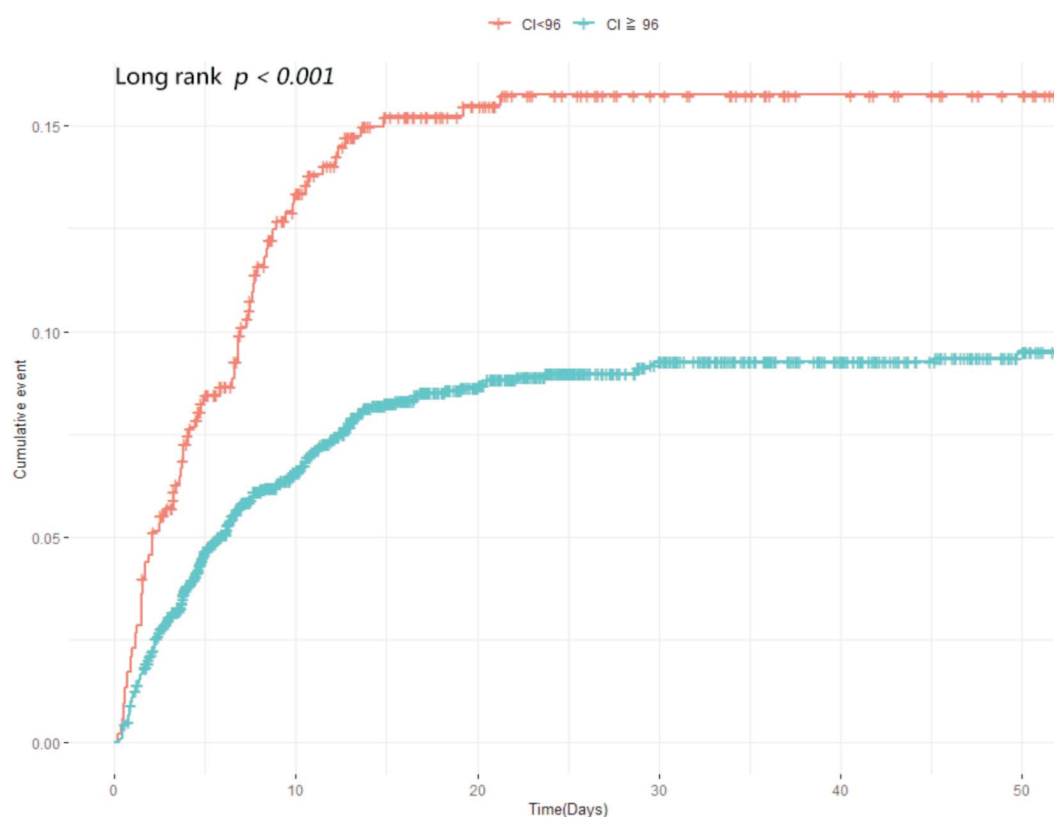


Figure 2. ICU mortality comparing the hypochloremia group and the normal group.

Table 4

The association between in-hospital mortality and chloride via comparing CI level (mEq/L) and hypochloremia/normal group.

	Univariate analysis				Multivariate analysis (continuous CI)				Multivariate analysis			
	OR	95% CI		p-value	aOR	95% CI		p-value	aOR	95% CI		p-value
		Lower	Upper			Lower	Upper			Lower	Upper	
In-hospital mortality												
CI level (mEq/L)	0.981	0.967	0.996	0.011*	0.971	0.955	0.987	< 0.001***				
CI group (CI < 96 vs. CI ≥ 96)	1.564	1.227	1.994	< 0.001***					1.464	1.095	1.956	0.010*
Female	1.091	0.891	1.334	0.399	1.191	0.936	1.515	0.154	1.198	0.942	1.524	0.140
Age (years)	1.032	1.023	1.041	< 0.001***	1.027	1.015	1.040	< 0.001***	1.027	1.015	1.040	< 0.001***
BMI (Kg/m ²)	0.991	0.978	1.003	0.132	1.001	0.987	1.016	0.848	1.002	0.988	1.017	0.747
Heart rate (bpm)	1.013	1.008	1.018	< 0.001***	1.007	1.002	1.013	0.009**	1.008	1.002	1.013	0.008**
MBP (mmHg)	0.992	0.986	0.997	0.003**	0.999	0.993	1.005	0.645	0.999	0.993	1.005	0.665
Respiratory rate (beats/min)	1.036	1.020	1.052	< 0.001***	1.021	1.002	1.040	0.030*	1.022	1.003	1.041	0.024*
Creatinine (mg/dL)	1.113	1.060	1.167	< 0.001***	0.962	0.891	1.040	0.333	0.971	0.900	1.049	0.458
Hemoglobin (gm/dL)	0.991	0.947	1.036	0.681								
Platelet (k/uL)	1.000	0.999	1.001	0.979								
WBC (K/uL)	1.018	1.009	1.028	< 0.001***	1.011	1.003	1.020	0.010**	1.011	1.003	1.020	0.010**
Urine output (mL)	0.999	0.998	0.999	< 0.001***	1.000	0.999	1.001	0.868	1.000	0.999	1.001	0.922
CCI score	1.172	1.126	1.219	< 0.001***								
SOFA score	1.279	1.245	1.316	< 0.001***								
GCS	0.815	0.793	0.837	< 0.001***								
SAPS II score	1.080	1.071	1.090	< 0.001***	1.021	1.008	1.035	0.002**	1.020	1.007	1.033	0.003**
LODS score	1.433	1.383	1.486	< 0.001***	1.355	1.288	1.426	< 0.001***	1.353	1.286	1.424	< 0.001***
Cerebrovascular disease	2.014	1.558	2.585	< 0.001***	2.153	1.592	2.910	< 0.001***	2.116	1.567	2.859	< 0.001***
Chronic pulmonary disease	0.835	0.670	1.035	0.104	0.819	0.635	1.055	0.122	0.830	0.644	1.069	0.148
Renal disease	1.496	1.224	1.832	< 0.001***	1.085	0.839	1.404	0.533	1.079	0.835	1.396	0.561
Diabetes mellitus	0.883	0.722	1.079	0.225								

aOR, adjusted odds ratio; BMI, body mass index; CI, chloride; LODS, Logistic Organ Dysfunction Score; MBP, mean blood pressure; OR, crude odds ratio; SAPS II, Simplified Acute Physiology Score II; WBC, white blood cell.

* $p < 0.05$. ** $p < 0.01$. *** $p < 0.001$.

the hypochloremia group compared to the normal group (p -value = 0.003, Figure 3). When further adjusted for age, gender, BMI, heart rate, MBP, respiratory rate, creatinine, WBC, urine output, SAPS II score, LODS score, rate of cerebrovascular disease, chronic pulmonary disease, and renal disease, the results for Cl level and hypochloremia group remained ($aOR = 0.971$, p -value < 0.001; $aOR = 1.464$, p -value = 0.01, respectively).

3.4. Total mortality

We further examined the long-term effect of chloride on total mortality rate (Table 5), the result suggested higher Cl level again showed a negative association for total mortality ($OR = 0.965$, p -value < 0.001). The hypochloremia group compared to the normal group exhibited a significant positive association with total mortality ($OR = 1.872$, p -value < 0.001). The result from Kaplan-Meier also indicated there were significantly more death events in the hypochloremia group compared to the normal group (p -value = 0.001, Figure 4). When adjusted for age, gender, BMI, heart rate, MBP, respiratory rate, creatinine, WBC, urine output, SAPS II score, LODS score, rate of cerebrovascular disease, chronic pulmonary disease, and renal disease, the significance remained for Cl level and hypochloremia group ($aOR = 0.958$, p -value < 0.001; $aOR = 1.762$, p -value ≤ 0.001 , respectively).

4. Discussion

In the current study, we discovered chloride level, whether in the form of continuous level or hyperchloremia/normal groups, obtain substantial prognostic potential for reflecting ICU mortality, in-hospital mortality, and total mortality. Specifically, we simultaneously observed shorter and longer prognostic effects of chloride in a maximum of 4-year follow-up period among HF patients admitted

to ICU. When further adjusted for multiple demographic and clinical characteristics, the aforementioned results remained significant.

The past literature consistently points out the prognostic role of baseline chloride levels in predicting the mortality rate. Several studies applied continuous Cl levels and exhibited a negative association with mortality. For instance, Grodin has shown the decrease of baseline chloride levels elevated by 14% of 2-month deaths, 9% of 6-month deaths, and 6% of < 1-year mortality, respectively.^{10,16} revealed chloride concentrations during admission are inversely associated with all-cause mortality (average follow-up time of 21 ± 9 months).¹⁷ The comparison between the hypochloremia/normal group also exhibited a positive association with mortality, with studies demonstrating that baseline hypochloremia strongly associated with 1-month, 3-month, and 12-month mortality.^{14,18,19} Our study has further extended the prognostic duration of chloride from ICU stay to a maximum 4-year follow-up, whether in the comparison of Cl level or hypochloremia/normal group.

We did not classify patients with hyperchloremia in the current study. Unlike the consensus reached in the association between low chloride levels and mortality, some debate exists regarding the prognostic role of high chloride levels. Some exhibited the inverse association with the hyperchloremia group,^{10,17,20} while some studies demonstrated the U shape pattern.^{9,12,14} Although the U shape relationship is presented, when focused on the statistics regarding the association between the high chloride/hyperchloremia group and mortality, most studies revealed insignificance or exhibited a similar trend compared to patients with the normal chloride group. These evidences highlight the relationship between hyperchloremia and mortality, unlike hypochloremia and mortality, warrants further investigation.

The current study has several limitations. Firstly, the selection bias existssince the selection process was based primarily on the ICD-10 code. Secondly, we only obtained the baseline chloride level

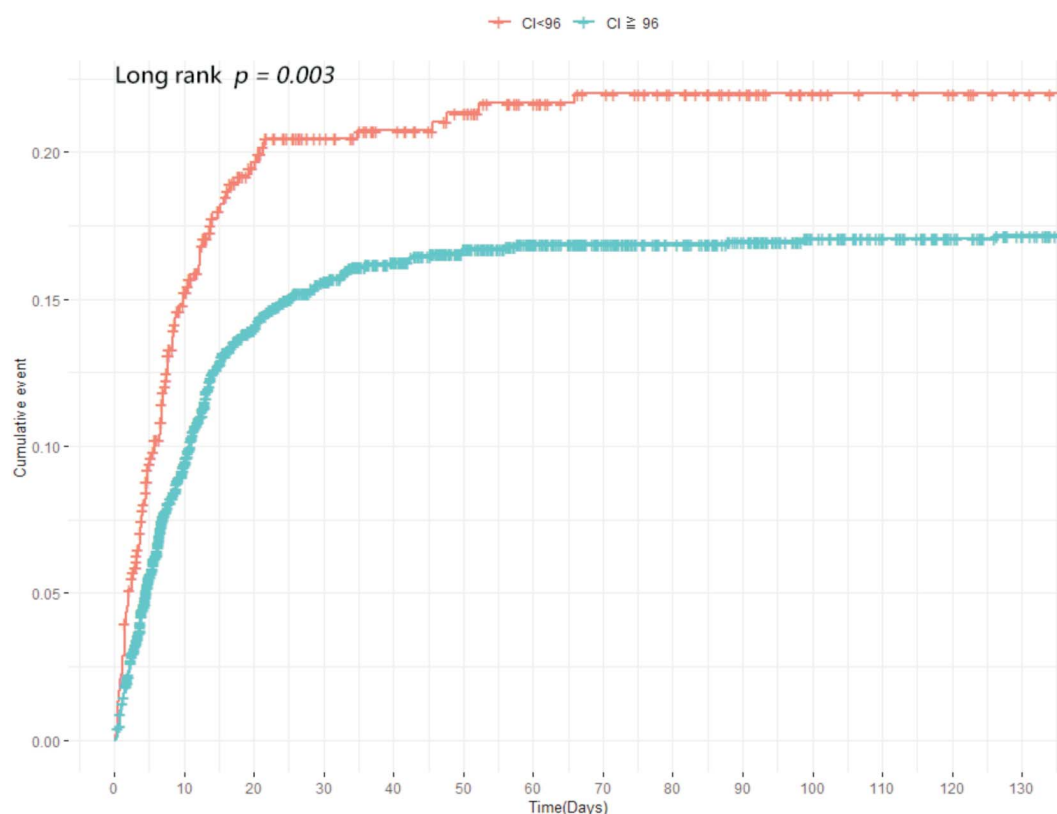


Figure 3. In-hospital mortality comparing the hypochloremia group and the normal group.

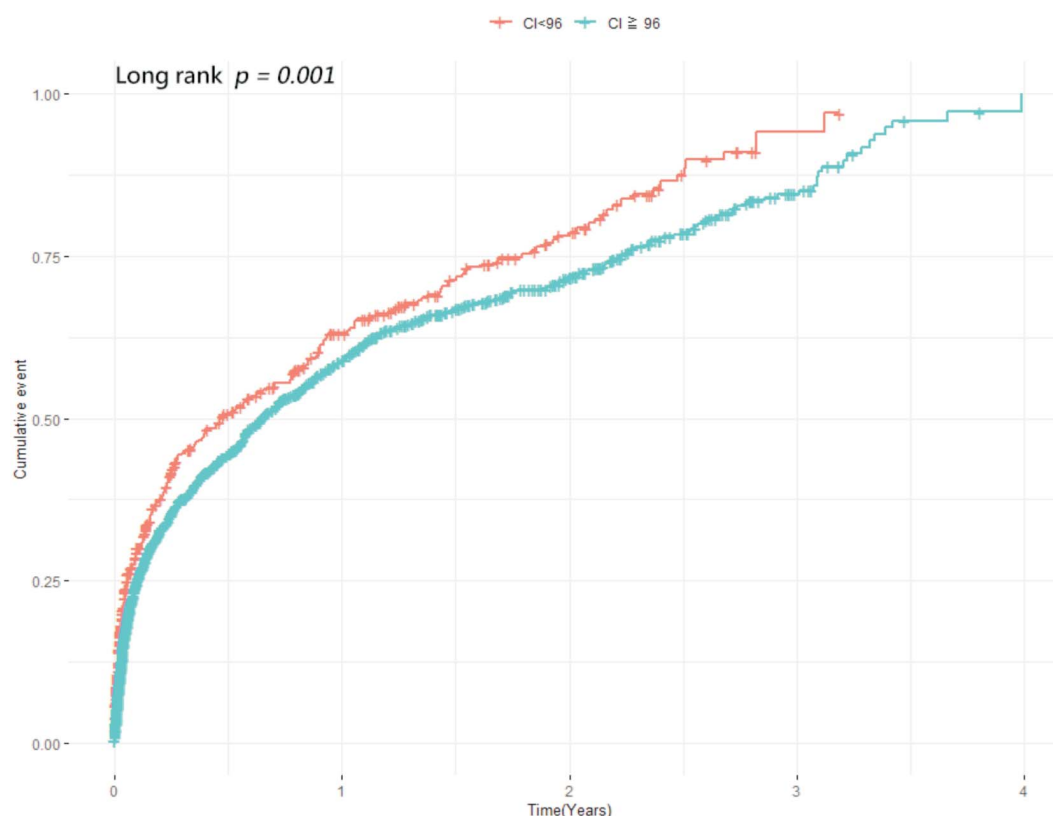
Table 5

The association between total mortality and chloride via comparing Cl level (mEq/L) and hypochloremia/normal group.

	Univariate analysis				Multivariate analysis (continuous Cl)				Multivariate analysis			
	OR	95% CI		p-value	aOR	95% CI		p-value	aOR	95% CI		p-value
		Lower	Upper			Lower	Upper			Lower	Upper	
Total mortality												
Cl level (mEq/L)	0.965	0.955	0.975	< 0.001***	0.958	0.947	0.970	< 0.001***				
Cl group (Cl < 96 vs. Cl ≥ 96)	1.872	1.548	2.264	< 0.001***					1.464	1.095	1.956	0.010*
Female	1.199	1.038	1.385	0.013*	1.148	0.973	1.355	0.102	1.198	0.942	1.524	0.140
Age (years)	1.046	1.039	1.053	< 0.001***	1.036	1.028	1.045	< 0.001***	1.027	1.015	1.040	< 0.001***
BMI (Kg/m ²)	0.968	0.959	0.977	< 0.001***	0.977	0.967	0.987	< 0.001***	1.002	0.988	1.017	0.747
Heart rate (bpm)	1.006	1.002	1.009	0.001**	1.002	0.998	1.007	0.235	1.008	1.002	1.013	0.008**
MBP (mmHg)	0.994	0.990	0.998	0.003**	0.999	0.995	1.003	0.625	0.999	0.993	1.005	0.665
Respiratory rate (beats/min)	1.039	1.027	1.052	< 0.001***	1.026	1.012	1.040	< 0.001***	1.022	1.003	1.041	0.024*
Creatinine (mg/dL)	1.133	1.086	1.184	< 0.001***	1.008	0.955	1.064	0.768	0.971	0.900	1.049	0.458
Hemoglobin (gm/dL)	0.942	0.912	0.973	< 0.001***								
Platelet (k/uL)	1.000	1.000	1.001	0.355								
WBC (K/uL)	1.007	0.999	1.015	0.089	0.999	0.992	1.007	0.845	1.011	1.003	1.020	0.010**
Urine output (mL)	0.999	0.999	1.000	< 0.001***	1.000	1.000	1.000	0.705	1.000	0.999	1.001	0.922
SAPS II score	1.062	1.055	1.069	< 0.001***	1.025	1.014	1.036	< 0.001***				
LODS score	1.235	1.203	1.268	< 0.001***	1.143	1.099	1.189	< 0.001***				
Cerebrovascular disease	1.339	1.089	1.648	0.006**	1.401	1.113	1.764	0.004**				
Chronic pulmonary disease	1.256	1.080	1.460	0.003**	1.366	1.153	1.620	< 0.001***	1.020	1.007	1.033	0.003**
Renal disease	1.757	1.522	2.029	< 0.001***	1.301	1.088	1.556	0.004**	1.353	1.286	1.424	< 0.001***
Diabetes mellitus	1.063	0.922	1.226	0.401								

aOR, adjusted odds ratio; BMI, body mass index; Cl, chloride; LODS, Logistic Organ Dysfunction Score; MBP, mean blood pressure; OR, crude odds ratio; SAPS II, Simplified Acute Physiology Score II; WBC, white blood cell.

* $p < 0.05$. ** $p < 0.01$. *** $p < 0.001$.

**Figure 4.** Total mortality comparing the hypochloremia group and the normal group.

and were not able to evaluate the prognostic effect for patients with changes in chloride patterns. Thirdly, the follow-up periods for subjects were heterogeneous, which indicates the loss of power for the inference of the relationship between chloride level and long-term mortality.

In conclusion, chloride serves as a prognostic marker for pre-

dicting mortality for HF patients admitted to ICU. The prognostic effect was revealed simultaneously in short-term mortality and long-term mortality. Although the implication of prognostic markers to real-world clinical usage requires much more effort, the add-on of chloride monitoring is beneficial to the future prevention of mortality of HF.

Conflicts of interest

None.

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