Association Between an Increase in Blood Urea Nitrogen at 24 Hours and Worse Outcomes in COVID-19 Pneumonia

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Research

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Abstract

Background and objectives: The dynamic change of blood urea nitrogen (BUN) have been proved to be related to the worse outcomes in various diseases such as pulmonary embolism, acute pancreatitis and acute nonvariceal upper GI bleeding. In the present study, we aimed to identify the association between blood urea nitrogen (BUN) change and clinical outcomes in patients presenting with COVID-19 pneumonia.

Methods: This is a retrospective study conducted in the Huoshenshan hospital. Patients with laboratory-confirmed COVID-19 from Feb 5th to March 5th in 2020 who had BUN level tested on admission and on the second day consecutively were included. Patients were stratified into two groups according to the BUN change (increase vs. no increase) during the first 24 hours. The primary outcome was in-hospital mortality. Moreover, other clinical outcomes were also compared. The potential risk factors of in-hospital mortality were analyzed.

Results: There were 266 patients included in the study. The mean change in BUN at 24 hours was 1.0 mg/dL, with 206 patients (77.4%) experiencing no increase in BUN and 60 patients (22.6%) experiencing an increase in BUN. In-hospital mortality was significantly higher in the BUN increase group compared to no increase group (30.0% vs. 5.8%, P<0.001). BUN increase group also had higher requirement for ICU admission, use of invasive mechanical ventilation and incidence of AKI (all P<0.001). After adjusted for related factors, the BUN increase was independently associated with the mortality with an odds ratio of 7.427[95% CI 2.370-23.279]. In the multivariable and survival analysis, BUN increase was also found to be associated with survival regardless of the admission BUN.

Conclusions: In patients with COVID-19, BUN increase at 24 hours was an independent predictor for a composite clinical outcome and in-hospital mortality. The association of BUN increase with worse outcomes further emphasizes the importance of monitoring BUN change and kidney function in the course of COVID-19.

Background

Since March 2020, coronavirus disease 2019 (COVID-19) has been declared a pandemic, which has subsequently affected 26 countries worldwide [1]. In general, COVID-19 is an acute self-limited disease but it can potentially be deadly [2-3]. The Chinese Center for Disease Control and Prevention summarized 72314 cases and reported that 5% patients were critical with respiratory failure, septic shock, and/or multiple organ failure, accounting for 49.0% case-fatality rate [4], Many factors has been reported to be related to increased mortality in COVID-19 pneumonia patients, including aging, obesity, presence of multiple comorbidity, depressed total lymphocytes, prolonged prothrombin time, elevated lactate dehydrogenase, etc [1, 2, 5-6].

Blood urea nitrogen (BUN), a routine laboratory test, is useful for risk stratification in various diseases such as heart failure, aortic dissection and peripheral artery disease [7-10]. In addition, BUN is considered

to be an independent predictor for mortality. An observational cohort study involving 13,384 patients, 69 hospitals showed that a strong association between extent of blood urea nitrogen (BUN) rise and mortality in acute pancreatitis even adjusted for confounding factors [11].However, there is no study assessing the relationship of dynamic change in BUN and worse outcomes in COVID-19 pneumonia.

In this study, we aimed to evaluate the relationship between dynamic change in BUN and clinical outcomes in patients admitted to a tertiary hospital with COCID-19 pneumonia.

Methods

Patients

This is a retrospective, observational, cohort study conducted in the Huoshenshan hospital, which is a newly-established, referral, portable hospital for the outbreak of COVID-19 in Wuhan. From Feb 5th to March 5th, patients with laboratory-confirmed COVID-19 were assessed for eligibility. Patients who had BUN level tested on admission and on the second day were included. Patients who had a known history of chronic kidney disease were excluded. An increase in BUN was defined as an increase in BUN at 24 hours of hospitalization compared with BUN at presentation. The study population was divided into two groups according to their BUN change in the first 24 hours from admission (Increase group and No increase group). This study was reviewed and approved by the institutional review board of Huoshenshan hospital.

Outcomes

The primary endpoint for the study was in-hospital death from any cause. Transfer to ICU, acute kidney injury, invasive mechanical ventilation and length of stay were also recorded.

Data Collection

Information of patient demographic and baseline clinical characteristics including age, gender, vital signs, comorbidities, laboratory values and coagulation function at admission were extracted from the electronic medical record system.

Statistical analyses

Statistical analyses were performed using SPSS software for Windows Version 25 and R software, version 3.6.2 (R Foundation for Statistical Computing). Continuous variables in the data were presented as mean value ± SD and categorical variables were presented as absolute numbers and percentage. Kolmogorov-Smirnov test was used to test the normality. The student t test or Mann-Whitney U test and Chi square or Fisher's exact tests were used to investigate the differences in quantitative and categorical variables, respectively between these groups.

Cox proportional-hazards models was used to evaluate the predictive factors for the survival rates. Multivariate COX regression only involved the variables that showed statistical significance in univariate COX analysis ($p<0.10$) with forced entry of variables such as age and gender. $P<0.05$ was considered significant for all analyses.

Results

Baseline characteristics

There were 266 patients included for analysis. The mean change in BUN at 24 hours was 1.0 mg/dL (SD 9.5 mg/dL), with 206 patients (77.4%) experiencing a decrease or no change in BUN and 60 patients (22.6%) experiencing an increase in BUN. Patients were divided into two groups according to whether BUN increased within 24 hours of admission in Table 1. The proportion of patients with history of hypertension in the BUN increased group is higher ($P<0.05$). Patients in the BUN increased group had faster respiratory rate ($P<0.05$), lower LYM, albumin and globulin level ($P<0.05$).

Clinical outcomes

To evaluate the association between BUN change and the mortality and clinical outcomes in COVID-19 patients more detailly, we analyzed the effect of BUN change both in patients with normal admission BUN level (<20mg/dl) or abnormal (≥20mg/dl) admission BUN level. Table 2 showed the in-hospital clinical outcomes of the study population, divided according to BUN increase (Yes vs. No). In-hospital mortality was significantly higher in the BUN increase group whatever admission BUN was normal or not (all $P<0.001$). Patients in the BUN increase group also had a higher incidence of transferring to intensive care unit, use of invasive mechanical ventilation and acute kidney injury (all $P<0.001$).

Association of BUN increase with in-hospital death

The association between BUN increase and the mortality of COVID-19 patients were further confirmed by logistic regression (Table 3). After adjusted for age, gender, hypertension, COPD, respiratory rate, LYM, ALB and GLO, the BUN increase was independently associated with the mortality of COVID-19 patients with an odds ratio (OR) of 7.427 [95% confidence interval (CI) 2.370-23.279]. However, the association was not significant in patients with history of hypertension after further adjusting for LYM, ALB and GLO.

The COX regression about BUN increase and the survival was summarized in table 4,5. Variables with a p value less than 0.05 in univariate regression analysis were included in the multivariate regression model. In the multivariable analysis, BUN increase (Yes vs. No) and admission BUN (<20mg/dL vs. ≥20 mg/dL) were associated with survival rate. BUN increase remained independent influence factor of survival with a hazard ratio (OR) of 6.838 [95% confidence interval (CI) 3.150-14.846].

Overall survival in the different patient groups is presented in figure 1. The survival curve of BUN increase group was significantly different from the survival curve of no increase group. Patients with BUN increase level had significant lower overall survival rate than patients with no increase group ($P<0.001$ Fig 1 A). In

pairwise comparison, patients with BUN increase had significant lower overall survival rate than patients with no BUN increase in normal admission BUN group (<20mg/dl) and abnormal admission group (≥20mg/dl) (Fig 1B, C).

Discussion

In this retrospective study we observed that a substantial proportion of patients had elevated serum BUN value at admission. Besides, 16.4% patients' BUN increased in 24 hours. We found that both elevated BUN at admission and BUN increase within first 24 hours were associated with higher in-hospital mortality.

Renal injury is not uncommon in patients with COVID-19, even in those who had no underlying kidney disease [12]. Early reports found that up to 30% of patients hospitalized with COVID-19 developed acute kidney injury [13]. Elevated BUN at admission and increasing BUN may be a sign of early kidney injury. One possible explanation of the high prevalence of kidney involvement is the immune response to the new coronavirus can be detrimental in some patients, leading to so-called a cytokine storm. In an attempt to kill the invading virus, this inflammatory reaction can destroy healthy tissue, including that of the kidneys. Besides, Angiotensin-converting enzyme and dipeptidyl peptidase-4, both expressed on renal tubular cells, were identified as binding partners for SARS-CoV and MERS-CoV, respectively. In kidney tissue and urine, COVID-19 RNA was also identified in COVID-19 patients [14-15]. Therefore, the kidney may be a susceptible target of this novel coronavirus.

Apart from injury of the kidney, the BUN increase may reflect these patients' health condition. Patients with BUN increase group had higher proportion of hypertension and COPD history and lower LYM, albumin and globulin level. Such patients may had functional defects in innate and adaptive immune cell populations who are vulnerable to COVID-19 and had worse prognosis.

In previous studies, AKI developed in 5% to 15% cases and carried a high (60%–90%) mortality rate in patients with SARS and MERS [16-18]. Early reports found that the incidence of AKI was 3-9% in patients with COVID-19 infection [19]. And in critically ill patients with COVID-19, the incidence of AKI can be up to almost 30% and the mortality was 80% in patients with AKI [20]. In our study, the incidence of AKI was 7.5%, and patients with increasing BUN in 24 hours had higher incidence of AKI and death. Therefore, monitoring BUN level might be of value even in patients with mild respiratory symptoms. Early detection of BUN and treatment of renal abnormalities, including avoidance of nephrotoxic drugs and adequate fluid therapy, may help improve the prognosis of these patients.

This is the first study showing an association between BUN change in 24 hours after admission and poor outcome in patients with COVID-19. The association of a rising BUN at 24 hours with worse clinical outcomes in COVID-19 may reflect under-resuscitation leading to pre-renal azotemia. In patients with COVID-19, early fluid therapy had never been studied before. Therefore, the fluid demand in COVID-19 patients should be evaluated. If these patients did not get adequate fluid supplementation in the course

of COVID-19, the kidney injury may be worsen consequently. And restoring intravascular volume may be a critical step in the early management of COVID-19.

There are some limitations in this study. First, patients had to have a BUN at presentation and at 24 hours of hospitalization to be included in the study, which raises the possibility of selection bias. Secondly, this was a single-center study at an referral hospital which only included 266 patients with COVID-19.

Conclusion

In conclusion, we found that an increase in BUN at 24 hours of hospitalization was a significant predictor of a composite clinical outcome and in-hospital mortality in patients with COVID-19. The association of a rise in BUN with worse outcomes further emphasizes the importance of monitoring BUN change and kidney function in the course of COVID-19.

Declarations

Ethical Approval and Consent to participate

This study was approved by the medical ethics committee of Huoshenshan Hospital (HSSLL036).

Consent for publication

Not applicable.

Availability of supporting data

The data sets supporting the results of this article are included within the article. Some data used during the study are available from the corresponding author by request.

Competing interests

The authors declare that they have no competing interests.

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Authors' contributions: Dr. Weiqin Li Zhihui Tong and Lu Ke design the work, Dr. Bo Ye, Jingjing Liang, and Hongbin Deng collect the data, Dr. Bo Ke and Hongbin Deng write the paper, Dr. Gang Li, Jing Zhou and Dr. Hanwei Zhao analyzed the data. All authors have read and approved the final manuscript.

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References

1. Guan WJ, Ni ZY, Hu Y, et al. Clinical Characteristics of Coronavirus Disease 2019 in China. N Engl J Med. 2020;382(18):1708-1720.
2. Yang X, Yu Y, Xu J, et al. Clinical course and outcomes of critically ill patients with SARS-CoV-2 pneumonia in Wuhan, China: a single-centered, retrospective, observational study. The Lancet Respiratory medicine 2020;8(5):475-481.
3. Murthy S, Gomersall CD, Fowler RA. Care for Critically Ill Patients With COVID-19. JAMA 2020. Online ahead of print.
4. Zunyou Wu, Jennifer M McGoogan. Characteristics of and Important Lessons From the Coronavirus Disease 2019 (COVID-19) Outbreak in China: Summary of a Report of 72 314 Cases From the Chinese Center for Disease Control and Prevention. JAMA. 2020. Online ahead of print.
5. Chen N, Zhou M, Dong X, et al. Epidemiological and clinical characteristics of 99 cases of 2019 novel coronavirus pneumonia in Wuhan, China: a descriptive study. Lancet. 2020;395(10223):507-513.
6. Wang Y, Zhou Y, Yang Z, et al. Clinical Characteristics of Patients with Severe Pneumonia Caused by the SARS-CoV-2 in Wuhan, China. Respiration. 2020;1-9.
7. Gerasimos Filippatos, Joseph Rossi, Donald M Lloyd-Jones, et al. Prognostic value of blood urea nitrogen in patients hospitalized with worsening heart failure: insights from the Acute and Chronic Therapeutic Impact of a Vasopressin Antagonist in Chronic Heart Failure (ACTIV in CHF) study. J Card Fail. 2007;13(5):360-4.
8. Jun Liu, Lian-Lian Sun, Jue Wang, et al. Blood urea nitrogen in the prediction of in-hospital mortality of patients with acute aortic dissection. Cardiol J. 2018;25(3):371-376.
9. Thomas Gary, Martin Pichler, Gernot Schilcher, et al. Elevated Blood Urea Nitrogen is Associated With Critical Limb Ischemia in Peripheral Arterial Disease Patients. Medicine (Baltimore). 2015;94(24):e948.
10. Doron Aronson, Murray A Mittleman, Andrew J Burger. Elevated blood urea nitrogen level as a predictor of mortality in patients admitted for decompensated heart failure. Am J Med. 2004;116(7):466-73.
11. Bechien U Wu, Richard S Johannes, Xiaowu Sun, et al. Early changes in blood urea nitrogen predict mortality in acute pancreatitis. Gastroenterology. 2009;137(1):129-35.
12. Meena P, Bhargava V, Rana DS, et al. COVID-19 and the kidney: A matter of concern. Curr Med Res Pract. 2020;10(4):165-168.
13. Darriverre L, Fieux F, de la Jonquière C. Acute renal failure during COVID-19 epidemic. Prat Anesth Reanim. 2020. Online ahead of print.
14. Werion A, Belkhir L, Perrot M, et al. SARS-CoV-2 Causes a Specific Dysfunction of the Kidney Proximal Tubule. Kidney Int. 2020;S0085-2538(20)30912-1.
15. He Q, Mok TN, Yun L, et al. Single-cell RNA sequencing analysis of human kidney reveals the presence of ACE2 receptor: A potential pathway of COVID-19 infection. Mol Genet Genomic Med.

2020;e1442.
16. Xia P, Wen Y, Duan Y, et al. Clinicopathological Features and Outcomes of Acute Kidney Injury in Critically Ill COVID-19 with Prolonged Disease Course: A Retrospective Cohort. J Am Soc Nephrol. 2020. Online ahead of print.
17. Rubin S, Orieux A, Prevel R, et al. Characterization of acute kidney injury in critically ill patients with severe coronavirus disease 2019. Clin Kidney J. 2020;13(3):354-361.
18. Gerges Harb J, Noureldine HA, Chedid G, et al. SARS, MERS and COVID-19: clinical manifestations and organ-system complications: a mini review. Pathog Dis. 2020;78(4):ftaa033.
19. Na KR, Kim HR, Ham Y, et al. Acute Kidney Injury and Kidney Damage in COVID-19 Patients. J Korean Med Sci. 2020;35(28):e257.
20. Gabarre P, Dumas G, Dupont T, et al. Acute kidney injury in critically ill patients with COVID-19. Intensive Care Med. 2020;46(7):1339-1348.

Tables

Table 1 Baseline characteristics of patients with an BUN increase versus decreased

or unchanged BUN at 24 hours

Demographics	No Increase	Increase	P
	(n = 206)	(n = 60)	
Age,years	64 ± 15	64 ± 14	0.898
Gender, male	116 (56.3)	29 (48.3)	0.625
Comorbidities			
Hypertension	77 (37.4)	33 (55)	0.022
Diabetes mellitus	42 (20.4)	12 (20)	0.999
Coronary heart disease	28 (13.6)	11 (18.3)	0.480
COPD	13 (6.3)	8 (13.3)	0.010
At admission			
Systolic blood pressure, mm Hg	125 ± 15	125 ± 14	0.724
Diastolic blood pressure, mm Hg	75 ± 10	76 ± 12	0.823
Heart rate, beats per minute	81 ± 13	85 ± 15	0.131
Respiratory rate, beats minute	20 ± 3	22 ± 5	0.034
Temperature , ℃	36.5 ± 0.4	36.6 ± 0.5	0.060
O2 saturation, %	96.6 ± 6.8	96.8 ± 3.0	0.876
Admission laboratory examination			
Creatinine (mg/dL)	71.98 ± 26.66	84.61± 24.63	0.197
RBC, $*10^{12}$ /L	3.73 ± 0.64	3.73 ± 0.59	0.256
Hemoglobin, g/dL	116.46 ± 21.41	114.0 ± 18.0	0.127
WBC, $*10^{9}$ /L	7.20 ± 2.93	7.39 ± 6.33	0.089
LYM, $*10^{9}$ /L	1.31 ± 0.65	1.13 ± 0.90	0.003
Neutrophil, $*10^{9}$ /L	5.22 ± 2.88	5.67 ± 6.22	0.261
Albumin, g/L	35.72 ± 4.79	33.87 ± 5.30	0.031
Globulin, g/L	28.33 ± 4.09	27.07 ± 3.93	0.036
ALT, U/L	43.43 ± 61.00	35.27 ± 52.73	0.130
AST, U/L	36.03 ± 44.12	30.80 ± 26.03	0.491
Blood urea nitrogen, mg/dL	17.28 ± 11.13	18.28 ± 15.83	0.259
D-dimer, ng/mL	1.58 ± 2.32	1.86 ± 2.21	0.229

CRP, mg/L	25.44 ± 37.62	40.00 ± 61.76	0.340
Admission coagulation function analysis			
PT, s	14.35 ± 6.76	14.25 ± 2.32	0.155
APTT, s	30.26 ± 11.16	29.43 ± 5.22	0.577
TT, s	15.60 ± 1.68	15.75 ± 1.77	0.446
PLT, *10^9 /L	227.96 ± 86.61	197.99 ± 80.88	0.086
FIB, g/L	3.25 ± 0.66	3.31 ± 0.61	0.408
INR	1.20 ± 0.56	1.19 ± 0.19	0.198

Table 2: Outcomes in patients with an BUN increase versus decreased or unchanged BUN at 24 hours

BUN			
Total (N=266)	No increase	Increase	
Transfer to Intensive care unit	28 (13.6)	23 (38.3)	P<0.001
Invasive mechanical ventilation	12 (5.80)	18 (30.0)	P<0.001
Acute kidney injury	7 (3.40)	13 (21.7)	P<0.001
All-cause mortality	12 (5.80)	18 (30.0)	P<0.001
Normal admission BUN (N=217)	No increase	Increase	
Transfer to Intensive care unit	15 (8.8)	13 (27.7)	P<0.001
Invasive mechanical ventilation	4 (2.4)	8 (17.0)	P<0.001
Acute kidney injury	1 (0.6)	6 (12.8)	P<0.001
All-cause mortality	4 (2.4)	8 (17.0)	P<0.001
Abnormal admission BUN (N=49)	No increase	Increase	
Transfer to Intensive care unit	12 (33.3)	11 (84.6)	P<0.001
Invasive mechanical ventilation	8 (22.2)	10 (76.9)	P<0.001
Acute kidney injury	5 (13,9)	8 (61.5)	P<0.001
All-cause mortality	7 (19.4)	10 (76.9)	P<0.001

Table 3 Odds ratios for death case associated with BUN Increase in whole population and in different

subgroups

	Model1		Model2		Model3	
	OR (95% CI)	P	OR (95% CI)	P	OR (95% CI)	P
Total	6.391 (2.845,14.360)	<0.001	5.964 (2.565,13.867)	<0.001	7.427 (2.370,23.279)	0.001
Subgroups						
Admission BUN						
<20mg/dL	7.262 (2.027,26.018)	0.002	6.475 (1.697,24.700)	0.006	4.235 (1.011,17.746)	0.048
≥20mg/dL	11.667 (2.576,52.845)	0.001	19.879 (3.225,122.539)	0.001	111.116 (3.359.,3675.461)	0.008
Hypertension						
Yes	3.750 (1.322,10.637)	0.013	3.984 (1.341,11.832)	0.013	6.342 (0.890,45.209)	0.065
No	10.937 (2.933,40.782)	<0.001	12.179 (3.049,48.641)	<0.001	12.223 (2.437,61.317)	0.002

Model1: unadjusted

Model2: adjusted for age, gender, hypertension, COPD and respiratory rate

Model3: adjusted for age, gender, hypertension, COPD, respiratory rate, LYM, ALB and GLO

OR odds ratio, CI confidence interval, COPD chronic obstructive pulmonary diseases LYM lymphocyte, ALB albumin, GLO globulin

Table 4. Single-factor Regression Analysis by Cox regression of death during hospitalization

Single-factor Regression Analysis			
Variable	HR	95%CI	P
Age,years	1.009	(0.983, 1.037)	0.498
Gender, male	1.005	(0.483, 2.092)	0.990
Comorbidities			
Hypertension	2.038	(0.957, 4.338)	0.065
Diabetes mellitus	1.868	(0.799, 4.372)	0.149
Coronary heart disease	1.995	(0.850, 4.680)	0.112
COPD	1.585	(0.477, 5.267)	0.452
At admission			
Systolic blood pressure, mm Hg	1.004	(0.982, 1.031)	0.600
Diastolic blood pressure, mm Hg	1.712	(0.777, 3.769)	0.182
Heart rate, beats per minute	1.025	(1.001, 1.050)	0.040
Respiratory rate, beats minute	1.031	(1.004, 1.058)	0.025
Temperature , ℃	1.613	(0.815, 3.192)	0.170
O2 saturation, %	0.919	(0.954, 1.006)	0.106
Admission laboratory examination			
Creatinine (mg/dL)	1.009	(1.005, 1.014)	P<0.001
RBC, $*10^{12}$ /L	0.834	(0.508, 1.370)	0.473
Hemoglobin, g/dL	0.994	(0.980, 1.009)	0.440
WBC, $*10^{9}$ /L	1.010	(0.985, 1.035)	0.434
LYM, $*10^{9}$ /L	0.128	(0.048, 0.343)	P<0.001
Neutrophil, $*10^{9}$ /L	1.079	(1.036, 1.122)	P<0.001
Albumin, g/L	0.836	(0.778, 0.898)	P<0.001
Globulin, g/L	0.979	(0.891, 1.076)	0.660
ALT, U/L	0.990	(0.976, 1.005)	0.192
AST, U/L	0.999	(0.998, 1.000)	0.166
D-dimer, ng/mL	1.138	(1.052, 1.232)	0.001
CRP, mg/L	1.011	(1.006, 1.016)	P<0.001

Admission coagulation function analysis			
PT, s	1.031	(0.985, 1.080)	0.186
APTT, s	1.027	(1.005, 1.048)	0.013
TT, s	1.204	(1.102, 1.316)	P<0.001
PLT, *10^9 /L	0.990	(0.985, 0.995)	P<0.001
FIB, g/L	0.840	(0.514, 1.373)	0.488
INR	1.395	(0.790, 2.466)	0.251
BUN Increase in 24hs	6.838	(3.150, 14.846)	P<0.001
BUN at admission≥20 mg/dl	5.881	(2.719, 12.718)	P<0.001

Table 5 Multipe-factor Regression Analysis by Cox regression of death during hospitalization

Multipe-factor Regression Analysis			
Variable	HR	95%CI	P
Age,y	1.009	(0.983, 1.037)	0.632
Gender, male	1.005	(0.483, 2.092)	0.163
At admission			
Heart rate, beats per minute	1.025	(1.001, 1.050)	0.312
Respiratory rate, beats minute	1.031	(1.004, 1.058)	0.039
Admission laboratory examination			
Creatinine (mg/dL)	1.009	(1.005, 1.014)	0.415
LYM, $*10^9$ /L	0.128	(0.048, 0.343)	0.284
Neutrophil , $*10^9$ /L	1.079	(1.036, 1.122)	0.683
Albumin, g/L	0.836	(0.778, 0.898)	0.704
D-dimer, ng/mL	1.138	(1.052, 1.232)	0.627
CRP, mg/L	1.011	(1.006, 1.016)	0.883
Admission coagulation function analysis			
APTT, s	1.027	(1.005, 1.048)	0.842
TT, s	1.204	(1.102, 1.316)	0.071
PLT, s	0.990	(0.985, 0.995)	0.340
BUN Increase in 24hs	6.838	(3.150, 14.846)	0.001
BUN at admission≥20 mg/dl	5.881	(2.719, 12.718)	0.017

Figures

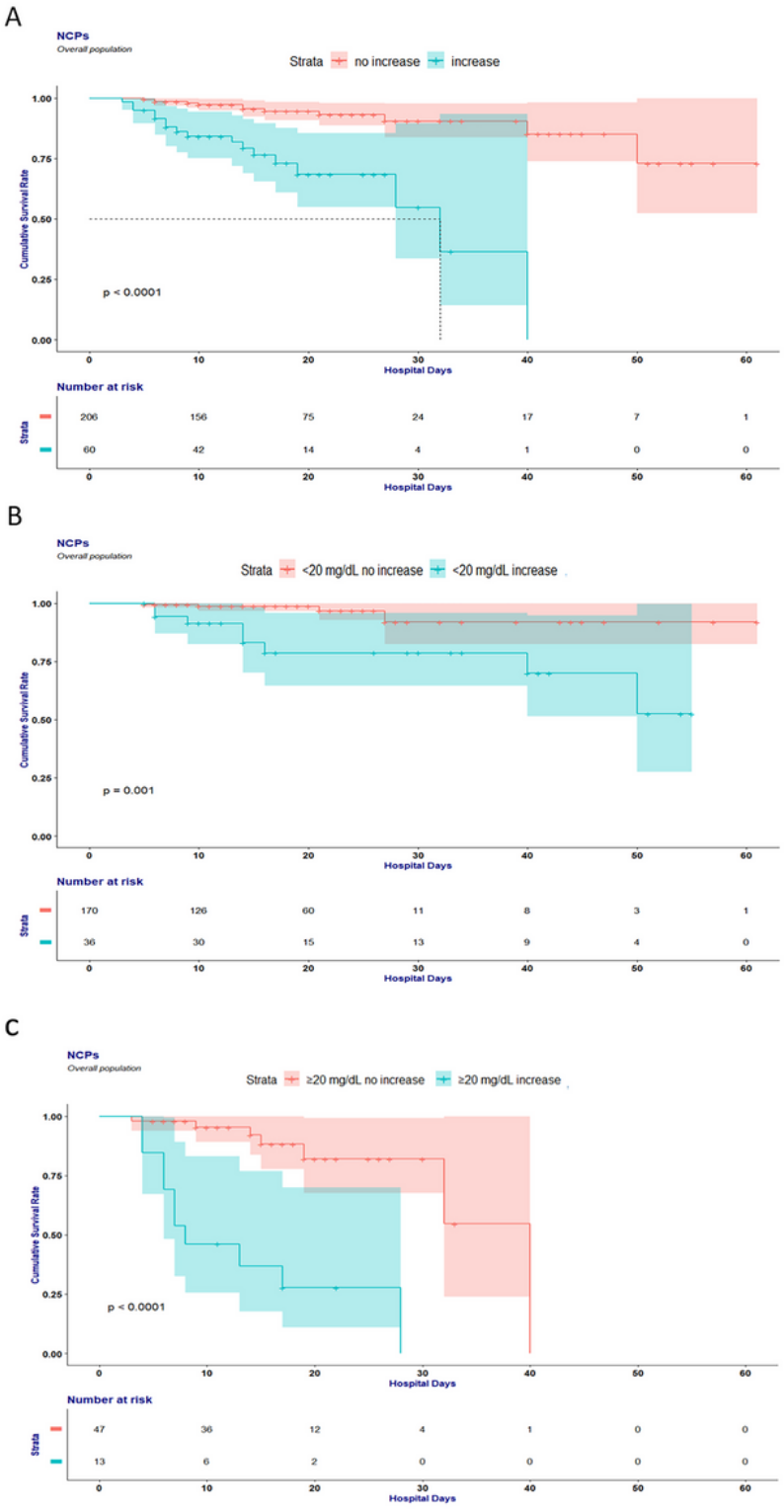

Figure 1

Cumulative incidence for in-hospital death of patients with coronavirus disease 2019 subgrouped by BUN value at admission and BUN change in 24 hours. A. Increase BUN versus no increase BUN at 24 hours B. Increase BUN versus no increase BUN at 24 hours when BUN at admission was normal (<20mg/dl) C. Increase BUN versus no increase BUN at 24 hours when BUN at admission was abnormal (≥20mg/dl)