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Diagnostic role of end-tidal carbon dioxide in differentiating chronic obstructive pulmonary disease and chronic heart failure: Association with NT-proBNP in dyspneic patients

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Abstract: Chronic heart failure (CHF) and chronic obstructive pulmonary disease (COPD) are increasingly prevalent among the elderly, and both frequently present with dyspnea as the primary symptom in emergency departments. Differentiating between the two conditions remains challenging, particularly in primary care, yet is essential given their distinct management approaches and prognostic implications. This study investigated the diagnostic utility of non-invasive end-tidal carbon dioxide ($ETCO_2$) measurements in patients presenting with dyspnea and assessed whether combining $ETCO_2$ with N-terminal pro-brain natriuretic peptide (NT-proBNP) enhances diagnostic accuracy. A total of 205 patients admitted to the Emergency Department of Kayseri City Hospital and subsequently diagnosed with either CHF or COPD were included. Demographic data, clinical history, treatments, vital signs, NT-proBNP levels, echocardiographic findings, arterial blood gas results, integrated pulmonary index (IPI) scores, $ETCO_2$ values, and clinical outcomes were recorded. Echocardiography was performed by a cardiologist, and $ETCO_2$ and IPI values were obtained using the Medtronic Capnostream™ 35 monitor. NT-proBNP ($p < 0.001$), $ETCO_2$ ($p < 0.001$), and IPI ($p = 0.038$) were all statistically significant in differentiating CHF from COPD, with $ETCO_2$ demonstrating the strongest association. The addition of NT-proBNP or IPI to $ETCO_2$ did not provide further diagnostic benefit. NT-proBNP was also predictive of hospital admission ($p < 0.001$). These findings indicate that quantitative $ETCO_2$ measurement, performed with a non-invasive and patient-friendly sidestream technique, is effective for diagnostic differentiation in acute dyspnea and has strong clinical applicability. $ETCO_2$ outperformed both NT-proBNP and IPI, and its use alone may be sufficient in this setting. Higher NT-proBNP cut-off values may be more appropriate in acute-onset dyspnea, and elevated NT-proBNP in COPD patients may hold prognostic value for poorer clinical outcomes.

Keywords: end-tidal carbon dioxide; COPD; CHF; Integrated Pulmonary Index; N-terminal pro B-type natriuretic peptide

INTRODUCTION

Dyspnea is one of the most frequent complaints encountered during visits to the emergency department (ED) and is most often attributable to underlying cardiac or pulmonary disorders. It is frequently associated with multiple comorbidities that are particularly common and clinically significant in older adults. The differential diagnosis includes congestive heart failure (CHF), chronic obstructive pulmonary disease (COPD), pulmonary thromboembolism, and pneumonia all conditions associated with substantial morbidity and mortality.

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Accurate and timely diagnosis is critical, as prognosis and therapeutic outcomes are highly dependent on the underlying etiology, and treatment strategies differ considerably. For example, corticosteroid therapy in patients with pulmonary edema or CHF may exacerbate fluid retention, worsen hemodynamic status, and negatively influence cardiac remodeling, whereas diuretics have limited therapeutic value in COPD management.[1,2]

CHF remains a key consideration in the differential diagnosis of acute dyspnea in the ED. It is characterized by structural or functional cardiac impairment that limits the ability of the heart to supply sufficient blood to meet metabolic demands. The prevalence of CHF continues to rise, and clinical presentation is often dominated by fluid and sodium retention. However, classical findings such as displacement of the cardiac apex, jugular venous distension, or pulmonary rales may be nonspecific and can overlap with other pathologies, complicating diagnosis.[1,3]

COPD, in contrast, is a progressive and irreversible disease most commonly caused by chronic exposure to noxious particles or gases, leading to structural damage to the airways and lung parenchyma. It manifests clinically as persistent airflow limitation accompanied by respiratory symptoms, and early recognition is essential to slow disease progression and improve outcomes.[4]

End-tidal carbon dioxide ($ETCO_2$) measurement has gained increasing attention as a non-invasive marker of ventilation and perfusion status in patients presenting with dyspnea. $ETCO_2$ represents the concentration of exhaled carbon dioxide at the end of expiration and is measured using capnography.[5] Although initially developed to confirm endotracheal tube placement, its clinical use has broadened to include monitoring during cardiopulmonary resuscitation, guiding management of COPD exacerbations, assessing respiratory status in patients under sedation or seizure monitoring, and evaluating overall ventilation. The technique is advantageous due to its non-invasive nature, real-time feedback, and applicability across diverse clinical settings. Both mainstream and sidestream methods are available; notably, sidestream capnography allows measurement in non-intubated patients using a nasal cannula, making it particularly suitable in ED and prehospital contexts.[5,6]

The Integrated Pulmonary Index (IPI) complements capnography by integrating $ETCO_2$, respiratory rate, oxygen saturation, and pulse rate into a single numerical score ranging from 1 to 10. Calculated through fuzzy logic algorithms, this index provides a dynamic, real-time assessment of ventilation and oxygenation adequacy. Lower values indicate a greater need for intervention, reflecting both underlying disease burden and acute ventilatory status.

The present study aimed to evaluate the diagnostic value of sidestream $ETCO_2$ measurement in non-intubated patients presenting with acute dyspnea to the ED, particularly in differentiating COPD from CHF. In addition, we examined whether combining $ETCO_2$ with NT-proBNP a biomarker that remains largely inaccessible in primary care and prehospital settings due to its laboratory requirements and IPI scores could improve diagnostic accuracy. We hypothesized that these findings would support more informed decision-making in both ED and primary care environments, ultimately facilitating earlier and more appropriate treatment.

MATERIAL AND METHOD

Study design and population

This prospective observational study was conducted in the Emergency Department of Kayseri City Training and Research Hospital between January 1 and September 1, 2019. Adult patients presenting with dyspnea and subsequently diagnosed with either chronic obstructive pulmonary disease (COPD) or congestive heart failure (CHF) were eligible. A total of 205 patients were enrolled.

Exclusion criteria included comorbid conditions that could potentially influence $ETCO_2$ values, such as sepsis, trauma, pulmonary embolism, pneumothorax, metabolic alkalosis or acidosis, acute renal failure, and intoxication.

Data collection

Demographic characteristics (age, sex), medical history, and treatments administered in the emergency department were recorded on standardized data collection forms. Vital signs (pulse rate, respiratory rate, oxygen saturation), laboratory parameters (NT-proBNP levels and arterial blood gas values), echocardiographic findings, $ETCO_2$ values, and Integrated Pulmonary Index (IPI) scores were documented at admission, prior to the initiation of treatment. Patient outcomes (hospitalization or discharge) were also noted. Final diagnoses were established collaboratively by emergency medicine physicians, cardiologists, and pulmonologists.

Measurements

$ETCO_2$ and IPI were measured using the sidestream technique with the Medtronic Capnostream™ 35 respiratory monitor and disposable nasal cannulas. NT-proBNP levels and arterial blood gases were analyzed using routine laboratory methods in the hospital's central laboratory. Transthoracic echocardiography was performed by experienced cardiologists in accordance with established guidelines.

Statistical analysis

Descriptive statistics were used to summarize study data. Continuous variables were expressed as mean ± standard deviation (SD) or as median with interquartile ranges (IQR), depending on distribution, while categorical variables were expressed as frequencies and percentages. Normality of numerical variables was tested using the Kolmogorov-Smirnov and Shapiro-Wilk tests. For group comparisons, the Independent Samples t-test was applied when distributions were normal, and the Mann-Whitney U test was used for non-normally distributed variables. Because age distribution was not homogeneous across groups, non-parametric ANCOVA was used for adjusted comparisons. The Pearson Chi-square test was employed for categorical variables when expected frequencies were ≥5. To assess the diagnostic performance of $ETCO_2$, NT-proBNP, IPI, SpO_2, respiratory rate, and heart rate in differentiating COPD from CHF, receiver operating characteristic (ROC) curve analysis was performed. The area under the curve (AUC), sensitivity, specificity, cut-off values, and 95% confidence intervals (CIs) were calculated.

All statistical analyses and figures were generated using Jamovi software (version 1.2.22, Jamovi Project, Sydney, Australia)[1], JASP (version 0.13, University of Amsterdam, Netherlands)[2], MedCalc Statistical Software (trial version, MedCalc Software bvba, Ostend, Belgium)[3], and R Studio (RStudio Inc., Boston, MA, USA). A two-tailed p-value <0.05 was considered statistically significant.

Ethical considerations

The study protocol was approved by the Erciyes University Clinical Research Ethics Committee. Written informed consent was obtained from all patients prior to study participation.

RESULTS AND DISCUSSION

A total of 205 patients were included in the study, with a mean age of 70.6 ± 12.2 years; 57% (n = 117) were male and 43% (n = 88) were female. Of these, 71.7% (n = 147) were diagnosed with COPD and 28.3% (n = 58) with CHF. Overall, 139 patients (67.8%) required hospitalization, while 66 (32.2%) were discharged after ED treatment (Table 1). When demographic data were analyzed by diagnosis, the mean age of CHF patients (75.3 ± 10.2 years) was significantly higher compared with COPD patients (68.7 ± 12.5 years; p = 0.045). No significant

differences were found between groups in terms of gender or hospitalization status (Table 2).

Significant differences were observed in several clinical and laboratory parameters. Median ejection fraction (EF), IPI score, $ETCO_2$, and PCO_2 were significantly higher in COPD patients compared with CHF patients ($p < 0.001$, $p = 0.038$, $p < 0.001$, and $p < 0.001$, respectively). In contrast, median NT-proBNP levels were significantly higher in CHF patients ($p < 0.001$). The mean $ETCO_2$ value was 36 mmHg in the COPD group and 22.5 mmHg in the CHF group, demonstrating a robust difference between groups ($p < 0.001$). Similarly, the mean NT-proBNP concentration was 6,015 pg/mL in CHF patients and 1,061 pg/mL in COPD patients ($p < 0.001$). The mean IPI score was 4 (IQR 2–7) in COPD and 3 (IQR 2–5) in CHF, with the difference reaching statistical significance ($p = 0.038$) (Table 3).

ROC analysis demonstrated that $ETCO_2$ had the highest discriminative ability, with a cut-off value of ≤29 mmHg (sensitivity 82.8%, specificity 78.9%, AUC 0.884; $p < 0.001$). For NT-proBNP, the cut-off was >1,480 pg/mL (sensitivity 91.2%, specificity 57.3%, AUC 0.808; $p < 0.001$). The IPI cut-off value of ≤5 yielded lower discriminative accuracy (sensitivity 79.3%, specificity 39.3%, AUC 0.592; $p = 0.025$) (Table 4). Pairwise ROC curve comparisons confirmed that $ETCO_2$ outperformed both NT-proBNP and IPI (Table 5). The addition of NT-proBNP or IPI to $ETCO_2$ did not provide a statistically significant improvement in diagnostic accuracy ($p = 0.085$ and $p = 0.092$, respectively) (Table 6; Figure 1). When outcomes were analyzed, hospitalized patients had significantly higher NT-proBNP levels compared with discharged patients (median 2,644 pg/mL vs 957 pg/mL; $p < 0.001$). However, no significant differences in EF, IPI, or $ETCO_2$ were observed between hospitalized and discharged groups (Table 7).

Dyspnea is a common reason for ED visits and may arise from both cardiac and pulmonary causes. In CHF, dyspnea typically results from impaired cardiac function and pulmonary congestion, while in COPD it is caused by airflow limitation and hyperinflation.[7,8] The clinical overlap between these conditions complicates early diagnosis, yet accurate differentiation is critical for guiding therapy and improving outcomes.[9,10]

Our findings support the diagnostic value of sidestream $ETCO_2$ measurement in distinguishing COPD from CHF. The mean $ETCO_2$ was significantly higher in COPD patients (36 mmHg) than in CHF patients (22.5 mmHg). ROC analysis identified an $ETCO_2$ cut-off of 29 mmHg, with strong sensitivity and specificity, confirming its utility. These results are consistent with prior studies by Lawrence et al,[14] Klemen et al,[15] and Grmec et al,[16] all of which reported significantly lower $ETCO_2$ values in CHF compared with COPD.

NT-proBNP also demonstrated diagnostic significance, with higher levels in CHF patients (median 6,015 pg/mL) compared with COPD (median 1,061 pg/mL). Our calculated cut-off value of 1,480 pg/mL yielded high sensitivity but moderate specificity. This threshold is substantially higher than the 300 pg/mL value recommended in the 2023 ESC guidelines for acute heart failure diagnosis,[1] reflecting the fact that our study included undifferentiated dyspneic patients with comorbidities such as advanced age, renal dysfunction, and atrial fibrillation all known to elevate NT-proBNP.[26,27] Age specific thresholds proposed by the ESC further support this observation, given the advanced age of our cohort (mean 70 years).[28]

Importantly, elevated NT-proBNP levels were also found in COPD patients, a phenomenon likely related to pulmonary hypertension, right ventricular strain, systemic hypoxemia, and exacerbations.[17,18] Similar results were reported by Ozdemirel et al[19] and Karakılıç et al,[22] who observed that BNP levels in COPD patients reflect both right- and left-ventricular function. In our study, elevated NT-proBNP was significantly associated with hospitalization in both groups, in line with

reports by Adrish et al[23] and Rubinsztajn et al,[24] suggesting its value as a prognostic marker beyond diagnostic differentiation.

The IPI, though statistically significant, demonstrated limited discriminative ability (AUC 0.592). This may be due to the reliance of the algorithm on multiple variables, including oxygen saturation, which is often reduced in COPD and may confound the contribution of $ETCO_2$. To our knowledge, this is the first study to evaluate IPI in differentiating COPD from CHF. While the IPI offers advantages such as non invasive monitoring and real-time assessment, its diagnostic utility remains limited compared with $ETCO_2$.

Overall, our data indicate that $ETCO_2$ is the most effective single parameter for differentiating COPD from CHF in patients presenting with dyspnea. The addition of NT-proBNP or IPI did not significantly enhance diagnostic accuracy. The practicality, non invasiveness, and rapid applicability of $ETCO_2$ measurement suggest its strong potential for use in ED and prehospital settings where NT-proBNP testing is often unavailable.

However, several limitations should be noted. This was a single-center study, which may restrict generalizability. Pulmonary function testing was not performed during the study period, and diagnoses were based on medical records and specialist consultations. Furthermore, although age was adjusted for using non-parametric ANCOVA, residual confounding by comorbidities cannot be excluded. Future multicenter studies with larger, more diverse populations and standardized pulmonary function testing are warranted.

CONCLUSION

In our study, NT-proBNP, $ETCO_2$, and IPI scores were all found to be statistically significant in differentiating between COPD and CHF. Quantitative $ETCO_2$ measurement using the non-invasive and patient-friendly sidestream technique proved effective both diagnostically and clinically. Among the three variables, $ETCO_2$ demonstrated the strongest association, while IPI showed the weakest. Given that $ETCO_2$ can be measured rapidly and non-invasively—even in prehospital settings such as ambulances—it holds promise as a valuable first-line tool for early clinical decision-making, particularly in environments where NT-proBNP testing is not readily available. Early and accurate differentiation is critical, as the administration of diuretics to a patient with COPD or beta-agonists to a patient with CHF may result in adverse outcomes.

AUTHORS' CONTRIBUTIONS

All authors have read and approved the final manuscript.

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DATA AVAILABILITY STATEMENT

The utilized data to contribute to this investigastion are available from the corresponding author on reasonable request.

DISCLOSURE STATEMENT

There is no conflict of interest.

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Table 1. Demographic and Clinical Characteristics of the Study Population

Gender	Male	117 (57)
	Female	88 (43)
Age		70,64 ± 12,22
$ETCO_2$		33,21 ± 10,2 / 32 [26 – 39]
EF		48,53 ± 10,08 / 50 [45 – 55]
Result	COPD	147 (71,71)
	CHF	58 (28,29)
IPI		4 [2 – 7]
Hospitlization status	Hospitalized	139 (67,8)
	Discharge	66 (32,2)
PCO_2		45,96 ± 10,66 / 45 [38 – 53]
nt-PRO BNP		4913,33 ± 7749,54 / 1954 [593 – 5594,5]
Oxygen Saturation		76,11 ± 21,11 / 88 [56 – 91]
Respiratory rate		26,11 ± 8,91 / 26 [20 – 31]
Heart rate		94,54 ± 18,46 / 92 [82 – 105]
Systolic Blood Pressure		129,19 ± 25,35 / 126,5 [111 – 141]
Diastolic Blood Pressure		79,59 ± 13,52 / 80 [70 – 85]

COPD: Chronic obstructive pulmoner disesase, CHF: Chronic heart failure, EF: Ejection Fraction, IPI: Integrated Pulmoner Index, NT-PRO BNP: N-terminal pro–B-type natriuretic peptide, $ETCO_2$: End-Tidal Carbon Dioxide, PCO_2: Partial Pressure of Carbon Dioxide. Descriptive statistics are presented as mean ± standard deviation or median [Q1–Q3] for numerical variables, and as frequency (percentage) for categorical variables

Table 2. Comparison of Demographic Characteristics Between COPD and CHF Patients

		COPD (n=147)	CHF (n=58)	*p*
Gender	Male	84 (57,1)	33 (56,8)	0,892*
	Female	63 (42,9)	25 (43,2)	
Age		68,7 ± 12,5	75,3 ± 10,2	**0,045****
Hospitalization status	Hospitalized	96 (65,3)	43 (74,1)	0,223*
	Discharge	51 (34,7)	15 (25,9)	

Descriptive statistics are presented as mean ± standard deviation for continuous variables and as number (percentage) for categorical variables
*Pearson Chi-Square test was used.
**Independent Samples T Test was used.
Bold p-values indicate statistical significance ($p < 0.05$).

Table 3. Comparison of EF, IPI, NT-proBNP, PCO_2, and $ETCO_2$ Between COPD and CHF Patients

	COPD	**CHF**	***p****	***Age (Covariate) p*** **
EF	55 [50 – 55]	40 [30 – 45]	<0.001	<0.001
IPI	4 [2 – 7]	3 [2 – 5]	0.038	0.093
nt-PRO BNP	1061 [324 – 3527]	6015 [2077 – 10717]	<0.001	<0.001
$ETCO_2$	36 [30 – 41]	22.5 [19 – 29]	<0.001	<0.001
PCO_2	47.5 [40 – 56]	39 [31.5 – 44.5]	<0.001	<0.001

EF: Ejection Fraction, IPI: Integrated Pulmoner Index, NT-PRO BNP: N-terminal pro–B-type natriuretic peptide, $ETCO_2$: End-Tidal Carbon Dioxide, PCO_2: Partial Pressure of Carbon Dioxide
*The Mann-Whitney U test was used. Descriptive statistics are presented as median [Q1 – Q3].
** For variables with significant differences, non-parametric ANCOVA was applied to control for age distribution, as it was not homogeneous across groups.

Table 4. ROC Analysis Results for $ETCO_2$, NT-proBNP, and IPI in COPD and CHF

	AUC	**Sensitivity**	**Specificity**	**Cut Off**	**%95 GA**	**p**
$ETCO_2$	0.884	82.76	78.91	≤29	0.832 – 0.925	<0.001
nt-PRO BNP	0.808	91.23	57.34	>1480	0.746 – 0.860	<0.001
IPI	0.592	79.31	39.31	≤5	0.521 – 0.661	0.025

IPI: Integrated Pulmoner Index, NT-PRO BNP: N-terminal pro–B-type natriuretic peptide, $ETCO_2$:

End-Tidal Carbon Dioxide Bold p-values are considered statistically significant (p<0.05).

Table 5. Pairwise ROC Curve Comparisons

	$ETCO_2$ ~ nt-PRO BNP	$ETCO_2$ ~ IPI	nt-PRO BNP ~ IPI
Difference Between Areas Under the Curve	0.079	0.291	0.212
Standard error	0.038	0.043	0.050
95% Confidence Interval	0.005 – 0.154	0.207 – 0.375	0.114 – 0.309
***p* value**	**0.036**	**<0.001**	**<0.001**

IPI: Integrated Pulmoner Index, NT-PRO BNP: N-terminal pro–B-type natriuretic peptide, $ETCO_2$: End-Tidal Carbon Dioxide
Bold p-values are considered statistically significant (p<0.05).

Table 6. Combined ROC Curve Comparisons

Prediction Model	AUC	95% CI	*P-value*
$ETCO_2$	0.884	0.833-0.936	
$ETCO_2$ + nt-PRO BNP	0.899	0.851-0.948	0.085
$ETCO_2$ + IPI	0.885	0.833-0.937	0.092

IPI: Integrated Pulmoner Index, NT-PRO BNP: N-terminal pro–B-type natriuretic peptide, $ETCO_2$: End-Tidal Carbon Dioxide

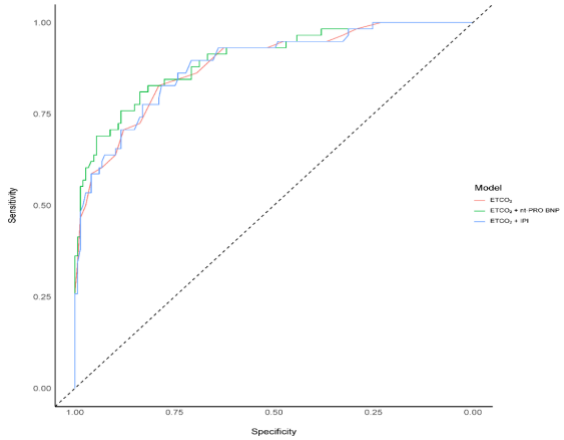

Figure 1. ROC Curves of $ETCO_2$, NT-proBNP, and IPI

Table 7. Comparison of EF, IPI, NT-proBNP, and $ETCO_2$ According to Hospitalization Status

	Hospitalized	Discharge	*p**
EF	50 [45 – 55]	55 [45 – 55]	0.060
IPI	4 [2 – 6]	5 [3 – 7]	0.068
nt-PRO BNP	2644 [945 – 6368.5]	957.5 [231 – 2799]	**<0.001**
$ETCO_2$	32 [26 – 41]	32 [27 – 38]	0.727

EF: Ejection Fraction, IPI: Integrated Pulmoner Index, NT-PRO BNP: N-terminal pro–B-type natriuretic peptide , $ETCO_2$: End-Tidal Carbon Dioxide
*The Mann-Whitney U test was used. Descriptive statistics are presented as median [Q1 – Q3].
Bold p-values are considered statistically significant (p<0.05).