Utility of NT-proBNP in predicting short-term outcomes in acute exacerbation of COPD without overt cardiac involvement

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Abstract

Background: Acute exacerbations of chronic obstructive pulmonary disease (AECOPD) are associated with substantial morbidity, mortality, prolonged hospitalization, and increased healthcare burden. Early identification of high-risk patients remains a clinical challenge because the severity of exacerbations often varies widely between individuals. Biomarkers capable of predicting disease severity and adverse outcomes may help optimize triage and management strategies. N-terminal pro–B-type natriuretic peptide (NT-proBNP), a marker released in response to myocardial wall stress, has been shown to rise in AECOPD even in the absence of overt cardiac disease due to hypoxia, pulmonary hypertension, and right ventricular strain [1-4].

Objectives: To evaluate the association between NT-proBNP levels and short-term adverse clinical outcomes in patients admitted with AECOPD without overt cardiac involvement, and to determine its predictive utility for ICU admission and ventilatory support.

Methods: This cross-sectional observational study included 90 consecutive patients admitted with AECOPD between July 2024 and June 2025. Patients with known heart failure, ischemic heart disease, significant valvular heart disease, cardiomyopathy, severe renal dysfunction, or echocardiographic evidence of cardiac dysfunction were excluded. NT-proBNP levels were measured at admission along with arterial blood gas (ABG) parameters and inflammatory markers. Outcomes assessed included ICU admission, need for ventilatory support, duration of ICU stay, and total hospital stay. Statistical analysis included Chi-square test, Mann–Whitney U test, Spearman correlation analysis, and receiver operating characteristic (ROC) curve analysis.

Results: The mean age of the study population was 65 years, with males comprising 69% of participants. ICU admission was required in 50% of patients, while 47.8% required ventilatory support. Median NT-proBNP level was 306.5 pg/mL. Higher NT-proBNP levels were significantly associated with ICU admission, ventilatory support, prolonged ICU stay, and longer hospital stay ($p < 0.0001$). NT-proBNP also showed significant correlations with worsening ABG parameters, including lower pH, higher $PaCO_2$, and lower PaO_2. ROC analysis demonstrated strong predictive performance, with an AUC of 0.87 for ICU admission at a cutoff of 452 pg/mL and an AUC of 0.84 for ventilatory support at a cutoff of 274 pg/mL.

Conclusion: NT-proBNP is a strong independent predictor of short-term adverse outcomes in AECOPD patients even in the absence of overt cardiac disease. Elevated NT-proBNP levels reflect physiological severity and may serve as a valuable biomarker for early risk stratification, clinical decision-making, and resource allocation in patients presenting with AECOPD.

Keywords: Chronic Obstructive Pulmonary Disease (COPD), Acute Exacerbation of COPD (AECOPD), NT-proBNP, Biomarkers, Risk stratification, Intensive Care Unit (ICU) admission, Ventilatory support, Arterial Blood Gas (ABG)

Introduction

Chronic obstructive pulmonary disease (COPD) is a progressive inflammatory airway disorder characterized by persistent airflow limitation and recurrent exacerbations that significantly impair quality of life and survival. COPD is currently among the leading causes of morbidity and mortality worldwide and is projected to remain a major global health burden in coming decades [1]. Acute exacerbations of COPD (AECOPD) contribute substantially to hospitalization rates, healthcare expenditure, accelerated decline in lung function, and mortality.

The clinical presentation of AECOPD is highly heterogeneous, ranging from mild worsening of symptoms to life-threatening respiratory failure requiring intensive care and ventilatory support. Early identification of patients at risk for poor outcomes is therefore essential for timely intervention and appropriate triage. Conventional clinical parameters and arterial blood gas findings may not always accurately predict disease severity, creating interest in biomarkers that can aid prognostication.

NT-proBNP is an inactive cleavage product released from ventricular myocardium in response to increased wall tension

and myocardial stress [2]. Although traditionally associated with heart failure, elevated NT-proBNP levels have also been observed in pulmonary disorders including AECOPD. Several mechanisms contribute to this elevation, including hypoxia-induced pulmonary vasoconstriction, increased pulmonary arterial pressures, right ventricular overload, and systemic inflammation [3-5].

Importantly, elevated NT-proBNP levels in AECOPD may occur even in patients without clinically overt cardiac disease. Previous studies have suggested that natriuretic peptides correlate with exacerbation severity, mortality, ICU admission, and need for ventilatory support in COPD exacerbations [6-11]. However, data remain limited regarding their predictive value specifically in patients without overt cardiac involvement.

The present study was therefore undertaken to evaluate the utility of NT-proBNP as a predictor of short-term adverse outcomes in patients admitted with AECOPD in the absence of clinically evident cardiac disease.

Materials and Methods

Study design and setting

This was a hospital-based cross-sectional observational study conducted over a one-year period from July 2024 to June 2025. The study included patients admitted with acute exacerbation of COPD to the Department of Pulmonary Medicine at a tertiary care teaching hospital.

Study population

A total of 90 consecutive patients diagnosed with AECOPD were enrolled after fulfilling eligibility criteria.

Inclusion criteria

Patients were included in the study if they fulfilled all of the following criteria:

Patients diagnosed with acute exacerbation of chronic obstructive pulmonary disease (AECOPD) requiring hospital admission.

No clinical or echocardiographic evidence of right heart involvement, defined as:

- Absence of right ventricular hypertrophy or dilatation on echocardiography
- Tricuspid annular plane systolic excursion (TAPSE) >17 mm
- No right atrial dilatation on echocardiography
- No echocardiographic evidence of pulmonary hypertension (pulmonary artery systolic pressure [PASP] <20 mmHg)

No clinical evidence of cor pulmonale, including:

- Pedal edema
- Raised jugular venous pressure (JVP)
- P pulmonale on electrocardiography

No clinical or echocardiographic evidence of significant left heart involvement, defined as:

- No left atrial dilatation
- Left ventricular ejection fraction (LVEF) ≥50%
- Absence of Grade III diastolic dysfunction
- No known ischemic heart disease
- No significant valvular heart disease
- No known cardiomyopathy

Exclusion criteria

Patients were excluded if any of the following conditions were present:

1. Significant cardiac pathology

Known heart failure with reduced or preserved ejection fraction accompanied by clinical heart failure

LVEF <50%

Grade III severe/restrictive diastolic dysfunction

Moderate to severe valvular heart disease

Acute coronary syndrome or myocardial infarction within the previous 3 months

Decompensated cor pulmonale

2. Severe renal dysfunction

Estimated glomerular filtration rate (eGFR) <30 mL/min/1.73 m²

3. Other confounding acute conditions

Active sepsis with hemodynamic instability

Acute pulmonary embolism

Severe anemia (hemoglobin <8 g/dL)

Conditions associated with hyperdynamic circulation, such as uncontrolled hyperthyroidism

Data collection

Detailed demographic and clinical data were recorded at admission, including:

Age and sex, Smoking history, Comorbidities, Respiratory rate and oxygen saturation, Requirement for ICU admission, Requirement for ventilatory support

Laboratory investigations included: NT-proBNP levels, Complete blood count, Neutrophil–lymphocyte ratio (NLR), C-reactive protein (CRP), Arterial blood gas (ABG) analysis.

All patients underwent echocardiography to exclude overt cardiac dysfunction.

Outcome measures

Primary outcomes

ICU admission

Need for ventilatory support

Duration of ICU stay

Total hospital stay

Secondary outcomes

Correlation of NT-proBNP with ABG parameters

Correlation of NT-proBNP with inflammatory markers

Statistical analysis

Data were analyzed using SPSS software. Continuous variables were expressed as mean ± standard deviation or median with interquartile range, depending on distribution. Categorical variables were analyzed using Chi-square test. Mann–Whitney U test was used for comparison of nonparametric variables. Correlations were assessed using Spearman correlation coefficient. ROC curve analysis was performed to determine optimal NT-proBNP cutoff values for predicting adverse outcomes. A *p*-value <0.05 was considered statistically significant.

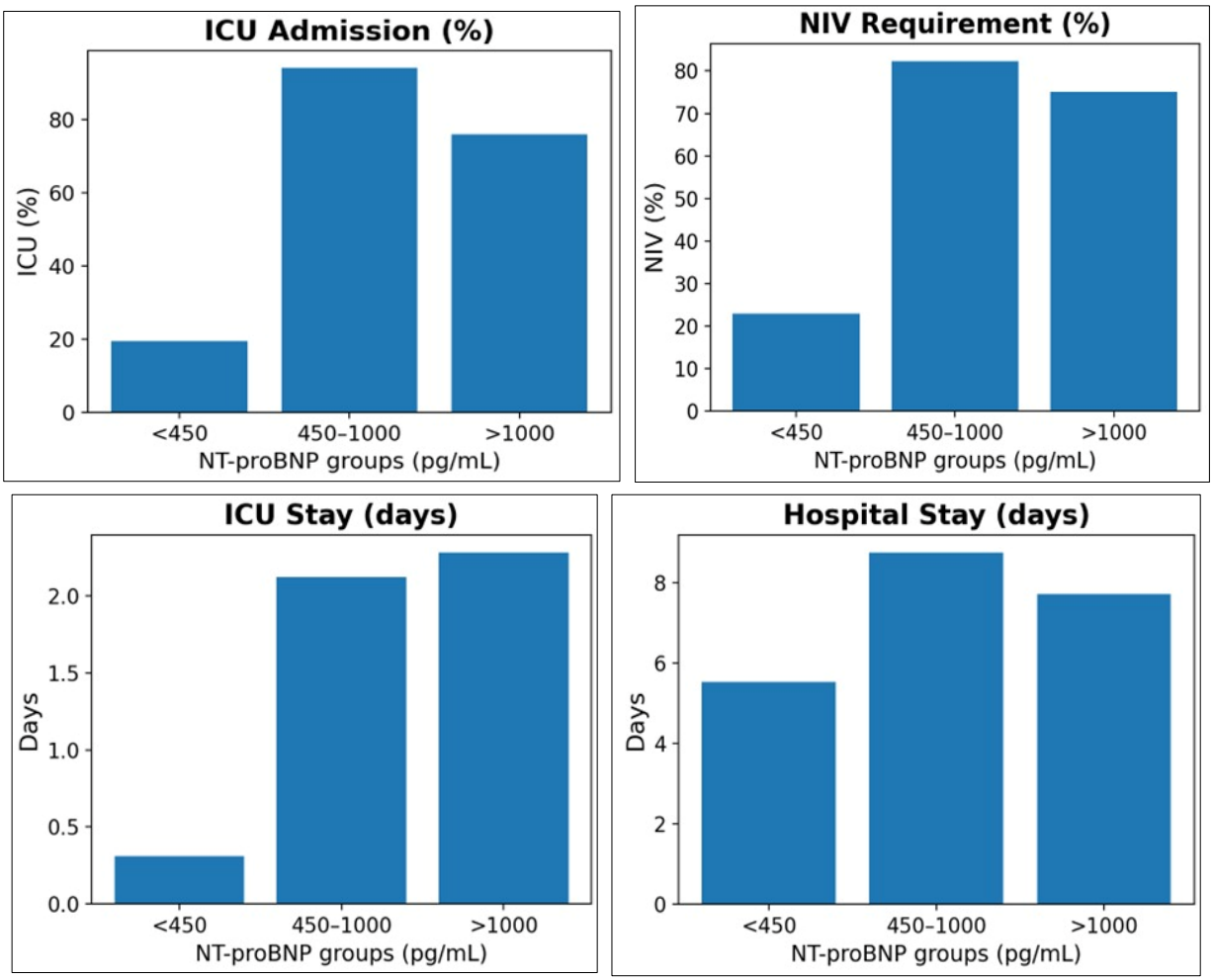
Results

Baseline characteristics

The study included 90 patients with a mean age of 65 years. Males constituted 69% of the study population, reflecting the higher prevalence of smoking-related COPD among men. ICU admission was required in 50% of patients, while ventilatory support was needed in 47.8%.

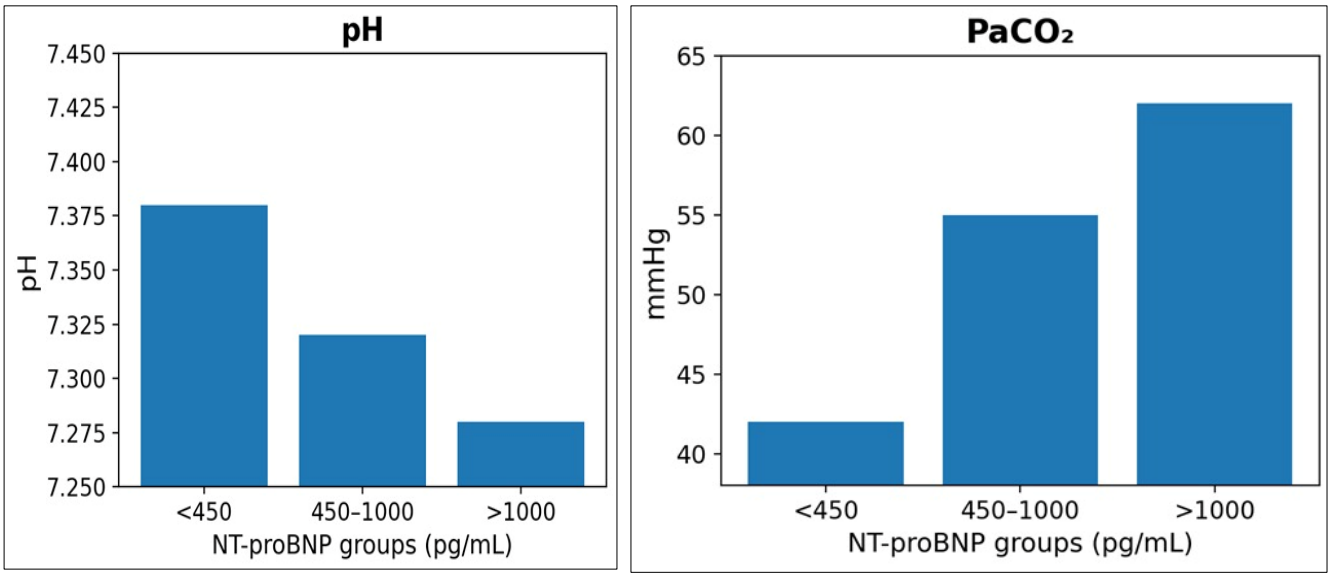
The median NT-proBNP level was 306.5 pg/mL, with significantly higher values observed among patients with severe exacerbations and poor clinical outcomes.

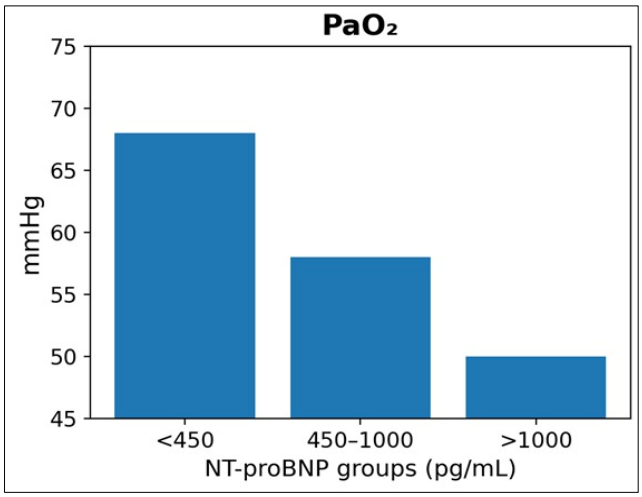
Association between NT-proBNP and clinical outcomes



Higher NT-proBNP levels were significantly associated with: ICU admission, Requirement for ventilatory support, Prolonged ICU stay, Longer hospital stay. These associations remained highly significant ($p < 0.0001$), suggesting that elevated NT-proBNP reflects greater physiological stress and disease severity.

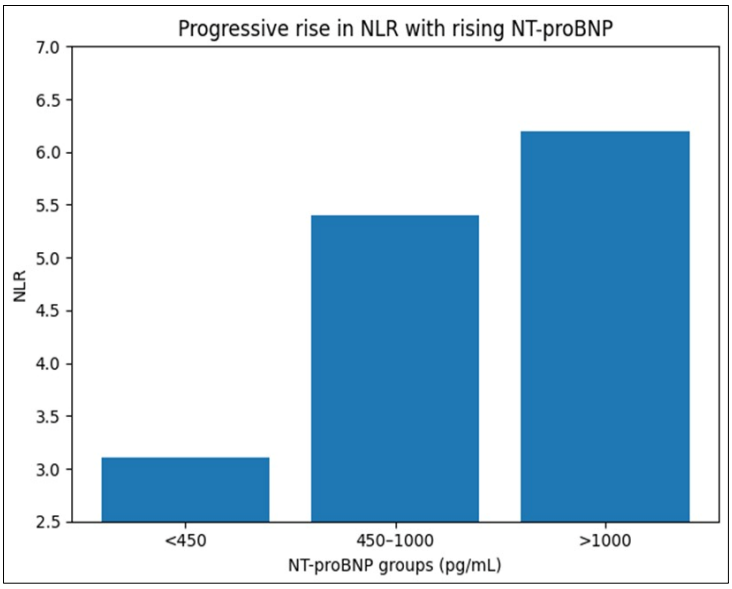
Correlation with ABG parameters





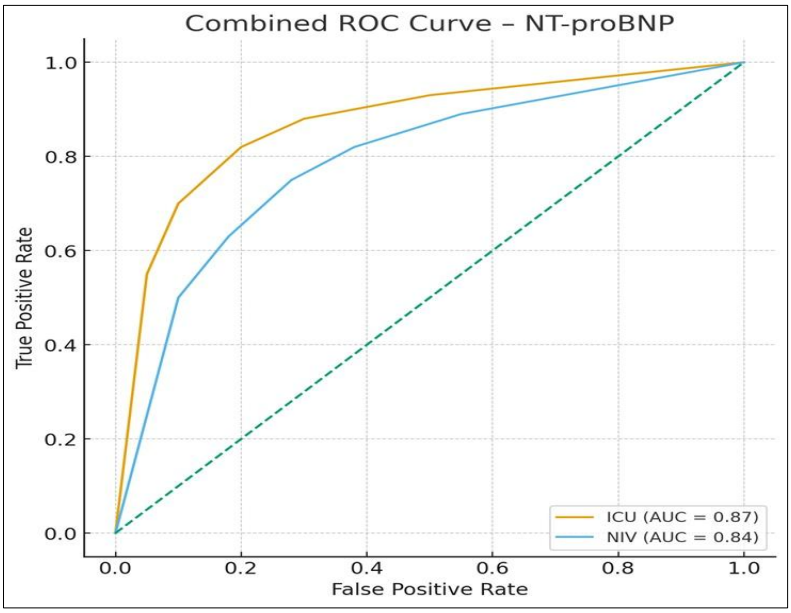
NT-proBNP levels demonstrated significant correlations with worsening arterial blood gas parameters: Negative correlation with pH, Positive correlation with $PaCO_2$, Negative correlation with PaO_2. These findings indicate that elevated NT-proBNP is associated with worsening respiratory failure, hypercapnia, and hypoxemia.

Correlation with inflammatory markers



NLR showed a statistically significant positive correlation with NT-proBNP levels ($p = 0.006$), suggesting an association between systemic inflammation and myocardial stress. CRP did not demonstrate a statistically significant relationship.

ROC curve analysis



ROC analysis demonstrated good predictive performance of NT-proBNP:
Prediction of ICU Admission, AUC = 0.87
Prediction of Non invasive Ventilatory Support- AUC = 0.84.
These findings indicate that NT-proBNP possesses good sensitivity and specificity for predicting short-term adverse outcomes in AECOPD.

Discussion

This study demonstrates that NT-proBNP is a strong predictor of adverse short-term outcomes in patients admitted with AECOPD even in the absence of overt cardiac disease. Elevated NT-proBNP levels were significantly associated with ICU admission, need for ventilatory support, and prolonged hospitalization.

The pathophysiological basis for elevated NT-proBNP in AECOPD is multifactorial. Acute hypoxia causes pulmonary vasoconstriction and increases pulmonary arterial pressure, leading to right ventricular strain and myocardial wall stress. Hyperinflation and increased intrathoracic pressure further impair cardiac filling and ventricular function. Systemic inflammation may additionally contribute to natriuretic peptide release [3–5,12].

The observed correlation between NT-proBNP and ABG derangements further supports its role as a marker of exacerbation severity. Patients with severe hypercapnia, respiratory acidosis, and hypoxemia exhibited higher NT-proBNP levels, indicating that worsening respiratory failure contributes to cardiac stress even in the absence of structural heart disease.

Several previous studies have demonstrated similar findings. Chang *et al*. reported that biochemical markers of cardiac dysfunction predicted mortality in AECOPD [3]. Stolz *et al*. found that BNP levels were associated with poor outcomes and longer hospital stay in COPD exacerbations [6]. Adrish *et al*. specifically demonstrated the significance of NT-proBNP in AECOPD patients without left ventricular dysfunction [4]. A systematic review by Pavasini *et al*. concluded that elevated NT-proBNP levels are associated with increased mortality and adverse outcomes in COPD [11,12].

The high AUC values observed in the present study highlight the clinical utility of NT-proBNP as a prognostic biomarker. Measurement of NT-proBNP at admission may aid clinicians in identifying high-risk patients who require closer monitoring, early ICU transfer, or aggressive respiratory support.

The study has certain limitations. The sample size was relatively small and the study was conducted at a single center, which may limit generalizability. Long-term outcomes and mortality were not assessed. Serial NT-proBNP measurements were also not performed. Larger multicenter studies are needed to validate these findings and establish standardized cutoff values.

Conclusion

NT-proBNP is strongly associated with adverse short-term outcomes in patients with acute exacerbation of COPD even in the absence of overt cardiac disease. Elevated levels correlate with ICU admission, need for ventilatory support, prolonged hospitalization, and worsening ABG abnormalities. Cutoff values of 452 pg/mL for ICU admission and 274 pg/mL for ventilatory support demonstrated good predictive accuracy. NT-proBNP may therefore serve as a valuable biomarker for early risk stratification and clinical decision-making in AECOPD.

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