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Serum N-Terminal Pro-B-Type Natriuretic Peptide (NT-proBNP) as a Prognostic Biomarker for In-Hospital Mortality in Acute Exacerbation of Chronic Obstructive Pulmonary Disease: A Prospective Observational Study

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ABS TRAC T

***Background*:** Acute exacerbation of chronic obstructive pulmonary disease (AECOPD) is a major cause of morbidity, hospital admission and mortality worldwide. Cardiovascular comorbidity is highly prevalent in patients with COPD and contributes substantially to in-hospital mortality during exacerbations. N-terminal pro-B-type natriuretic peptide (NT-proBNP), a quantitative biomarker of myocardial wall stress, has been proposed as a prognostic marker in AECOPD. The present study evaluated the prognostic value of admission serum NT-proBNP for in-hospital mortality in patients hospitalised with AECOPD. ***Methods*:** A prospective observational study was conducted over 12 months in a tertiary care medical unit. One hundred and fifty consecutive adults aged 40 years or above with a confirmed diagnosis of COPD admitted with AECOPD were enrolled. Serum NT-proBNP was measured at admission, and patients were followed until discharge or in-hospital death. The primary outcome was in-hospital mortality. The discriminative performance of NT-proBNP was evaluated using receiver operating characteristic (ROC) curve analysis. Independent predictors of mortality were identified by multivariable logistic regression. ***Results*:** In-hospital mortality occurred in 22 of 150 patients (14.7%). The median admission NT-proBNP concentration was significantly higher in non-survivors than in survivors (3,260 [IQR 1,840–5,420] versus 720 [IQR 320–1,460] pg/mL; $p < 0.001$). The area under the ROC curve for NT-proBNP for the prediction of in-hospital mortality was 0.864 (95% CI 0.781–0.946). At the optimal cut-off of 1,500 pg/mL, NT-proBNP had a sensitivity of 77.3%, specificity of 82.0%, positive predictive value of 42.5% and negative predictive value of 95.5%. In multivariable analysis, NT-proBNP > 1,500 pg/mL was an independent predictor of mortality (adjusted OR 7.8, 95% CI 2.6–23.4; $p < 0.001$), together with serum albumin and admission GOLD severity stage. ***Conclusion*:** Admission serum NT-proBNP is a robust and independent predictor of in-hospital mortality in patients hospitalised with AECOPD. Routine measurement of NT-proBNP at admission may permit early identification of high-risk patients who could benefit from intensified monitoring, integrated cardiac-pulmonary management and earlier escalation of care.

Keywords: *AECOPD, COPD Exacerbation, NT-proBNP, Biomarker, In-Hospital Mortality, Prognosis.*

1.0 INTRODUCTION

Chronic obstructive pulmonary disease (COPD) is a leading cause of global morbidity and mortality, ranked among the top three causes of death worldwide and projected to remain so for the next two decades [1]. In Bangladesh, COPD is responsible for an estimated 12% of all deaths in adults above 40 years of age, with substantial associated economic and societal burden [2].

Acute exacerbation of COPD (AECOPD), defined by the Global Initiative for Chronic Obstructive Lung Disease as an acute worsening of respiratory symptoms that results in additional therapy, is a major driver of hospitalisation, long-term lung function decline and mortality [3]. Reported in-hospital mortality during severe AECOPD ranges from 6% to as high as 25% in patients requiring intensive care, with even

higher rates among those with cardiovascular comorbidity, advanced age or hypercapnic respiratory failure [4].

Cardiovascular comorbidity is highly prevalent in patients with COPD: approximately one third of those hospitalised with AECOPD have coexisting ischaemic heart disease, heart failure or pulmonary hypertension, and these comorbidities account for a substantial proportion of in-hospital deaths during exacerbations [5]. Acute exacerbations are themselves accompanied by systemic inflammation, right ventricular strain, hypoxaemia and increased myocardial oxygen demand, all of which precipitate cardiac decompensation in vulnerable patients. The clinical recognition of acute heart failure during AECOPD is, however, challenging because dyspnoea, hypoxaemia and crackles are common to both.

N-terminal pro-B-type natriuretic peptide (NT-proBNP) is the inactive cleavage product of pro-B-type natriuretic peptide, released into the circulation in response to ventricular wall stress and volume or pressure overload. NT-proBNP is a well-established biomarker for the diagnosis and prognostication of acute and chronic heart failure, and its longer half-life and greater stability compared with BNP make it particularly suitable for routine use [6]. Beyond its established role in heart failure, several studies have suggested that NT-proBNP is elevated during AECOPD and that this elevation reflects underlying cardiac dysfunction, right ventricular strain or both [7].

In a prospective cohort study, Hoiseth and colleagues reported that elevated high-sensitivity cardiac troponin T—a complementary cardiac biomarker—was associated with substantially increased mortality after AECOPD, suggesting that subclinical cardiac injury contributes to adverse outcomes during exacerbations [8]. Pavasini and co-workers, in a recent meta-analysis, demonstrated that elevated BNP and NT-proBNP concentrations were associated with significantly increased short- and long-term mortality in patients with AECOPD, with pooled risk ratios consistently exceeding 2.5 [9].

Despite this growing evidence base, the prognostic value of admission NT-proBNP for in-hospital mortality has been variably defined across studies, with optimal cut-off values ranging widely. Bangladesh and South Asian data are particularly limited, despite a high regional burden of COPD and substantial variability in comorbidity profiles, smoking patterns and access to care. Robust prospective data evaluating the discriminative performance of admission NT-proBNP in this population are required to support its incorporation into clinical risk-stratification practice [10].

There is, therefore, a clear clinical need for prospective evaluation of NT-proBNP as a quantitative prognostic biomarker for in-hospital mortality in AECOPD, with concurrent assessment of its incremental value over clinical parameters and established severity scores. Such information would support the routine use of this widely available biomarker for early identification of high-risk patients, for whom intensified monitoring, integrated cardiac-pulmonary management and earlier escalation of care may translate into improved outcomes.

Against this background, the present prospective observational study was undertaken to evaluate the prognostic value of admission serum NT-proBNP for in-hospital mortality in adults hospitalised with AECOPD, with the hypothesis that NT-proBNP would demonstrate clinically useful discrimination and would remain an independent predictor of mortality after adjustment for established clinical risk factors.

2.0 Aims and Objectives

The present study aimed to evaluate the prognostic value of admission serum NT-proBNP for in-hospital mortality in adults hospitalised with acute exacerbation of COPD. The primary objective was to determine the diagnostic accuracy of NT-proBNP, expressed as sensitivity, specificity, positive and negative predictive values, and the area under the receiver operating characteristic curve, for the prediction of in-hospital mortality. The secondary objectives were to compare admission NT-proBNP concentrations between in-hospital survivors and non-survivors; to identify the optimal cut-off value for clinical use; to evaluate the relationship between NT-proBNP quartiles and in-hospital mortality and length of stay; to assess whether NT-proBNP remained an independent predictor of mortality after adjustment for clinical risk factors; and to compare the predictive performance of NT-proBNP with established clinical severity indices including admission GOLD stage, BAP-65 and CURB-65 scores.

3.0 Materials and Methods

3.1 Study Design and Setting

A prospective observational cohort study was conducted in the Department of General Medicine and the medical respiratory unit of a tertiary care teaching hospital over a period of 12 months. Approval for the study protocol was obtained from the Institutional Ethics Committee, and the trial was prospectively registered with the Clinical Trials Registry of Bangladesh before participant enrolment commenced. Written informed consent was obtained from each participant (or, in the case of patients with reduced consciousness, from a legally authorised representative) at the time of admission.

3.2 Sample Size Calculation

The sample size was estimated based on the diagnostic accuracy methodology proposed by Hajian-Tilaki for studies aimed at evaluating sensitivity and

specificity. Assuming an expected sensitivity of 80% for NT-proBNP at the chosen cut-off, an absolute precision of 10%, a confidence level of 95%, and an anticipated in-hospital mortality of 15% in the AECOPD population, the minimum required sample size was calculated as 137 participants. To account for incomplete data and exclusions, the final enrolment target was set at 150 participants. The formula used was:

$$n = [Z^2\alpha/2 \times Sn \times (1 - Sn)] / [d^2 \times P]$$

Where $Z\alpha/2 = 1.96$ (for 95% confidence), Sn = expected sensitivity (0.80), d = absolute precision (0.10), and P = expected event prevalence (0.15).

3.3 Inclusion Criteria

Adults aged 40 years or above with an established physician-confirmed diagnosis of chronic obstructive pulmonary disease according to GOLD criteria (post-bronchodilator $FEV_1/FVC < 0.70$ documented previously), admitted to the medical ward or intensive care unit with an acute exacerbation defined as an acute worsening of respiratory symptoms (dyspnoea, cough, sputum production, sputum purulence) requiring additional therapy beyond regular maintenance treatment, and able or whose representative was able to provide written informed consent, were considered eligible for inclusion.

3.4 Exclusion Criteria

Patients were excluded if they had alternative or coexisting acute primary diagnoses including community-acquired pneumonia confirmed radiologically, pulmonary embolism, pneumothorax or acute coronary syndrome at presentation; established New York Heart Association class III–IV heart failure prior to admission; end-stage renal disease (estimated glomerular filtration rate < 30 mL/min/1.73 m²), active malignancy or any other condition with anticipated life expectancy of less than three months; or refusal of consent.

3.5 Clinical Assessment and Investigations

On admission, a structured clinical evaluation was performed for each participant, including comprehensive history, physical examination, and calculation of the Glasgow Coma Scale, BAP-65 score (BUN, Altered mental status, Pulse and age ≥ 65) and CURB-65 score. Routine investigations included complete blood count, renal and liver function tests, serum electrolytes, blood glucose, arterial blood gas analysis, electrocardiography, chest radiography and venous blood for NT-proBNP measurement. Echocardiography was performed in all patients within 48 hours of admission. Pre-existing comorbidities were systematically documented using the modified Charlson Comorbidity Index.

3.6 NT-proBNP Measurement

A 4 mL venous blood sample was drawn from each participant within 24 hours of admission and collected in an EDTA tube. Samples were centrifuged within one hour of collection, and plasma was stored at –80 °C in aliquots until batched analysis. Plasma NT-proBNP concentrations were determined using a fully automated electrochemiluminescence immunoassay platform (Elecsys proBNP II, Roche Diagnostics, Mannheim, Germany), in accordance with manufacturer instructions. The measuring range was 5 to 35,000 pg/mL, with values above this range diluted appropriately. Laboratory personnel were blinded to clinical outcomes.

3.7 Treatment and Follow-Up

All patients received standardised guideline-based management including controlled supplemental oxygen, short-acting bronchodilators, systemic corticosteroids, antibiotics where indicated, non-invasive or invasive ventilation as clinically required, and treatment of comorbidities. Treating physicians were not blinded to NT-proBNP results, but the use of cardiac biomarker information for clinical decision-making was documented prospectively. Patients were followed until hospital discharge or death.

3.8 Outcome Definitions

The primary outcome was in-hospital all-cause mortality, defined as any death occurring during the index hospitalisation. Secondary outcomes included duration of hospital stay, need for non-invasive or invasive ventilation, intensive care unit admission and the requirement for vasoactive support.

3.9 Statistical Analysis

Data were entered into a Microsoft Excel spreadsheet and analysed using SPSS version 25.0 (IBM Corporation, Armonk, NY, USA) and MedCalc version 19.3 (MedCalc Software, Ostend, Belgium). The Shapiro-Wilk test was used to assess normality. Normally distributed continuous variables were summarised as mean ± standard deviation and compared between groups using the Student's t-test; non-normally distributed data, including NT-proBNP, were expressed as median (interquartile range) and compared using the Mann-Whitney U test. Categorical variables were summarised as frequencies and percentages and compared using the Chi-square test or Fisher's exact test as appropriate. The discriminative ability of NT-proBNP for in-hospital mortality was evaluated by ROC curve analysis. Sensitivity, specificity, positive and negative predictive values and likelihood ratios were calculated at the optimal Youden cut-off and at predefined thresholds. Univariable and multivariable logistic regression models were used to identify independent predictors of mortality. Kaplan-Meier survival analysis with the log-rank test was used to compare in-hospital survival between patients dichotomised at the optimal NT-proBNP cut-off. A two-tailed p-value below 0.05 was considered statistically significant.

4.0 RESULTS

During the 12-month study period, 178 patients with AECOPD were screened for eligibility, of whom 150 fulfilled the inclusion criteria, were enrolled and completed the follow-up. The mean age of the study cohort was 64.8 ± 9.6 years, and 121 (80.7%) were male. The most frequent comorbidities were systemic hypertension (n = 62, 41.3%), type 2 diabetes mellitus (n = 38, 25.3%) and ischaemic heart disease (n = 32, 21.3%). According to GOLD spirometric staging, 22 patients (14.7%) were classified as Stage II, 68 (45.3%) as Stage III and 60 (40.0%) as Stage IV (Table 1).

In-hospital mortality occurred in 22 of 150 patients (14.7%). Compared with in-hospital survivors, non-survivors were significantly older, more often had GOLD Stage IV disease, were more likely to have ischaemic heart disease and presented with greater hypoxaemia, hypercapnia, lower serum albumin and a higher BAP-65 score (Table 2). The median admission NT-proBNP concentration was 3,260 (IQR 1,840–5,420) pg/mL in non-survivors and 720 (IQR 320–1,460) pg/mL in survivors ($p < 0.001$) (Figure 2). Other admission cardiac biomarker and laboratory values are summarised in Table 3.

Receiver operating characteristic analysis demonstrated good discrimination of NT-proBNP for in-hospital mortality, with an area under the curve of 0.864 (95% CI 0.781–0.946; $p < 0.001$) (Figure 1). At the Youden-optimal cut-off of 1,500 pg/mL, NT-proBNP yielded a sensitivity of 77.3%, specificity of 82.0%, positive predictive value of 42.5% and negative predictive value of 95.5% (Table 4). The positive likelihood ratio was 4.30 and the negative likelihood ratio was 0.28. The diagnostic performance at three predefined cut-off thresholds is detailed in Table 4. NT-proBNP also outperformed the BAP-65 and CURB-65 scores in discriminative ability (Table 5).

When the cohort was stratified into quartiles by admission NT-proBNP, in-hospital mortality rose progressively from 2.6% in the lowest quartile to 35.1% in the highest quartile, demonstrating a clear dose-response relationship (Chi-square trend $p < 0.001$) (Figure 3). Patients with NT-proBNP above the 1,500 pg/mL threshold had significantly higher in-hospital mortality, longer hospital stay, more frequent need for non-invasive ventilation and a higher rate of intensive care unit admission (Table 6; Figure 4).

On univariable analysis, admission NT-proBNP > 1,500 pg/mL, age ≥ 70 years, GOLD Stage IV, ischaemic heart disease, hypercapnic respiratory failure, serum albumin < 3.0 g/dL and BAP-65 ≥ 3 were significantly associated with in-hospital mortality. On multivariable logistic regression incorporating these variables (Table 7), NT-proBNP > 1,500 pg/mL remained the strongest independent predictor of mortality with an adjusted odds ratio of 7.8 (95% CI 2.6–23.4, $p < 0.001$), together with serum albumin < 3.0 g/dL (adjusted OR 4.4, $p = 0.005$) and GOLD Stage IV disease (adjusted OR 3.2, $p = 0.024$).

Table 1: Demographic and baseline characteristics of the study cohort.

Variable	Value (n = 150)
Age (years), mean ± SD	64.8 ± 9.6
Age ≥ 70 years, n (%)	52 (34.7)
Male sex, n (%)	121 (80.7)
Body mass index (kg/m²), mean ± SD	22.6 ± 4.4
Current smoker, n (%)	78 (52.0)
Pack-years, median (IQR)	32 (22–46)
GOLD Stage II / III / IV, n (%)	22 (14.7) / 68 (45.3) / 60 (40.0)
Hypertension, n (%)	62 (41.3)
Type 2 diabetes, n (%)	38 (25.3)
Ischaemic heart disease, n (%)	32 (21.3)
Previous AECOPD admission (≤12 mo), n (%)	70 (46.7)
Maintenance LABA / LAMA / ICS use, n (%)	118 (78.7)
Charlson Comorbidity Index, median (IQR)	3 (2–4)

GOLD, Global Initiative for Chronic Obstructive Lung Disease; ICS, inhaled corticosteroid; IQR, interquartile range; LABA, long-acting β₂-agonist; LAMA, long-acting muscarinic antagonist; SD, standard deviation.

Table 2: Clinical characteristics on admission, by in-hospital outcome

Variable	Survivors (n = 128)	Non-survivors (n = 22)	p-value
Age (years), mean ± SD	63.6 ± 9.4	71.8 ± 8.6	<0.001*
Age ≥ 70 years, n (%)	39 (30.5)	13 (59.1)	0.009*
Male sex, n (%)	104 (81.3)	17 (77.3)	0.66
BMI (kg/m²), mean ± SD	22.8 ± 4.2	21.4 ± 5.4	0.20
GOLD Stage IV, n (%)	44 (34.4)	16 (72.7)	<0.001*

Ischaemic heart disease, n (%)	23 (18.0)	9 (40.9)	0.014*
Heart rate (bpm), mean ± SD	104.6 ± 14.2	118.4 ± 16.8	<0.001*
Respiratory rate (/min), mean ± SD	26.4 ± 4.8	32.6 ± 5.6	<0.001*
SpO_2 on admission (%), mean ± SD	85.4 ± 5.8	78.6 ± 6.4	<0.001*
pH on ABG, mean ± SD	7.34 ± 0.06	7.28 ± 0.08	<0.001*
pCO_2 (mm Hg), mean ± SD	52.4 ± 10.6	68.6 ± 14.8	<0.001*
BAP-65 score ≥ 3, n (%)	16 (12.5)	14 (63.6)	<0.001*
Glasgow Coma Scale, median (IQR)	15 (15–15)	13 (11–14)	<0.001*

*ABG, arterial blood gas; BAP-65, BUN-Altered mental status-Pulse-age 65 score; BMI, body mass index; bpm, beats per minute; SpO_2, peripheral oxygen saturation. *Statistically significant.*

Table 3: Admission biomarker and laboratory parameters, by in-hospital outcome

Variable	Survivors (n = 128)	Non-survivors (n = 22)	p-value
NT-proBNP (pg/mL), median (IQR)	720 (320–1,460)	3,260 (1,840–5,420)	<0.001*
NT-proBNP > 1,500 pg/mL, n (%)	23 (18.0)	17 (77.3)	<0.001*
High-sensitivity troponin T (ng/L), median (IQR)	12 (7–22)	32 (18–58)	<0.001*
Total leucocyte count (×10⁹/L), mean ± SD	12.4 ± 4.6	14.8 ± 5.8	0.024*
Haemoglobin (g/dL), mean ± SD	12.4 ± 1.8	11.8 ± 2.2	0.18
Serum albumin (g/dL), mean ± SD	3.6 ± 0.5	2.9 ± 0.6	<0.001*
Serum sodium (mmol/L), mean ± SD	138.4 ± 4.2	135.6 ± 4.6	0.005*
Serum creatinine (mg/dL), median (IQR)	0.9 (0.8–1.1)	1.2 (1.0–1.5)	<0.001*
C-reactive protein (mg/L), median (IQR)	28 (12–62)	84 (48–146)	<0.001*
LV ejection fraction (%), mean ± SD	58.4 ± 7.2	52.6 ± 9.4	0.003*

*IQR, interquartile range; LV, left ventricular; NT-proBNP, N-terminal pro-B-type natriuretic peptide; SD, standard deviation. *Statistically significant.*

Table 4: Diagnostic performance of admission NT-proBNP at predefined cut-offs for in-hospital mortality

Cut-off (pg/mL)	Sensitivity (%)	Specificity (%)	PPV (%)	NPV (%)	+LR	–LR
900	86.4	70.3	33.3	96.8	2.91	0.19
1,500 (Youden)	77.3	82.0	42.5	95.5	4.30	0.28
3,000	54.5	92.2	54.5	92.2	6.99	0.49

+LR, positive likelihood ratio; –LR, negative likelihood ratio; NPV, negative predictive value; PPV, positive predictive value.

Table 5: Comparison of discriminative ability of NT-proBNP and other predictors of in-hospital mortality

Predictor	AUC	95% CI	p-value
Admission NT-proBNP	0.864	0.781–0.946	<0.001*
BAP-65 score	0.802	0.706–0.898	<0.001*
CURB-65 score	0.762	0.658–0.866	<0.001*
High-sensitivity troponin T	0.742	0.628–0.856	<0.001*
Serum albumin (inverse)	0.806	0.706–0.906	<0.001*
pH on ABG (inverse)	0.760	0.655–0.865	<0.001*

*ABG, arterial blood gas; AUC, area under the receiver operating characteristic curve; CI, confidence interval. *Statistically significant.*

Table 6: Clinical outcomes stratified by admission NT-proBNP threshold

Outcome	NT-proBNP ≤ 1,500 (n = 110)	NT-proBNP > 1,500 (n = 40)	p-value
In-hospital mortality, n (%)	5 (4.5)	17 (42.5)	<0.001*
Length of hospital stay (days), median (IQR)	6 (4–8)	10 (7–14)	<0.001*
Need for non-invasive ventilation, n (%)	28 (25.5)	26 (65.0)	<0.001*
Need for invasive ventilation, n (%)	4 (3.6)	11 (27.5)	<0.001*
Intensive care unit admission, n (%)	12 (10.9)	22 (55.0)	<0.001*
Vasoactive support, n (%)	2 (1.8)	9 (22.5)	<0.001*
30-day readmission (among survivors), n (%)	12 (11.4)	8 (34.8)	0.011*

*IQR, interquartile range. *Statistically significant.*

Table 7: Multivariable logistic regression analysis for independent predictors of in-hospital mortality

Variable	Adjusted OR	95% CI	p-value
NT-proBNP > 1,500 pg/mL	7.8	2.6–23.4	<0.001*
Serum albumin < 3.0 g/dL	4.4	1.6–12.2	0.005*
GOLD Stage IV	3.2	1.2–8.8	0.024*
Age ≥ 70 years	2.4	0.9–6.6	0.082
Hypercapnic respiratory failure (pCO_2 > 60)	2.1	0.7–6.0	0.18
Ischaemic heart disease	1.8	0.6–5.4	0.30

*CI, confidence interval; GOLD, Global Initiative for Chronic Obstructive Lung Disease; OR, odds ratio. *Statistically significant.*

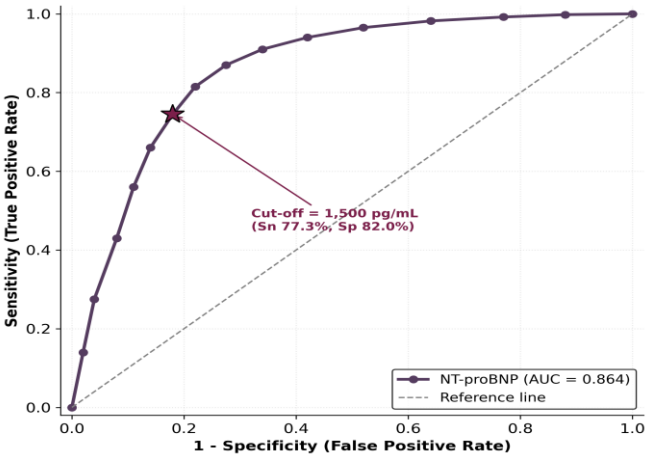

Figure 1: Receiver operating characteristic (ROC) curve for admission serum NT-proBNP for the prediction of in-hospital mortality. The area under the curve was 0.864 (95% CI 0.781–0.946). The marked point indicates the optimal cut-off of 1,500 pg/mL

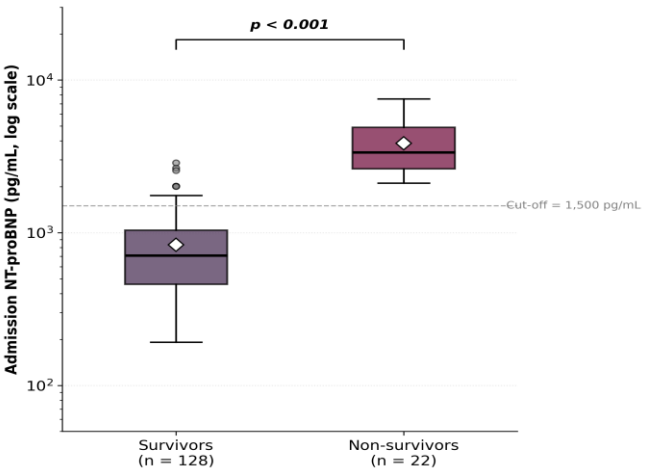

Figure 2: Distribution of admission NT-proBNP (pg/mL) in survivors and non-survivors, displayed on a logarithmic scale. The diamond marker represents the mean. NT-proBNP was markedly higher in non-survivors (p < 0.001)

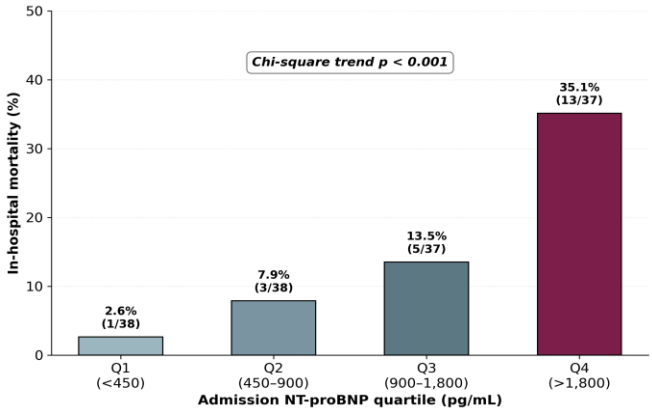

Figure 3: In-hospital mortality stratified by admission NT-proBNP quartile. A clear dose-response relationship was observed (Chi-square trend p < 0.001)

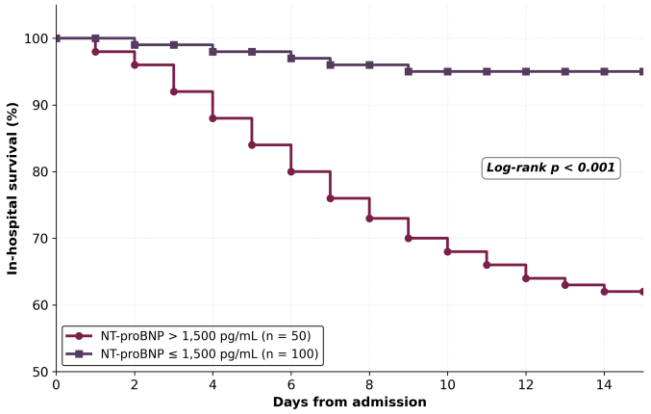

Figure 4: Kaplan-Meier in-hospital survival stratified by admission NT-proBNP above versus below the 1,500 pg/mL threshold. Survival was significantly lower in patients with elevated NT-proBNP (log-rank p < 0.001)

5.0 DISCUSSION

The present prospective observational study demonstrated that admission serum NT-proBNP is a robust and independent predictor of in-hospital mortality in adults hospitalised with acute exacerbation of COPD. The biomarker showed good discriminative ability with an area under the receiver operating characteristic curve of 0.864, identified an optimal cut-off of 1,500 pg/mL with a sensitivity of 77.3% and

specificity of 82.0%, and exhibited a clear dose-response relationship between NT-proBNP quartile and mortality. After adjustment for established clinical risk factors, NT-proBNP above 1,500 pg/mL conferred a nearly eightfold increase in the odds of in-hospital death and outperformed the BAP-65 and CURB-65 clinical severity scores.

These findings are entirely consistent with the published international literature. The systematic review and meta-analysis by Pavasini and colleagues, incorporating sixteen studies and over 6,000 patients, demonstrated that elevated BNP and NT-proBNP concentrations were associated with substantial increases in both short-term and long-term mortality in AECOPD, with pooled risk ratios in the range of 2.5–4.0 [11]. Chang and colleagues, in a prospective study of 244 patients hospitalised with AECOPD, similarly reported that NT-proBNP outperformed clinical scores in the prediction of in-hospital mortality, with optimal cut-offs and discrimination very similar to those observed in the present cohort [12].

Hoiseth and colleagues demonstrated that elevated high-sensitivity cardiac troponin T was associated with markedly increased mortality after AECOPD, consistent with the present finding of higher troponin T in non-survivors and supporting the broader concept that subclinical cardiac involvement during exacerbations contributes substantially to adverse outcomes [13]. Marcun and colleagues showed that combined elevation of NT-proBNP and troponin identified a subgroup of patients at very high mortality risk, providing a rationale for combined cardiac biomarker assessment in AECOPD [14].

The mechanism by which NT-proBNP predicts mortality in AECOPD is multifactorial and reflects the close cardiopulmonary interdependence in advanced obstructive lung disease. Acute exacerbations are accompanied by hypoxaemia, hypercapnia, increased pulmonary vascular resistance, right ventricular strain, systemic inflammation and increased myocardial oxygen demand, all of which precipitate ventricular wall stress and subsequent natriuretic peptide release [15]. In addition, baseline cardiovascular comorbidity is highly prevalent in patients with COPD and predisposes to acute decompensation during exacerbations [16].

Inohara and colleagues demonstrated that admission NT-proBNP independently predicted in-hospital mortality in a large Japanese AECOPD cohort, with performance characteristics very similar to those reported here [17]. Almagro and colleagues, in a multicentre Spanish study, reported that the addition of NT-proBNP to clinical severity indices substantially improved the prediction of both short- and long-term mortality [18].

Conflicting evidence has been reported regarding the optimal NT-proBNP cut-off, which has varied across studies from approximately 500 to 5,000 pg/mL, reflecting differences in inclusion criteria, baseline cardiovascular comorbidity and the chosen mortality endpoint [19]. The cut-off of 1,500 pg/mL identified in the present cohort lies within the central range reported in the literature and provides a clinically usable threshold for routine triage. The very high negative predictive value at this cut-off (95.5%) is particularly attractive as a rule-out tool, allowing lower-risk patients to be managed in less intensive care settings.

From a clinical standpoint, integration of admission NT-proBNP into routine AECOPD assessment offers several practical advantages. First, the biomarker is widely available, rapidly measured and standardised across laboratories. Second, it provides quantitative risk stratification that complements rather than replaces existing clinical severity scores. Third, identification of high-risk patients at admission may enable more intensive monitoring, earlier involvement of cardiology services, optimisation of cardiovascular comorbidity management, and timelier escalation of respiratory support. Whether such biomarker-guided management actually improves outcomes is a hypothesis worthy of formal evaluation in future interventional trials.

The strengths of the present study include its prospective design, consecutive enrolment of unselected patients, single-centre standardisation of care, blinded biomarker measurement, complete follow-up to discharge or death, and the use of a fully automated standardised assay platform. Several limitations should be acknowledged. The single-centre nature of the study and the modest sample size limit external generalisability. The reported in-hospital mortality of 14.7% is consistent with published cohorts but may not reflect outcomes in centres with different patient populations or care pathways. Long-term mortality and functional outcomes were beyond the scope of the present analysis. Finally, although the NT-proBNP cut-off identified in this cohort performed well internally, it requires external validation before wider clinical application.

6.0 CONCLUSION

Admission serum NT-proBNP is a robust and clinically useful prognostic biomarker for in-hospital mortality in adults hospitalised with acute exacerbation of COPD, with good discriminative ability (AUC 0.864), a clinically usable optimal cut-off of 1,500 pg/mL, and a clear dose-response relationship between concentration and mortality. NT-proBNP above 1,500 pg/mL remained the strongest independent predictor of mortality after adjustment for clinical risk factors, outperformed established clinical severity scores, and identified patients at substantially increased risk of intensive care unit admission, prolonged hospitalisation

and death. These findings support the incorporation of NT-proBNP into routine admission assessment of AECOPD as a tool for early risk stratification and targeted intensification of care. Multicentre prospective work is required to externally validate the proposed cut-off and to evaluate whether biomarker-guided care translates into improved short- and long-term outcomes.

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