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Evaluation of The Diagnostic Value of Brain Natriuretic Peptide for Detection of Left Ventricular Systolic Dysfunction and Pulmonary Hypertension in Patients with Acute Exacerbation of Chronic Obstructive Pulmonary Disease

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ABSTRACT

Background: One of the most critical health concerns of our day is acute deterioration of chronic obstructive lung disease (COPD). Detecting concurrent heart illness in these individuals might be challenging.

Objective: Aims of this study were determining the diagnostic value of B-type natriuretic peptide (BNP) levels in the identification of acute COPD exacerbations (AECOPD) that were linked with left ventricular (LV) dysfunction and pulmonary hypertension. **Methods:** a prospective study of 100 patients with acute COPD exacerbations was done. All research participants were subjected to history taking, clinical examination, laboratory testing, blood gas analysis, echocardiography, and NT-pro BNP plasma level estimation.

Results: Receiver operating characteristic (ROC) curve for BNP as a diagnostic for LV systolic dysfunction showed that area under the curve (AUC) was 0.923 at cut off point of 72.1 ng/ml with sensitivity of 93.3% and specificity of 84.6% (P<0.001).

Conclusion: Heart failure is confirmed when the average natriuretic (NT)-BNP level in the left ventricle during AECOPD is higher than normal, which should prompt quick treatment for both conditions.

Key words: Acute exacerbation of COPD, Brain natriuretic peptide, Cardiac dysfunction, Pulmonary hypertension

INTRODUCTION

Despite recent advances, COPD continues to be a major public health problem. It has significant extrapulmonary effects and may aggravate the sickness in certain patients [(1)].

A COPD flare-up is defined as "a change in the patient's baseline dyspnea, cough, and/or sputum that exceeds normal daily changes, is abrupt in start, and may justify a change in routine therapy in a patient with underlying COPD" [(2)]. Exacerbations are most frequently caused by infection of the tracheobronchial tree and air pollution, while roughly one-third of severe exacerbations are unknown [(3)].

Detecting left ventricular heart failure caused by a systolic left ventricular systolic dysfunction (LVSD) or diastolic (LVDD) etiology during an acute COPD exacerbation is particularly difficult due to the clinical presentation overlap [(4)]. Misdiagnosis of left ventricular heart failure during a COPD exacerbation might result in a bad prognosis and perhaps death [(5)].

Pulmonary arterial hypertension (PAH) is related with the development of severe hypoxemia late in the natural history of COPD patients [(6)]. COPD causes right ventricular hypertrophy (referred to as the "cor pulmonale"), with a dismal prognosis [(7)].

Echocardiography can be used to diagnose PAH and LVSD. Due to the fact that chest hyperinflation alters the propagation of sound waves in the chest, measurements cannot be taken in all scenarios [(8)].

Despite their broad use in the identification of cardiac disease, acute COPD exacerbation biomarkers have received little attention. Previously, biomarkers for respiratory sickness were investigated utilising the B-type natriuretic peptide (BNP) as a biomarker [(9)]. Apart from sodium regulation, vasodilation, renin–angiotensin–aldosterone suppression, and protection against unfavorable ventricular remodeling, B-type natriuretic peptide has an effect on cardiorenal homeostasis [(10)].

The current study's objective is to determine BNP levels in individuals with acute COPD exacerbations associated with reduced LV function and elevated pulmonary hypertension.

PATIENTS AND METHODS

This was a prospective observational study done in Alemeis Hospital and Alhayat National Hospital, Jazan, KSA and was conducted on 100 patients suffering from acute exacerbation of COPD.

Written informed permission, an acute exacerbation of pre-existing COPD, a minimum age of 18 years, and the capacity to undergo echocardiography were all included as inclusion criteria. Abrupt right ventricular overload confirmed by echocardiography, pulmonary embolism, severe pneumonia, renal failure, acute coronary event, mitral and aortic stenosis, and

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severe mitral and aortic stenosis were all excluded criteria.

Demographic data were collected from all patients as age, sex, chronic diseases (history of ischemic heart disease (IHD), hypertension, dyslipidemia or diabetes mellitus). Clinical examination with assessment of heart rate and blood pressure was done.

Q waves, ST depression or elevation, or T wave inversion were all looked for on every patient's electrocardiogram. In order to get a full blood picture, renal and liver function tests, fasting blood glucose level, prothrombin activity, total serum protein, albumin and lactate dehydrogenase content and C-reactive protein were performed on the venous blood sample.

Hydrogen ion concentration (pH), partial pressure of arterial oxygen (PaO_2) and partial pressure of arterial carbon dioxide ($PaCO_2$), oxygen saturation and bicarbonate (HCO_3) level were determined from a radial artery blood sample examined for these parameters

Chest radiography (CXR) was used to look for symptoms of heart failure (cardiomegaly, pleural effusion, or vascular redistribution), as well as radiologic markers of COPD (such as emphysema, decreased lung capacity, and decreased lung volume; defined by hyperinflation and flattened diaphragm).

An echocardiogram (Philips Affiniti 70G, Philips Ultrasound, Inc., USA) was used to evaluate blood flow in the pulmonary vessels by analyzing the pulmonary flow velocity, the pulmonary artery ejection time (AT), the ventricular end systolic and diastolic dimensions, the right ventricular ejection fraction, and the left ventricular end diastolic dimension (LVEF).

Enzyme-Linked Fluorescent Array (ELFA) on Vidas machine (bioMérieux Industry, Hazelwood, MO, USA) detected BNP quantitatively within 48 hours of hospitalization.

Ethical approval:

The study was approved by the Ethics Board of Alemeis Hospital and an informed written consent was taken from each participant in the study. This work has been carried out in accordance with The Code of Ethics of the World Medical Association (Declaration of Helsinki) for studies involving humans.

RESULTS

Table 1 shows that mean age was 58.14 years with mean BMI of 27.58 kg/m^2. Majority of the patients were males. Regarding clinical characteristics, the most predominant was cor pulmonale followed by crackles. Mean FEV1 was 67.9 and FVC was 56.43 with FEV1/FVC was 96.4 while mean pH value was 7.3 and mean SAPS II was 29.35.

Table 1: Baseline characteristics

Variable	AECOPD Patients (n=100)
Age (years)	58.14 ± 10.16
BMI (kg/m^2)	27.58 ± 4.54
Sex, n (%)	
Male	64 (64%)
Female	36 (36%)
Clinical characteristics, n (%)	
Crackles	31 (31%)
Wheezing	29 (29%)
Cor pulmonale	32 (32%)
Comorbidities, n (%)	
DM	40 (40%)
HTN	43 (43%)
Smoking	69 (69%)
HR (beat/min)	97.42 ± 18.96
RR (cycle/min)	26.7 ± 5.96
FEV_1	67.9 ± 7.17
FVC	56.43 ± 14.76
FEV/FVC	96.4 ± 10.53
pH	7.3 ± 0.107
PaO_2	87.15 ± 6.38
$PaCO_2$	46.98 ± 9.48
HCO_3	23.56 ± 5.076
$PaCO_2$:FiO_2	217.17 ± 9.44
SAPS II	29.35 ± 2.43

FVC: Forced vital capacity. FEV1: Forced expiratory volume. FiO_2: fraction of inspired oxygen. SAPS II: new Simplified Acute Physiology Score. Quantitative data were expressed as mean ±SD and qualitative data were expressed as number and percentage.

Table 2 shows the laboratory parameters of the studied patients.

Table 2: Laboratory parameters

Variable	AECOPD Patients (n=100)
Hb (g/dL)	12.38 ± 1.17
PLT (x10^3/L)	286.33 ± 48.15
TLC (x10^3/L)	10.7 ± 2.63
RBS (mg/dL)	149.76 ± 32.92
Total cholesterol (mg/dL)	206.1 ± 35.15
Triglycerides (mg/dL)	199.8 ± 31.16
LDL (mg/dL)	96.5 ± 3.83
HDL (mg/dL)	44.92 ± 7.71
Creatinine (mg/dL)	1.02 ± 0.3
Troponin T (ng/L)	393.88 ± 15.26
BNP (ng/ml)	53.95 ±11

All variables were expressed as mean ±SD except for BNP expressed as median (IQR).

Table 3 shows the echocardiographic parameters of the patients. Patients with pulmonary hypertension (defined as PAP>30 mmHg) were 62%.

Table 3: Echocardiography parameters

Variable	AECOPD Patients (n=100)
LVEDD (mm)	46.91 ± 5.03
LVESD (mm)	29.49 ± 4.62
LV-GLS (%)	-11.67 ± 1.33
EF (%)	45.97 ± 11.63
FS (%)	18.5 ± 3.05
PAP (mmHg)	49.3 ± 17.96
Pulmonary hypertension	
PAP ≤ 30 mmHg	38 (38%)
PAP > 30 mmHg	62 (62%)

LVEDD: left ventricular end-diastolic diameter. LVEDS: left ventricular end-systolic diameter. GLS: global longitudinal strain. EF: ejection fraction. FS: fraction shortening. PAP: pulmonary artery pressure. Quantitative data were expressed as mean ±SD and qualitative data were expressed as number and percentage.

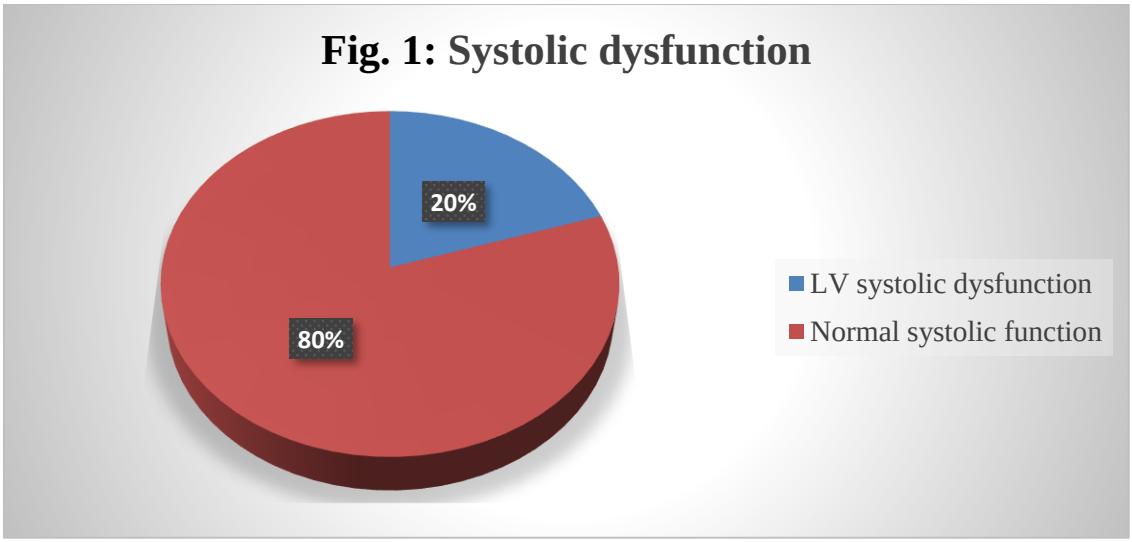

Fig. 1 shows that the prevalence of LV systolic dysfunction was 20%.

BNP should be considered as a diagnostic tool for LV systolic dysfunction and pulmonary hypertension.

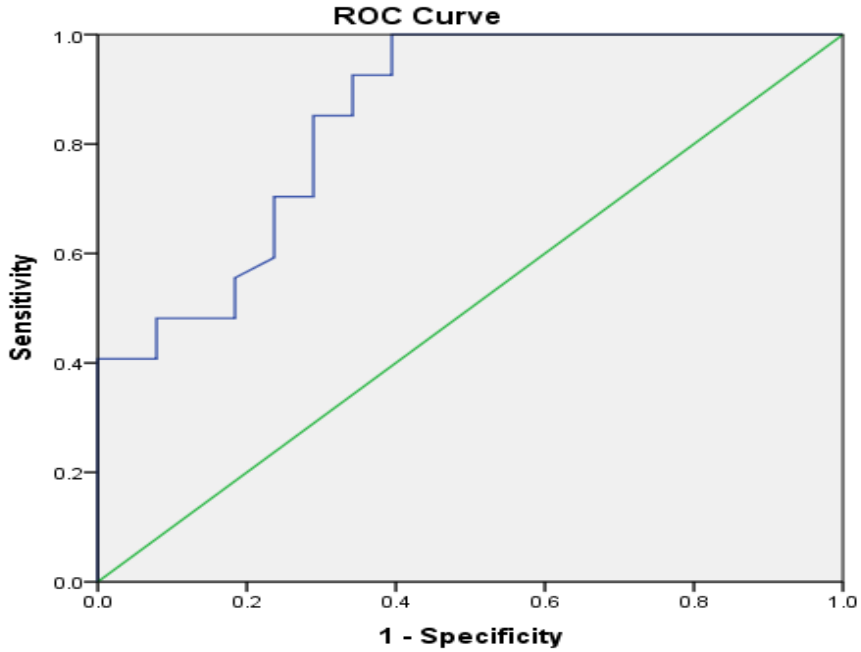

Fig 2: ROC curve for BNP as a diagnostic for pulmonary hypertension.
AUC=0.849 at cut off point of 50.3 ng/ml with sensitivity of 81.7% and specificity of 87.6% (P<0.001).

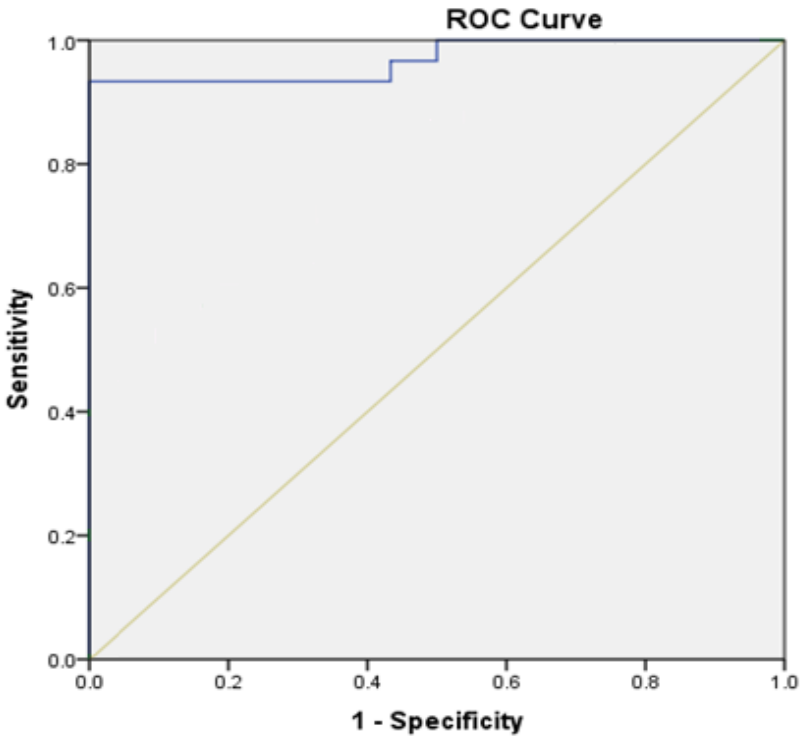

Fig. 3: ROC curve for BNP as a diagnostic for LV systolic dysfunction.
AUC=0.923 at cut off point of 72.1ng/ml with sensitivity of 93.3% and specificity of 84.6% (P<0.001).

DISCUSSION

We included 100 subjects in our study whose mean age was 58.14 years with SD of 10.16 and mean BMI was 27.58 kg/m^2 with SD of 4.54. Most of them were males. Crackles were found in 31% of patients, cor pulmonale in 32% of patients and wheezing in 29% of patients. Similar to our findings **Abroug *et al.*** [11] reported that median age was 68 years; males represented 81.1% of included subjects. Cor pulmonale was found in 39% of patients, crackles in 52.7% of patients and wheezing in 64.9% of patients.

In our study hypertension (HTN) was found in 43% of patients, most of them (69%) were smokers and diabetes mellitus (DM) was found in 40% of patients. Less than our study **Andrijevic *et al.*** [5] reported that diabetes was found in 19.59% of patients. However, HTN was found in 77.84% of patients. Close to our study **Andrijevic *et al.*** [12] reported that 41.63% of patients were smokers.

Regarding vital signs heart rate reached a mean of 97.42 beat/min with SD of 18.96 and respiratory rate (RR) reached a mean of 26.7 cycle/min with SD of 5.96. In our study pH mean was 7.3, PaO_2 mean was 87.15, and $PaCO_2$ mean was 46.98 and $PaCO_2$:FiO_2 mean was 217.17 and SAPS II was 29.35. Close to our study **Abroug *et al.*** [11] reported that HR reached median of 100 beats/min, RR reached median of 28 breaths/min. PH median was 7.27, baseline PaO_2 reached median of 70 and baseline $PaCO_2$ reached median of 48. Baseline FEV1 reached median of 0.7. PaO_2 /FIO_2 median was 212 and SAPSII median was 27.

In our study BNP reached median of 53.95 ng/mL and IQR was (11.85-90.11). A study by **Sato *et al.*** [13] reported that Average BNP mean reached 47.57ng/ml. Regarding echo parameters LVEDD reached mean of 46.91 mm and LVESD reached mean of 29.49 mm. Ejection fraction mean was 45.97% and fraction shortening reached a mean of 18.5%. Pulmonary artery pressure (PAP) reached a mean of 49.3 mmHg. PAP in 38% of patients was ≤ 30 mmHg and in 62% of patients was > 30 mmHg. A similar study by **Xia *et al.*** [14] about COPD and cardiac parameters, reported LVEDD reached mean of 64.98 mm in mild cases and less in moderate and severe cases. LVESD reached a mean of 28.11 mm. Also **Sato *et al.*** [13] reported that LV ejection fraction reached 60% in COPD patients. **Arian *et al.*** [15] reported that PAP in patients reached mean of 49.2 mmHg.

ROC curve for BNP as a diagnostic for pulmonary hypertension showed that AUC was 0.849 at cut off point of 50.3 ng/ml with sensitivity of 81.7% and specificity of 87.6%. ROC curve for BNP as a diagnostic for LV systolic dysfunction showed that AUC was 0.923 at cut off point of 72.1 ng/ml with sensitivity of 93.3% and specificity of 84.6%.

To our knowledge it is the first trial to evaluate the diagnostic value of brain natriuretic peptide for detection of left ventricular systolic dysfunction and pulmonary hypertension in patients with acute exacerbation of chronic obstructive pulmonary disease as all previous trials depended on proBNP.

In a previous trial by **Ouanes *et al.*** [16] it was shown that median NT-proBNP levels were

significantly higher in patients with LVSD and AECOPD irrespective of whether renal function was normal or impaired. More than our values, in this trial, sensitivity and specificity were 94 and 82%. **Prosen and associates** [(17)], found 92% sensitivity, 89% specificity, 86% negative predictive value (NPV), and 90% positive predictive value (PPV) for diagnosis of heart failure in AECOPD. In the latest study by **Andrijevic *et al.*** [(12)] sensitivity, specificity, PPV, and NPV were 76.6, 83.33, 57.14, and 92.47%. They were close to our results.

CONCLUSION

Heart failure is confirmed when the average NT-BNP level in the left ventricle during AECOPD is higher than normal, which should prompt quick treatment for both conditions.

Declarations:

Consent for publication: I confirm that all authors accept the manuscript for submission

Availability of data and material: Available

Competing interests: none

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Conflicts of Interest: The authors declare no conflicts of interest regarding the publication of this paper.

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