Association Between the Level of Plasma B-type Natriuretic Peptide and in-hospital Mortality in Patients With Acute Exacerbation of COPD Without a History of Coronary Ischemic Heart Disease: A Retrospective Study

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Keywords: B-type natriuretic peptide, chronic obstructive pulmonary disease, mortality, mechanical ventilation

Posted Date: December 29th, 2020

DOI: https://doi.org/10.21203/rs.3.rs-135746/v1

Abstract

Background

Previous studies suggested that plasma B-type natriuretic peptide (BNP) level was often elevated in patients with acute exacerbations of chronic obstructive pulmonary disease (AECOPD) and was associated with increased mortality. However, most studies did not consider the fact that conditions such as coronary ischemic heart disease can also increase BNP level. Therefore, we aimed to explore the association between BNP level and in-hospital mortality in patients with AECOPD without a history of coronary ischemic heart disease.

Methods

In this retrospective cohort study, data on patients with AECOPD but without a history of coronary ischemic heart disease who were admitted in a comprehensive hospital from January 2017 to December 2019 and were identified using International Statistical Classification of Diseases and Related Health Problems, Nineth Revision (ICD-9) codes were included. BNP level was determined within 24 hours after admission, and the value was $\log_2$ transformed. The primary outcome was in-hospital mortality, and the secondary outcome was a composite outcome of in-hospital mortality or invasive mechanical ventilation.

Results

A total of 300 patients were included in this study (mean ages, 76.88 years; SD, 9.87; men, 63.33%). Sixteen patients (5.33%) showed in-hospital mortality; 29(9.67%) and 22 (6.67%) patients were assisted with invasive mechanical ventilators and noninvasive positive pressure ventilators, respectively. Univariate cox regression analysis showed that the unadjusted HRs of the primary and secondary outcomes were 1.85 (95% CI, 1.39-2.47) and 1.42 (95% CI, 1.19-1.71), respectively. After adjustment for age, sex, past medical history, smoking status, drinking status, CURB65 (Confusion, Urea > 7mmol/L, Respiratory rate≥30/min, Blood pressure systolic < 90 mmHg or diastolic <60 mmHg and age > 65 years), arterial partial pressure of O_2(PaO_2), arterial partial pressure of CO_2 ($PaCO_2$), neutrophil count, and D-dimer level (only secondary outcome), the adjusted HRs of the primary and secondary outcomes were 2.44 (95% CI, 1.43-4.14) and 1.36 (95% CI, 1.07-1.74), respectively. The results of subgroup analysis by age, sex, and lung function were robust.

Conclusions

The plasma $\log_2$BNP level was significantly associated with in-hospital mortality and a composite outcome of in-hospital mortality or invasive mechanical ventilation

Introduction

Chronic obstructive pulmonary disease (COPD) is a global public health challenge because of its high prevalence and the related disability and mortality.[1] COPD has become the third leading cause of death worldwide and is estimated to become the source of the seventh highest burden worldwide in 2030.[2] Prevalence was higher in men than in women, and in individuals aged ≥40 years, it was 13.7% in China; [1] 6.4% of Americans reported receiving a diagnosis of COPD. [3]

Plasma brain natriuretic peptide and N-terminal fragment of pro-B-type natriuretic peptide (BNP; NT-pro-BNP) are cardiac neurohormones that are synthesized and released from ventricular myocytes in response to myocardial stretching. [4] It had been proven that BNP and NT-pro-BNP are diagnostic and prognostic biomarkers of congestive heart failure [5] and established that BNP and NT-pro-BNP are independent predictors of death and cardiovascular events in patients with stable coronary artery disease.[6] Furthermore, they were found to be elevated with right ventricular overload and to be associated with a poor prognosis in patients with pulmonary arterial hypertension and pulmonary thromboembolism. [7-9]

Previous studies have shown that BNP and NT-pro-BNP are probably useful in predicting the outcomes of COPD. A prospective, single-center study on acute exacerbation of COPD (AECOPD) suggested that elevated NT-pro-BNP level was associated with an increase in 30-day mortality. [10] Another prospective study showed that NT-pro-BNP level was associated with in-hospital mortality and 1-year mortality in patients with exacerbations of COPD; however, in their studies, about 35.9% of patients had congestive heart failure. [11] Stolz et al. found that BNP accurately predicted the need for intensive care unit (ICU) treatment, [12] and BNP was an independent predictor of requirement for noninvasive ventilation, mechanical ventilation, and noninvasive ventilation failure in patients with AECOPD along with preserved left ventricular function. [13] However, some studies have found that NT-pro-BNP level was not associated with the requirement for noninvasive positive pressure ventilation, mechanical ventilation, or in-hospital mortality in patients with AECOPD without underlying left ventricular dysfunction. [14]

We aimed to assess the association between BNP level and in-hospital mortality or requirement for invasive mechanical ventilation in patients hospitalized for AECOPD without a history of coronary ischemic heart disease.

Methods

Ethics Committees of Jinan Central Hospital reviewed and approved this retrospective study protocol in accordance with the precepts established by the Declaration of Helsinki (the assurance number 2020-137-01), and waived the need for obtaining informed consent from patients.

Data Sources

All data were obtained from electronic patient files and medical data intelligence platform of Jinan Central Hospital. The medical data intelligence platform is administered by Jinan Central Hospital, and all

local in-patient and out-patient information was registered in it since January 2009.

Study Patients and Covariates

In this retrospective cohort study, patients who were diagnosed with AECOPD using International Statistical Classification of Diseases and Related Health Problems, Nineth Revision (ICD-9 codes) between January 2017 and December 2019 were included (explicit ICD-9 codes J44.0, J44.1 and J44.9). Patients with a medical history of coronary ischemic heart disease and advanced renal disease were excluded. Patients were excluded if the discharge diagnosis included acute asthma, bronchiectasis, bronchial lung cancer, and acute myocardial infarction. If patients were admitted more than once during the study period, only the first admission was included in the analysis. We obtained medical history and physiological variables that were recorded on admission. These data were used to compile two prognostic scores: CURB65 and BAP65 (BUN level > 25 mg/dL, Altered mental status, Pulse > 109 beats/min, Age≥65 years). [15-16] If laboratory parameters were measured more than once during the in-hospital stay, data obtained from the first measurement within 24 h of admission alone were collected. The plasma BNP was a continuous variable. In this retrospective cohort study, there were 2 outcomes of interest, primary outcome, in-hospital mortality; secondary outcomes, (1) a composite outcome of in-hospital mortality or invasive mechanical ventilation and (2) invasive mechanical ventilation.

Statistical Analysis

Continuous variables with normal distribution are presented as mean ± standard deviation (SD). Non-normally distributed variables are presented as median (interquartile range [IQR]). Categorical variables are presented as percentage. Differences between groups were compared using the Kruskal-Wallis test for continuous variables or Wilcoxon-Mann-Whitney Test for categorical variables. BNP was $\log_2$ transformed. Outcomes were compared using cox regression, both unadjusted and adjusted. Adjusted models included the following covariates: age; sex; smoking status of never, ex-smoker, and current smoking; drinking status of never, ex-drinker, and current drinker; past medical history of hypertension, diabetes, cerebral vascular disease, renal dysfunction, atrial fibrillation, and malignancy; variables with $p \leq 0.1$ in univariate analysis (CURB65, blood neutrophil count, D-dimer level, arterial partial pressure of O_2 [PaO_2], and arterial partial pressure of CO_2 [$PaCO_2$]). Subgroup analyses (by sex, age and missing of lung function) were performed, and differences in HRs between subgroups were tested by Wald tests for statistical interaction. Statistical analysis was performed using Packages R (The R Foundation, Vienna, Austria); a statistical significance level of 0.05 was used.

Results

In this retrospective cohort study designed to examine the association of BNP level with the outcomes of patients with AECOPD, medical records of 722 patients hospitalized with AECOPD were reviewed, and those on 300 patients were included. Patient selection is shown in the Figure 1. The demographic and baseline characteristics of all the included patients are shown in Table 1. Among the patients, 63.33%

were men. The mean age of patients was 76.88 ± 9.53 years. Sixteen patients died during hospitalization, 29 patients were assisted with invasive mechanical ventilator, and 22 patients were assisted with noninvasive positive pressure ventilation. The duration of hospital stay was 12.04 ± 6.35 days. BNP levels of 300 (100%) patients were available. Its median was 65.50 pg/ml (IQR, 30.00, 181.50). C-reactive protein level, findings of arterial blood gas test, and lung function data were missing in the study, but the missing data was processed according to the median value. After median replacement of missing data, there was no difference in the findings of multivariable cox regression models (Table 1s).

In univariate cox regression analysis, we used all baseline variables of the entire cohort to assess factors associated with the primary outcome and the secondary outcomes (Table 2, Table 2b and Table 2c). The in-hospital mortality was 5.33% (16/300). Table 3 shows the unadjusted and adjusted HRs from the Cox regression analysis. A higher $\log_2$BNP value was significantly associated with a greater risk of in-hospital mortality in the unadjusted analysis (HR, 1.85 [95% CI, 1.39-2.47]), and the association was still significant after accounting for age, sex, smoking status, drinking status, past medical history, CURB65, PaO_2, and $PaCO_2$ (HR, 2.44 [95% CI, 1.43-4.14]).

The secondary outcome of in-hospital mortality or invasive mechanical ventilation was observed 10.67% (32/300). Table 3 shows the unadjusted and adjusted HRs derived from the Cox regression analysis. As in the case of the primary outcome of in-hospital mortality, a higher $\log_2$BNP value was significantly associated with a higher risk of the combined end point of in-hospital mortality or invasive mechanical ventilation in unadjusted analysis (HR, 1.42 [95% CI, 1.19-1.71]), and this association was still significant after adjusting for age, sex, smoking status, drinking status, past medical history, CURB65, blood neutrophil count, D-dimer level, PaO_2, and $PaCO_2$ (HR, 1.36 [95% CI, 1.07-1.74]).

The secondary outcome of invasive mechanical ventilation was observed in 9.67% (29/300) of patients. Table 3 shows the unadjusted and adjusted HRs derived from the Cox regression analysis. As in the case of the primary outcome of in-hospital mortality, a higher $\log_2$BNP value was significantly associated with a higher risk of invasive mechanical ventilation in unadjusted analysis (HR, 1.48 [95% CI, 1.22-1.80]), and this association was still significant after adjusting for age, sex, smoking status, drinking status, past medical history, CURB65, blood neutrophil count, D-dimer level, PaO_2, and $PaCO_2$ (HR, 1.45 [95% CI, 1.11-1.88]).

In this study, among patients with AECOPD, subgrouping was performed according to (1) sex, (2) age, and (3) missing lung function data were examined. The results were similar to the overall results, and all tests for interaction with these covariates were not statistically significant (P >0.05) (Table 4).

Discussion

Among patients diagnosed with exacerbations of COPD, this study found significant association between log_2BNP and in-hospital mortality, a composite outcome of in-hospital mortality or mechanical ventilation, and mechanical ventilation, after adjusting for baseline demographics, comorbidities and other hematological data; results of the subgroup analysis were stable; and this suggests that BNP can be used as an important biomarker of prognosis in patients with COPD exacerbations.

A previous prospective study by Chang et al. found that elevated NT-pro-BNP levels (>220 pmol/L) were associated with increased 30-day mortality, and this finding is consistent with that of our study. [10] Another study by Hai et al. found that NT-pro-BNP level (≥551.35 ng/l) was associated with in-hospital mortality and 1-year mortality in patients with exacerbations of COPD, but in their study, about 35.9% of patients had congestive heart failure. [11] A systematic review and meta-analysis also found that elevated NT-pro-BNP values were associated with all-cause in-hospital mortality in patients with and without exacerbation of COPD. [17]

Stolz et al. found that BNP was not associated with 6-month or 2-year mortality in patients with exacerbations of COPD, but BNP accurately predicted the need for ICU treatment, and the need for mechanical ventilation was the most common reasons for ICU admission. [12] This is confirmed in our study, we also found that the association between log_2BNP and invasive mechanical ventilation was strong in multivariate analysis. This was consistent with the finding of previous studies in which BNP was an independent predictor of higher noninvasive ventilation requirement, mechanical ventilation use, and noninvasive ventilation failure in patients with AECOPD with preserved left ventricular function, but they did not assess the association of BNP and in-hospital mortality. [13] Another previous retrospective study by Muhammad et al. demonstrated that log-transformed NT-pro-BNP levels were positively associated with echocardiographically estimated right ventricular systolic pressure; however, NT-pro-BNP was not associated with the need for noninvasive positive pressure ventilation/mechanical ventilation or with in-hospital mortality in patients with AECOPD without underlying left ventricular dysfunction. [18]

Plasma brain natriuretic peptide and NT-pro-BNP are cardiac neurohormones that are synthesized and released from ventricular myocytes in response to myocardial stretch. [4] It was established that NT-pro-BNP is a diagnostic and prognostic biomarker of congestive heart failure, [5] and it has also been found to be a significant and independent predictor of death and cardiovascular events in stable coronary artery disease.[6] In our study, we had excluded patients with a past medical history of coronary ischemic heart disease; however, we had not obtained the echocardiographic data; therefore, a small number of patients with undiagnosed heart failure may have been included. The meta-analysis performed by Pavasini et al. suggested that having a history of heart failure did not influence the relationship between elevated NT-pro-BNP levels and long-term mortality. [18]

The pathophysiological processes underlying the elevation of BNP level in patients with exacerbations of COPD are unknown. Hypoxia often occurs in severe COPD, especially in patients with AECOPD. In our research, oxygen tension on arterial blood gas measurement was strongly associated with in-hospital

mortality (P=0.008), composite outcome of in-hospital mortality or mechanical ventilation(P=0.009), and mechanical ventilation(P=0.014) in univariate analysis. Hypoxia can cause pulmonary hypertension and right ventricular dysfunction by pulmonary vasoconstriction. [7] Concentration of NT pro-BNP was significantly higher in those with a higher pulmonary hypertension than in those with a lower pulmonary hypertension, and they found that NT pro-BNP was an excellent discriminator of right-ventricular impairment but not of cor pulmonale. [8] Previous studies have found that BNP and NT-pro-BNP levels were elevated in patients with pulmonary thromboembolism, and BNP may be a useful determinant of the short-term outcome. [9]

Coronary artery ischemia may be more likely to occur in patients with AECOPD. Gavin et al found that exacerbations of COPD increase the risk of myocardial infarction. [14] This finding may be related to hypoxic ischemia of myocardium caused by hypoxia. Hypoxic myocardial ischemia leads to a decrease in myocardial contractility, which increases the burden on the heart and increases BNP or NT-pro-BNP secretion. In our study, 12 patients had acute myocardial infarction during hospitalization and were excluded.

There are some limitations to our research. First, our study was observational; no causal inference can be obtained, and relationships should be interpreted as associations. Second, COPD specific diagnostic codes for the identification of patients were adopted. Spirometry data of some patients were not available completely. However, we reviewed the electronic patient files and medical data intelligence platform of Jinan Central Hospital and found that they were hospitalized many times and inhaled maintenance drugs of COPD for a long time; in subgroup analysis, irrespective of whether data on the lung function were missing or not, the results were consistent. Third, although our study was a retrospective single-center trial, it was closer to real-world clinical practice, and the patient treatments by clinicians were not influenced by the study. Considering that no multicenter study has been performed so far, a multi-center prospective study is urgently needed to further explore the prognostic efficiency of BNP for AECOPD.

Conclusions

This study suggests that a higher $\log_2$BNP value was significantly associated with in-hospital mortality and invasive mechanical ventilation in patients with AECOPD, and BNP is a promising prognostic marker of in-hospital mortality and invasive mechanical ventilation in patients with AECOPD. These findings justify that a multi-center prospective study is urgently needed to further explore the prognostic efficiency of BNP for AECOPD.

Abbreviations

AECOPD, Acute exacerbations of chronic obstructive pulmonary disease; BAP65, BUN level > 25 mg/dL, Altered mental status, Pulse > 109 beats/min, Age≥65 years; BNP, B-type natriuretic peptide; COPD, Chronic obstructive pulmonary disease; CURB65, Confusion, Urea > 7mmol/L, Respiratory rate≥30/min,

Blood pressure systolic < 90 mmHg or diastolic <60 mmHg and age > 65 years; ICD-9, International Statistical Classification of Diseases and Related Health Problems, Nineth Revision; ICU, Intensive care unit; SD, Standard deviation

Declarations

Ethics approval and consent to participate

Ethics Committees of Jinan Central Hospital reviewed and approved this retrospective study protocol.

Consent for publication

Not applicable.

Availability of data and materials

The datasets used and/or analyzed during the current study are available from the corresponding author on reasonable request.

Competing interests

The authors declare that they have no competing interests.

Funding

No funding.

Authors' contributions

DL conceived and designed the study; JC and JL devised the analysis of the data. JC, JW, ML and CX performed the study and drafted the manuscript. JL proofed the manuscript.

Acknowledgements

Not Applicable.

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Tables

Table 1: Cohort characteristics of the study patients

Variables	All (n=300)
Sex, n (%)	
male	190 (63.33)
female	110 (36.67)
Age, mean in years (SD)	76.88 (9.53)
Smoking status, n (%)	
Never	104 (34.67)
Ex-smoker	156 (52.00)
Current smoking	40 (13.33)
Drinking status, n (%)	
Never	195 (65.00)
Ex-drinker	88 (29.33)
Current drinker	17 (5.67)
Past medical history	
Hypertension, n (%)	79 (26.33)
Diabetes, n (%)	35 (11.67)
Cerebral vascular disease, n (%)	38 (12.67)
Renal dysfunction, n (%)	4 (1.33)
Malignancy, n (%)	7 (2.33)
Atrial fibrillation, n (%)	10 (3.33)
Duration of hospital stay, mean in days (SD)	12.04 (6.35)
Lung function, mean (SD)	
FVC (litres)	2.95 (0.71)
FEV1 (litres)	2.22 (0.63)
FEV1 (%predicted)	70.39 (19.75)
FEV1/FVC (%)	56.38 (10.41)
Clinical scores	
CURB65, mean (SD)	1.24 (0.69)
BAP, mean (SD)	2.33 (0.73)

BMI	24.15 (4.14)
Arterial blood gas	
$PaCO_2$	49.40 (17.06)
PaO_2	79.97 (25.31)
pH	7.39 (0.08)
Neutrophil count, $\times 10^9$/l	6.70 (4.25)
CRP, mg/l	16.9 (3.48, 47.10)
Creatinine, umol/l	68.50 (56.60, 87.10)
Urea, mmol/l	5.20 (4.00, 6.70)
Albumin, g/l	37.90 (4.96)
D-dimer, mg/l	0.54 (0.31, 1.33)
BNP, pg/ml	65.50 (30.00, 181.50)
Treatment, n (%)	
Systemic corticosteroids	300 (100)
Table 1 continued	
Antimicrobial therapy	300 (100)
Bronchodilators	300 (100)
Non-invasive ventilation	20 (6.67)
Invasive ventilation	29 (7.33)
In-hospital mortality	16 (5.33)
In-hospital mortality or invasive ventilation	32 (10.67)

Abbreviations: CRP, C reactive protein; BMI, body mass index; PaO_2, arterial partial pressure of O_2; $PaCO_2$, arterial partial pressure of CO_2; BNP, plasma B-type natriuretic peptide; FEV1, forced expiratory volume in 1 s; FVC, forced vital capacity.

Table 2: Univariate associations with in-hospital mortality

Variables	All (n=300)	P Value
Sex, n (%)		
female	110 (36.67)	NA
male	190 (63.33)	0.573
Age, mean in years (SD)	76.88 (9.53)	0.191
Smoking status, n (%)		
Never	104 (34.67)	NA
Ex-smoker	156 (52.00)	0.301
Current smoking	**40 (13.33)**	**0.050**
drinking status, n (%)		
Never	195 (65:00)	NA
Ex-drinker	88 (29.33)	0.369
Current drinker	17 (5.67)	0.372
Past medical history		
Hypertension, n (%)	79 (26.33)	0.701
Diabetes, n (%)	35 (11.67)	0.311
Cerebral vascular disease, n (%)	38 (12.67)	0.154
Renal dysfunction, n (%)	4 (1.33)	NA
Malignancy, n (%)	7 (2.33)	0.430
Atrial fibrillation, n (%)	**10 (3.33)**	**0.062**
Lung function, mean (SD)		
FVC (litres)	2.94 (0.71)	0.580
FEV1(litres)	2.21 (0.63)	0.483
FEV1(%predicted)	70.19 (19.82)	0.174
FEV1/FVC (%)	56.28 (10.42)	0.301
Clinical scores		
CURB65, increment by 1	**1.24 (0.69)**	**0.017**
BAP, increment by 1	2.33 (0.73)	0.121
BMI	24.15 (4.14)	0.480

$PaCO_2$	49.40 (17.06)	0.839
PaO_2	**79.97 (25.31)**	**0.008**
pH	7.39 (0.08)	0.433
Neutrophil count, $\times 10^9$/l	6.70 (4.25)	0.189
CRP, mg/l	35.01(45.01)	0.840
Creatinine, umol/l	78.26 (43.24)	0.732
Urea, mmol/l	6.07 (3.96)	0.166
Albumin, g/l	37.90 (4.96)	0.125
D-dimer, mg/l	1.17 (1.67)	0.412
BNP, pg/ml	**207.82 (378.35)**	**0.001**

Abbreviations: CRP, C reactive protein; BMI, body mass index; PaO_2, arterial partial pressure of O_2; $PaCO_2$, arterial partial pressure of CO_2; BNP, plasma B-type natriuretic peptide; FEV1, forced expiratory volume in 1 s; FVC, forced vital capacity.

Table 2b Univariate associations with composite of in-hospital mortality or Invasive ventilation

Variables	All (n=300)	P Value
Sex, n (%)		
female	110 (36.67)	NA
male	190 (63.33)	0.426
Age, mean in years (SD)	76.88 (9.53)	0.191
Smoking status, n (%)		
Never	104 (34.67)	NA
Ex-smoker	156 (52.00)	0.541
Current smoking	40 (13.33)	0.115
drinking status, n(%)		
Never	195 (65:00)	NA
Ex-drinker	88 (29.33)	0.545
Current drinker	17 (5.67)	0.925
Past medical history		
Hypertension, n (%)	79 (26.33)	0.714
Diabetes, n (%)	35 (11.67)	0.900
Cerebral vascular disease, n (%)	38 (12.67)	0.165
Renal dysfunction, n (%)	4 (1.33)	NA
Malignancy, n (%)	7 (2.33)	0.756
Atrial fibrillation, n (%)	10 (3.33)	0.291
Lung function, mean (SD)		
FVC (litres)	2.94 (0.71)	0.285
FEV1 (litres)	2.21 (0.63)	0.550
FEV1(%predicted)	70.19 (19.82)	0.492
FEV1/FVC (%)	56.28 (10.42)	0.687
Clinical scores		
CURB65, increment by 1	**1.24 (0.69)**	**<0.001**
BAP, increment by 1	**2.33 (0.73)**	**0.011**
BMI	24.15 (4.14)	0.514

PaCO2	**49.40 (17.06)**	**0.001**
PaO2	**79.97 (25.31)**	**0.009**
pH	**7.39 (0.08)**	**0.001**
Neutrophil count, $\times 10^9$/l	**6.70 (4.25)**	**0.013**
CRP, mg/l	35.01 (45.01)	0.962
Creatinine, umol/l	78.26 (43.24)	0.303
Urea, mmol/l	6.07 (3.96)	0.136
Albumin, g/l	37.90 (4.96)	0.317
D-dimer, mg/l	**1.17 (1.67)**	**0.063**
BNP, pg/ml	**207.82 (378.35)**	**0.008**

Abbreviations: CRP, C reactive protein; BMI, body mass index; PaO_2, arterial partial pressure of O_2; $PaCO_2$, arterial partial pressure of CO_2; BNP, plasma B-type natriuretic peptide; FEV1, forced expiratory volume in 1 s; FVC, forced vital capacity.

Table 2c Univariate associations with invasive ventilation

Variables	All (n=300)	P Value
Sex, n (%)		
female	110 (36.67)	NA
male	190 (63.33)	0.434
Age, mean in years (SD)	**76.88 (9.53)**	**0.183**
Smoking status, n (%)		
Never	104 (34.67)	NA
Ex-smoker	156 (52.00)	0.305
Current smoking	**40 (13.33)**	**0.050**
drinking status, n(%)		
Never	195 (65:00)	NA
Ex-drinker	88 (29.33)	0.708
Current drinker	17 (5.67)	0.634
Past medical history		
Hypertension, n(%)	79 (26.33)	0.679
Diabetes, n(%)	35 (11.67)	0.843
Cerebral vascular disease, n(%)	**38 (12.67)**	**0.050**
Renal dysfunction, n(%)	4 (1.33)	NA
Malignancy, n(%)	7 (2.33)	0.674
Atrial fibrillation, n(%)	10 (3.33)	0.256
Lung function, mean (SD)		
FVC (litres)	2.94 (0.71)	0.200
FEV1(litres)	2.21 (0.63)	0.169
FEV1(%predicted)	70.19 (19.82)	0.893
FEV1/FVC (%)	56.28 (10.42)	0.969
Clinical scores		
CURB65, increment by 1	**1.24 (0.69)**	**<0.001**
BAP, increment by 1	**2.33 (0.73)**	**<0.001**
BMI	24.15 (4.14)	0.514

PaCO2	**49.40 (17.06)**	**<0.001**
PaO2	**79.97 (25.31)**	**0.014**
PH	**7.39 (0.08)**	**<0.001**
Neutrophil count, $\times 10^9$/l	**6.70 (4.25)**	**0.007**
CRP, mg/l	35.01 (45.01)	0.905
Creatinine, umol/l	78.26 (43.24)	0.419
Urea, mmol/l	**6.07 (3.96)**	**0.072**
Albumin, g/l	37.90 (4.96)	0.305
D-dimer, mg/l	**1.17 (1.67)**	**0.038**
BNP, pg/ml	**207.82 (378.35)**	**0.007**

Abbreviations: CRP, C reactive protein; BMI, body mass index; PaO_2, arterial partial pressure of O_2; $PaCO_2$, arterial partial pressure of CO_2; BNP, plasma B-type natriuretic peptide; FEV1, forced expiratory volume in 1 s; FVC, forced vital capacity.

Figures

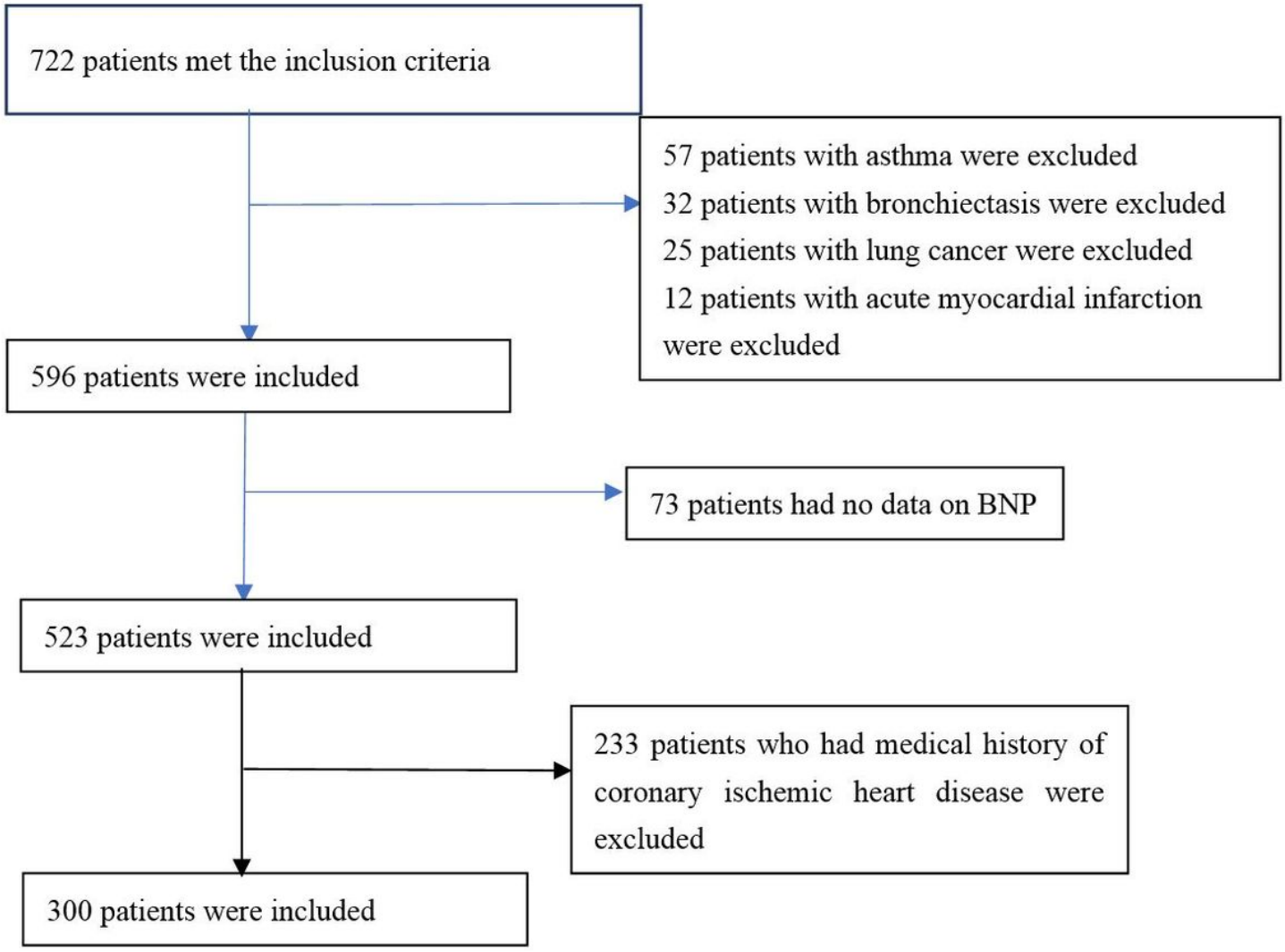

Figure 1

Flowchart of patient selection

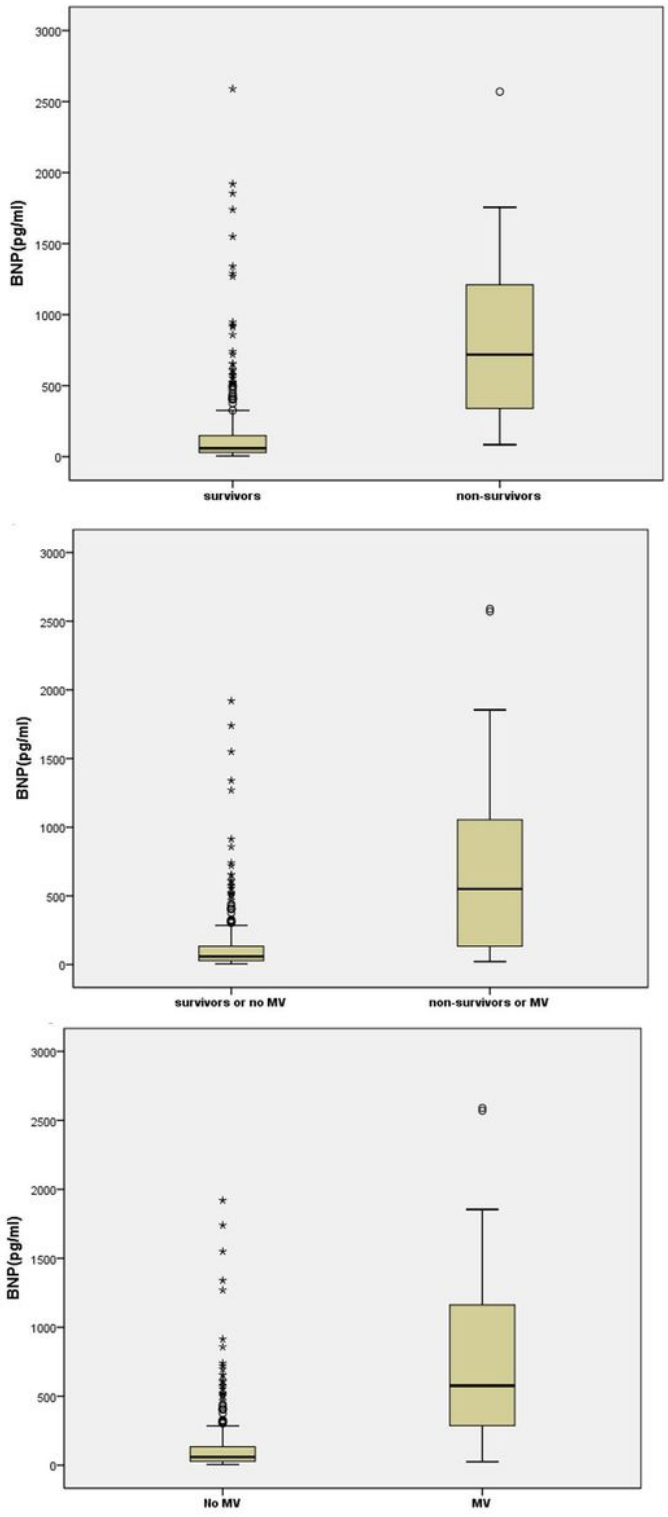

Figure 2

a BNP levels in non-survivors and survivors. b BNP levels in non-survivors or mechanical ventilation and survivors or no mechanical ventilation. c BNP levels in mechanical ventilation and or no mechanical ventilation.

Supplementary Files

This is a list of supplementary files associated with this preprint. Click to download.

- Table1s.csv
- Table3.csv
- Table4.csv