

## Prognostic value of NT-pro Brain Natriuretic Peptide levels in patients with AECOPD in Intensive Care Unit

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### Abstract

**Background:** In patients with acute aggravation of chronic obstructive pulmonary disease, the predictive relevance of amino terminal pro-brain natriuretic peptide levels has not been clearly demonstrated. Amino terminal pro-brain natriuretic peptide levels in patients with acute exacerbation COPD who need ICU hospitalisation were evaluated in this study. **Methods:** From May 2020 to March 2021, 80 patients with acute aggravation of chronic obstructive pulmonary disease were enrolled in this prospective observational research at Benha University Hospital's chest ICU. The following information was gathered: demographics, use of noninvasive mechanical ventilation, necessity of invasive mechanical ventilation, level of amino terminal pro-brain natriuretic peptide, duration of mechanical ventilation, intensive care unit and hospital stay, success in weaning, and mortality rates. The research comprised a total of 80 individuals (74 men and 6 women). Participants ranged in age from 53 to 84 years on average. Noninvasive mechanical ventilation success was associated with lower levels of the amino terminal pro-brain natriuretic peptide than noninvasive mechanical ventilation failure (320.50 – 991.90). In addition, patients who required invasive mechanical breathing assistance had considerably greater levels of the amino terminal pro-brain natriuretic peptide (1004.90 – 1188.30,  $p=0.001$ ) than those who did not. Patients on IMV who saw an increase in their amino terminal pro-brain natriuretic peptide levels had a considerably greater death rate (12.5 percent). **Conclusion** The measurement and trend monitoring of amino terminal pro-brain natriuretic peptide may be a valuable asset in predicting mortality, noninvasive mechanical ventilation, weaning success, and the need for invasive mechanical ventilation in cases of acute exacerbation of chronic obstructive pulmonary disease requiring mechanical ventilation.

**Keywords:** NT-pro Brain Natriuretic Peptide, AECOPD.

### 1. Introduction

Common, curable, and preventive, Chronic Obstructive Pulmonary Disease (COPD) is defined by persistent respiratory symptoms and airflow restriction that is caused by anomalies in airways and/or alveoli. [9] COPD is a leading cause of illness and death worldwide. For many years, it has been predicted that this would become the third biggest cause of mortality in the globe. [9]

To put it simply, AECOPD refers to a "acute worsening of respiratory symptoms that requires additional medications" in the context of COPD [9].

As many as 26% to 74% of patients in critical care units (ICUs) need mechanical ventilation assistance owing to hypoxemic or hypercapnic respiratory failure, respectively. Even though up to one-third of AECOPD patients have an unknown origin, viral and/or bacterial infections are the most common culprits [17].

The most prevalent complication of COPD is cardiovascular disease, which affects up to 30% of patients. As a result of their association with higher mortality, these conditions are significant prognostic indicators [15].

When cardiac function is compromised, the ventricles produce natriuretic peptides such as brain natriuretic peptide (BNP) and amino terminal pro-BNP (NT-pro BNP). Cardiac failure biomarkers may be detected using these peptides [19].

Primary pulmonary hypertension, myocarditis, right ventricular failure, and sepsis have all been linked to elevated BNP levels [2].

COPD primarily affects the right ventricle, although AECOPD may affect both ventricles. A greater risk of death in AECOPD may be associated with elevated levels of BNP and NT-pro BNP, suggesting that these biomarkers have predictive significance (4).

### 2. Aim of the work

The aim of this work is to evaluate the prognostic value of amino terminal pro-brain natriuretic peptide levels in patients with acute exacerbation COPD who need ICU admission due to their need to mechanical ventilation either invasive or non invasive.

### 3. Patients And Methods

This Prospective observational study Included 80 patients who were admitted to intensive care unit at Benha university hospital in the period from may 2020 to march 2021.

Approval from ethical committee in the faculty of medicine (Institutional Research Board IRB).

#### Inclusion criteria

- Patients with acute exacerbation COPD who were admitted at ICU due to their need for mechanical ventilation,

#### NIMV

- types of devices used include
- CPAP
- BIPAP
- Criteria suggestive use of NIMV include

Acute hyper capnic respiratory failure with PH(7.25-7.35). [3].

- Criteria suggestive success of NIMV,
- Clinical improvement as regard(heart rate,respiratory rate,blood pressure).
- Laboratory improvement of ABG two hours after use.(Ediboglu o et al.,2017).

#### IMV

- Criteria suggestive use of IMV include,
- Major criteria (respiratory arrest, loss of consciousness, psychomotor agitation requiring sedation, hemodynamic instability with a systolic BP less than 70 or greater than 180 mmHg, HR less than 50 beats/minute with loss of alertness, gasping for air).
- Minor criteria(RR >35 breath/min, worsening acidemia or pH < 7.25, paO<sub>2</sub> < 40 mmHg or paO<sub>2</sub>/FiO<sub>2</sub> < 200 despite oxygen therapy, decreasing level of consciousness.) (3).

#### Criteria of successful weaning,

Weaning started once the cause of the exacerbation was adequately treated and the patient is hemodynamically stable.

Physiologic parameters must be followed intensively. It's targeted MV < 15 L, RR < 30 breaths/minute, TV > 325 ml, rapid shallow breathing index (RSBI) <105, maximum inspiratory pressure (MIP) < -15. (Gaprestad E et al., 2007).

#### Exclusion criteria

- Myocarditis.
- Right ventricular failure.
- Renal failure.
- Sepsis.

#### Study description

##### All patients were subjected to the following:

- 1.Full medical history:** age, sex, residence, occupation, smoking and other special habits of medical importance.
- 2.Thorough physical examination:** general and local chest examination.
- 3.Routine laboratory investigations in the form of:**
  - Complete Blood picture, erythrocyte sedimentation rate (ESR), coagulation profile.
  - Liver function tests: (ALT,AST and serum albumin).
  - Kidney function tests: in the form of serum urea and serum creatinine.
  - Arterial blood gases
  - Level of NT-pro BNP;

It was measured before induction of mechanical ventilation.

By ELISA KIT supplied by **Shanghai Korain Biotech CO.,Ltd Cat.No E1239Hu**

#### Assay Principle

This kit is an Enzyme-Linked Immunosorbent Assay (ELISA). The plate has been pre-coated with Human NT-pro BNP antibody. NT-pro BNP present in the sample is added and binds to antibodies coated on the wells. And then biotinylated Human NT-proBNP Antibody is added and binds to NT-pro BNP in the

sample. Then Streptavidin-HRP is added and binds to the Biotinylated NT-pro BNP antibody. After incubation unbound Streptavidin-HRP is washed away during a washing step. Substrate solution is then added and color develops in proportion to the amount of Human NT-pro BNP. The reaction is terminated by addition of acidic stop solution and absorbance is measured at 450 nm.

#### Intended Use

This sandwich kit was used for the accurate quantitative detection of Human N-terminal pro-brain natriuretic peptide (also known as NT-pro .BNP) in serum.

Allow serum to clot for 10-20 minutes at room temperature. Centrifuge at 2000-3000 RPM for 20 minutes. Collect the supernatant without sediment.

- Sample concentrations was predicted before being used in the assay.
- Samples were used within 5 days were stored at 2-8°C.
- Samples should were brought to room temperature before starting the assay.
- Centrifugation were done to collect sample before used.
- When sediments occurred during storage, centrifugation were performed again.

#### 4. Radiological examination including:

- Plain chest X-ray postero-anterior and lateral views.
- CT scan of the chest when indicated.
- Echocardiography.

#### Data management and Statistical Analysis :

All data were collected, tabulated and statistically analyzed using statistical package of special science SPSS version 22 (SPSS Inc. Chicago, IL, U.S.A) as follow:

1. Editing and coding
2. Data entry in computer.
3. Quantitative data were expressed as mean ± SD (standard deviation) for parametric data median and range for non- parametric data.
4. Qualitative data were expressed as frequencies and relative percentage.
5. Data were tested for normal distribution using Shapiro-Wilk's test.
6. Data were handled using appropriate statistical tests of significance such as :
  - A.** Independent t-test and mann whitney test were used to calculate difference between quantitative variables in two groups.
  - B.** Paired t-test was used to compare between two dependent groups of normally distributed variables.
  - C.** Chi square test ( $\chi^2$ ) and fisher exact was used to calculated difference between qualitative variables.
  - D.** All statistical comparison were two tailed with significance level of p-value  $\leq 0.05$  indicates significant, p- value <0.001 indicates highly significant difference while p-value > 0.05 indicates non significant difference.

### 3. Results

**Table (1)** Distribution of studied sample according to patient's demographic data.

	Number	Percent
<b>Age (years)</b>		
Range	53-84	
Mean±S.D.	69.30±6.934	
<b>Sex</b>		
Male	74	92.5
Female	6	7.5
<b>Smoking</b>		
Smoker	79	98.75
Non smoker	1	1.25
<b>Smoking index</b>		
Range	400-1800	
Mean±S.D.	994.94±331.623	
<b>Invasive Mechanical Ventilation</b>		
No	48	60.0
Yes	32	40.0

This Table shows demographic data of the studied group. Age ranged from 53-84 years with mean value 69.30±6.934 years. Male cases were 74(92.5%) while female cases were 6(7.5%). The majority of our cases were smoker (98.75%). Smoking index ranged between 400-1800 with mean value 994.94±331.623. Invasive Mechanical Ventilation were detected in 32 patients (40%).

**Table (2)** Distribution of studied sample according to patient's arterial blood gases.

	Min. – Max.	Mean±S.D.
PaO <sub>2</sub> (mm Hg)	40 – 56	47.49±5.166
PaCO <sub>2</sub> (mm Hg)	56 – 111	80.84±12.896
PH	2.28 – 7.33	7.15±0.563
PaO <sub>2</sub> /FiO <sub>2</sub>	50 – 340	230.63±73.007

This table show patient's arterial blood gases; PaO<sub>2</sub> was ranged from 40 – 56 with a mean value of 47.49±5.166. Patient's PaCO<sub>2</sub> was ranged from 56 – 111 with a mean value of 80.84±12.896. Patient's PH was ranged from 2.28 – 7.33 with a mean value of 7.15±0.563. Patient's PaO<sub>2</sub>/FiO<sub>2</sub> was ranged from 50 – 340 with a mean value of 230.63±73.007.

**Table (3)** Distribution of studied sample according to patient's Duration of mechanical ventilation and I.C.U stay.

	Mechanical Ventilation		P value
	NIMV	IMV	
<b>Duration of mechanical ventilation</b>			
Min. – Max.	3 – 14	4 – 11	0.381
Mean±S.D.	8.15±2.858	7.53±1.665	
<b>Duration of ICU stay</b>			
Min. – Max.	4 – 21	4 – 14	0.255
Mean±S.D.	9.90±3.360	8.97±2.148	

This table show patient's Duration of mechanical ventilation and I.C.U stay and it show no statistically significant differences between IMV and NIMV.

**Table (4)** Distribution of studied sample according to patient's NT-Pro BNP.

	Min. – Max.	Mean±S.D.
NT-Pro PNP	320.50 – 1188.30	874.53±233.998

This table show patient's duration of ventilation and it was ranged from 320.50 – 1188.30 with a mean value of 874.53±233.998.

**Table (5)** Distribution of studied sample according to patient's mortality in cases of IMV.

Mortality	Number	Percent
No	70	87.5
Yes	10	12.5
<b>Total</b>	<b>80</b>	<b>100</b>

This table shows invasive ventilation of the studied group and it show that 10(12.5%) were died.

**Table (6)** Comparison between levels of NT-Pro BNP in patients who needed invasive mechanical ventilation and those who didn't need invasive mechanical ventilation.

NT-Pro PNP	Invasive Ventilation		P value
	No	Yes	
Min. – Max.	320.50 – 991.90	1004.90 – 1188.30	<0.001*
Mean±S.D.	739.08±208.526	1077.71±50.903	

This table shows comparison between levels of NT-Pro BNP in patients who needed invasive mechanical ventilation and those who didn't need invasive mechanical ventilation and it show highly statistically significant difference between them.

**Table (7)** Relation between NT-Pro BNP and mortality.

NT-Pro PNP	Mortality		P value
	No	Yes	
Min. – Max.	320.50 – 1099.60	1102.50 – 1188.30	<0.001*
Mean±S.D.	837.14±226.303	1136.25±31.840	

This table shows relation between NT-Pro BNP and mortality and it show highly statistically significant difference between them.

**Table 8:** Correlation between levels of NT-Pro BNP and different patients parameters

	NT-Pro PNP	
	R	P
Age	-0.184	0.102
PH	0.321	0.004*
PaO <sub>2</sub>	0.021	0.853
PaCO <sub>2</sub>	-0.252	0.024*
PaO <sub>2</sub> /FiO <sub>2</sub>	0.309	0.005*
ICU stay	0.374	0.001*

Correlation between levels of NT-Pro BNP and different patients parameters show highly positive significant correlation between levels of NT-Pro BNP and each of PH ( $r=0.321$ ,  $P=0.004$ ), PaO<sub>2</sub>/FiO<sub>2</sub> ( $r=0.309$ ,  $P=0.005$ ) and ICU stay ( $r=0.374$ ,  $P=0.001$ ) and negative significant correlation between levels of NT-Pro BNP and PaCO<sub>2</sub> ( $r=-0.252$ ,  $P=0.024$ )

6)

**Table 9:** ROC curve analysis of NT-Pro BNP levels as a predictor of need for invasive mechanical ventilation and mortality

	Cut of Value	NT-Pro PNP					P
		Sensitivity	Specificity	PPV	NPV	AUC	
IMV	>991.9	100%	100%	100	100	1.000	<0.001*
Mortality	>1099.6	100%	100%	100	100	1.000	<0.001*

Table( 9) show that NT-Pro BNP levels was a best predictor of need for invasive mechanical ventilation and mortality at cut off point of >991.9 and >1099.6 respectively with high sensitivity and specificity 100% for each.

#### 4. Discussion

Worldwide, COPD is a primary cause of illness and death, and it is linked with a considerable economic burden because of its high prevalence. COPD was diagnosed in 15.7 million people in the United States in 2014. COPD's prevalence rises with age, from 2.6 percent in persons aged 18–34 to 12.3 percent in those aged 75 and above [24].

More than half of individuals with chronic obstructive pulmonary disease (COPD) have no idea they have it, according to research. COPD not only restricts everyday activities, but it also increases the financial burden of those suffering from the disease. People with COPD are estimated to participate in the workforce at a lower rate than their non-COPD counterparts because of the lower number of days they

can spend working and the lower quantity of labour they can do in a year (varying from only 27 to 63 days) [20].

One of the leading causes of acute hospitalisation is acute aggravation of a chronic obstructive pulmonary disease (AECOPD). One of the various features of chronic obstructive pulmonary disease (COPD) has been revealed to be cardiovascular in origin. Acute myocardial infarction (AMI) and chronic heart failure (HF) may both be linked with AECOPD, however the usual presentation of a particular cardiac ailment in clinical practise is quite rare [12].

Myocytes release the 108-amino acid precursor protein, pro-BNP, which is split into two pieces and produces BNP and the 76-amino acid N-terminal fragment of pro-BNP (NT-pro-BNP), both of which are essential for the synthesis of BNP [5].

For diagnosis, risk classification, and therapy of heart failure (HF), BNP and NT-pro-BNP are established biomarkers. Natriuretic peptide levels have also been shown to be elevated in individuals with COPD who do not have heart failure. BNP gene expression is increased in the right ventricle when there is pulmonary hypertension, coronary artery disease, or hypoxemia in the bloodstream [8].

BNP has been shown to be useful in predicting the outcomes of patients with COPD, according to a number of studies. The association between NT-pro-BNP and mortality was found in a prospective, single-center study of stable patients with COPD in the ambulatory setting, but it was not significant when adjusting for the presence of dilated left atrium, aortic stenosis, and left ventricular systolic dysfunction in the population. There was a connection between higher NT-proBNP levels and mortality in individuals with AECOPD, according to another research. Only individuals with established cardiovascular disease were included in this research. There was a correlation between long-term mortality in individuals with AECOPD and NT-proBNP, however only 12% of those patients had Spirometrically verified COPD. According to Buchan et al's meta-analysis, NT-pro-BNP levels were correlated with COPD in the majority of studies that examined the relationship [4].

Amino terminus pro-brain natriuretic peptide levels in patients with acute COPD exacerbation requiring mechanical ventilation, either invasive or non-invasive, were the focus of this investigation.

At Benha University Hospital, a total of 80 patients with acute exacerbation COPD were studied in this cross-sectional research. The research was carried out over a period of six to twelve months.

The following are the findings of this study:

As far as the demographics of the study group are concerned. With an average age of 69.306.934 years, participants were aged 53 to 84 years. As a result, there were 74 males and six females in the study (7.5 percent). Tobacco use was a prominent factor in most of our instances (98.75 percent). Between 400 and 1800, the smoking index had a mean value of 994.94331.623. There were 32 cases of invasive mechanical ventilation (40 percent).

According to [6], a total of 110 patients (75 of them were male) from a total of 1228 individuals were included in the research. At 69 years old, the median APACHE II score was 19 (61-76). [15, 23].

It was also found that patients' characteristics, including the average and standard deviation (SD) age of all 20 patients, ranged from the 47th to the 75th years of age. Males accounted for eighteen of the cases, while females accounted for the remaining four. Nonsmokers outnumbered smokers in this study by a factor of five to one. Smoking duration ranged from 15 to 43 years, and the mean length was 32 years (SD = 8.71).

COPD is the third biggest cause of death globally, behind ischemic heart disease (IHD) and stroke, and it affects hundreds of millions of people throughout the globe. It is well accepted that comorbidities and

exacerbations add to the disease's complexity and mortality [14].

One of the most frequent and significant occurrences in COPD is an acute exacerbation of the condition. As the severity of COPD increases, so does the frequency with which patients have exacerbations (frequent exacerbators). A lower quality of life and faster deterioration in lung function are also seen in frequent exacerbators [12]. PaO<sub>2</sub> varied from 40 to 56 in this research, with a mean value of 47.495.166, according to the results. From 56 to 111, the patient's PaCO<sub>2</sub> varied from 80.84 to 12.896. The patient's PH varied from 2.28 to 7.33, with a mean value of 7.150.563, according to the study. Pupil's PAO<sub>2</sub>/FiO<sub>2</sub> varied from 50-340, and the average was 230.63/73.007 (p=0.001)."

In addition to common risk factors like age and smoking, people with COPD have an increased risk of cardiovascular comorbidity in general, and IHD in particular. The existence of IHD in COPD has a detrimental influence on health status, symptoms, exercise ability, exacerbation recovery time, hospitalizations, and death [20].

Detection of pulmonary hypertension and cor pulmonale may be made by using echocardiography. In individuals with chest hyperinflation, however, measuring is impossible because sound waves cannot travel through the chest normally. It is still the "gold standard" method of measuring pulmonary arterial pressure by right cardiac catheterization [17].

It is the only main cause of death for which death rates are rising. Objective risk-stratification assessments, systematic comorbidity management, and medicines that extend life are still lacking. Cardiovascular illness accounts for one-third of fatalities in COPD, which is equivalent to or exceeds pulmonary mortality. Despite the fact that cardiovascular medicines have been shown to improve mortality and morbidity, they are seldom used since the condition is not well known. In order to improve the outcomes of COPD patients with cardiovascular illness (especially heart failure), simple, generalizable, and cost-effective methods are required [10].

IMV and NIMV had no statistically significant differences in terms of length of mechanical ventilation or time in the intensive care unit, according to the results of the research we have in our hands. 10 people (12.5%) lost their lives.

However, in the research of [6], 69 patients with type 2 respiratory failure were given noninvasive mechanical ventilation. 68.11% of patients with noninvasive mechanical ventilatory success had NT-pro BNP levels lower than those with noninvasive mechanical ventilatory failure (2004 pg/mL vs. 3977 pg/mL, p=0.05). pH, pCO<sub>2</sub>, and PaO<sub>2</sub>/FiO<sub>2</sub> ratio did not change between patients who were successful and those who were unsuccessful in their use of noninvasive mechanical ventilation (NIMV). 63 individuals were given invasive mechanical ventilation (41 due to noninvasive mechanical ventilation failure).

The most prevalent complication of COPD is cardiovascular disease, which affects up to 30% of patients. For this reason, these disorders are regarded to be key prognostic factors. For the diagnosis, follow-up, and management of heart failures, echocardiography is critical. An significant diagnostic technique for heart failure, echocardiographic assessment has a number of drawbacks, including imaging difficulties and user reliance during mechanical ventilation in the intensive care unit (ICU). When cardiac function is compromised, the ventricles produce natriuretic peptides such as brain natriuretic peptide (BNP) and amino terminal pro-BNP (NT-pro BNP). Cardiac failure biomarkers may be detected using these peptides [19].

There are a number of disorders that may cause elevated BNP levels, including primary pulmonary hypertension, myocarditis and cardiac allograft rejection. COPD primarily affects the right ventricle, although AECOPD may affect both ventricles. As a result, elevated BNP and NT-pro BNP levels are associated with higher mortality in patients with AECOPD [10].

To compare levels of NT-Pro BNP, the current research found that patients who required invasive mechanical ventilation had significantly lower levels of NT-Pro BNP than those who didn't need mechanical ventilation. When it comes to the correlation between NT-Pro BNP and mortality, the results are statistically significant. Correlations between levels of NT-Pro BNP and various patient parameters show a highly positive correlation between PH ( $r=0.321$ ,  $P=0.004$ ),  $PaO_2/FiO_2$  ( $r=0.309$ ,  $P=0.005$ ) and ICU stay ( $r=0.374$ ,  $P=0.001$ ), as well as a highly negative correlation between levels of NT-Pro BNP and  $PaCO_2$  ( $r=-0.252$ ,  $P=0.024$ ). At the cutoff points of  $>991.9$  and  $>1099.6$ , NT-Pro BNP levels were the greatest predictors of the requirement for invasive mechanical ventilation and death, respectively, with excellent sensitivity and specificity of 100% for each.

Study [6], which demonstrated a lower mean level of amino terminal pro-brain natriuretic peptide in situations where noninvasive mechanical ventilation was successful than in cases where noninvasive mechanical ventilation failed ( $p=0.053$ ), corroborated our findings. Those who required invasive mechanical breathing assistance had a substantially higher mean amino terminal pro-brain natriuretic peptide level (4740 pg/mL vs. 3004 pg/mL,  $p=0.001$ ) than patients who did not. In patients with rising levels of amino terminal pro-brain natriuretic peptide ( $p=0.015$ ) during hospitalisation, the death rate was considerably greater than in individuals with decreasing levels (59 percent vs. 23 percent). With a predicted area under curve of 0.84 ( $p<0.0001$ , 95 percent confidence interval: 0.75 to 0.93), the receiver operating characteristic analysis predicted mortality in patients in the intensive care unit and predicted the need for mechanical ventilation with an area under curve of 0.68, both based on the rising trend of amino terminal pro-brain natriuretic peptide levels.

When compared to recovery, BNP levels were significantly higher during the acute exacerbation (65

pg/mL; interquartile range [IQR], 34 to 189 pg/mL, and vs. 40 to 85 pg/mL; IQR, 25 to 85;  $p<0.001$ ), particularly in those patients who required ICU treatment (105 pg/mL; IQR, 6 to 553; vs. 60 pg/mL; IQR, 31 to 169 pg/mL, and the P values were 0.007 and 0.07, respectively). An increase in BNP of 100 pg/mL (hazard ratio, 1.13; 95% confidence interval [CI], 1.03 to 1.24;  $p=0.008$ ) reliably predicted the requirement for ICU treatment in multivariate Cox regression analysis. Analysis of receiver operating characteristic curves found that BNP levels may predict short-term and long term death rates with a 0.55 (SD 0.71; 95 percent CI, 0.41 to 0.68) and 0.56 area under the curve, respectively, in the short-term and long-term mortality rates (SD, 0.53; 95 percent CI, 0.45 to 0.66, respectively).

Marcun et al., 2012 [15] NT-pro BNP and troponin T were found to be increased in 60% and 36% of patients at admission and 28% and 19% at discharge, respectively. Patients were hospitalised in 53 (42% of the total) and died in 17 (13%) of the follow-up visits. NT-pro BNP on admission and troponin T at discharge were used in Kaplan Meier analysis of survival curves to discriminate between died and surviving patients ( $p=0.011$  and 0.017, respectively). In the adjusted Cox proportional hazard model, discharge troponin T (hazard ratio 2.89, 95 percent confidence range 1.13–7.36) and admission NT-pro BNP (hazard ratio 4.20, 95 percent confidence interval 1.07–14.01) predicted hospitalisation and death, respectively.

According to a study published in [16], hospitalised patients had a higher BNP level (interquartile range) than those with stable COPD: 18.3 (10.0–45.3) pg/mL for Global Initiative for Chronic Obstructive Lung Disease (GI-COPD) grade I; 25.8 (11.0–53.7) pg/mL for grade II; 22.1 (9.1–52.6) for grade III; and 17.2 (9.6–22.99) pg/mL for grade IV, all  $P<0.001$ . The median plasma BNP level was 19.4 pg/mL before AECOPD, 72.7 pg/mL during AECOPD, and 14.6 pg/mL after AECOPD ( $P=0.0033$  and  $P=0.0013$ , respectively) in 15 participants evaluated prospectively. At AECOPD, BNP levels were substantially higher in 10 unsuccessfully discharged patients (260.5 pg/mL vs. 48 successfully released patients 48.5 pg/mL) than in 48 successfully discharged patients (48.5 pg/mL). Systolic dysfunction was seen in only 5.6% of AECOPD patients and 7.4% had poor relaxation characterised as an E/A wave velocity ratio 0.8 and an E deceleration time of E  $>240$  ms, respectively, in this study. However, a Spearman's rank correlation coefficient of 0.353/ $P=0.018$  indicates that BNP levels are strongly linked with the E/peak early diastolic velocity of the mitral annulus ratio (Ea) (Spearman's rank correlation coefficient =0.353,  $P=0.018$ ).

According to El Mallawany and colleagues in 2014, BNP NT-pro exhibited a statistically significant connection with pH ( $p=0.005$ ), E/A ( $p=0.007$ ), E/A ( $p=0.016$ ), and both left ventricular dimensions ( $p=0.008$ ) and E/A ( $p=0.016$ ) (El Mallawany et al, 2014). Following AECOPD, the NT-pro BNP dropped considerably ( $p=0.030$ ).

A follow-up analysis of (13), however, found that although patients with elevated admission NT-pro BNP levels had decreased follow-up levels ( $P = 0.04$ ), their NT-pro BNP levels remained higher than those in the control group. The missing data were found in two of the eight individuals admitted with elevated levels (one had died and one declined).

Furthermore, (9) indicated that COPD patients with higher NT-pro BNP readings were associated with an increased risk of all-cause death (hazard ratio (HR): 2.87,  $p = 0.0001$  and HR: 3.34,  $p = 0.04$ , respectively) in both patients with and without exacerbation. Meta-regression analysis for confounding variables corroborated the findings (previous cardiovascular history, hypertension, HF, forced expiratory volume at 1 second and mean age). Prognostic biomarker of poor prognosis in COPD patients may be NT-pro BNP.

However, in the research of (1), NT-pro-BNP levels were not linked with COPD severity or concomitant conditions. Echocardiographically measured right ventricular systolic pressure was significantly linked with log-transformed levels of NT-pro-BNP ( $r=0.3658$ ; 95 percent confidence interval [CI]: 0.2060–0.5067;  $P=0.0001$ ,  $P=0.0207$ ) and ( $P=0.0052$ ) patients with increased NT-pro-BNP levels were more likely to need intensive care and to spend more time in the hospital. Neither the requirement for noninvasive positive pressure ventilation ( $P=0.1245$ ) nor mechanical ventilation ( $P=0.9824$ ) nor in-hospital mortality ( $P=0.5273$ ) differed significantly. Our study's inclusion criteria may be to blame for the discrepancy.

## 5. Conclusion

- The measurement and trend monitoring of amino terminal pro-brain natriuretic peptide in cases of acute exacerbation of chronic obstructive pulmonary disease requiring mechanical ventilation may be a valuable asset in predicting mortality, noninvasive mechanical ventilation, weaning success, and the need for invasive mechanical ventilation in such cases.
- There was no financial support for this research.
- There was no one author who was not engaged in the study's design or analysis or interpretation of the data or revision of its content. Every one of the writers has agreed to take full responsibility for the work in every way.
- There are no conflicts of interest between the authors and any organisations or entities having financial interests in or conflicts of interest with the subject matter or materials covered in this paper. In this category, you'll see things like jobs, consulting gigs, fees for expert testimony, grants or patents that have been granted or are still pending, and royalties.
- The Benha University Faculty of Medicine's Research Ethics Committee has given its blessing to the investigation. It was made clear to all participants that they had the option of withdrawing from the research at any time.

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