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RESEARCH

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Role of exhaled carbon monoxide in assessment of chronic obstructive airway disease severity

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Abstract

Background Chronic obstructive pulmonary disease (COPD) is a critical public health issue. Spirometric measurements are used to diagnose chronic obstructive lung disease, as per the guidelines of the GOLD initiative. Post-bronchodilator forced expiratory volume in 1 s (FEV1) is a predictor of mortality from COPD and helps to classify the disease's severity. Smoking contributes to the high levels of exhaled CO. Evidence suggests that the exhaled CO level in COPD patients varies with degree of blockage and can be used to assess treatment response. Estimating the exhaled CO level can help assess airway inflammation and severity of airflow obstruction in individuals with COPD.

Aim Evaluate role of exhaled CO in assessment of severity of COPD.

Materials and methods This cross-sectional study included 132 patients who visited the outpatient clinics or were admitted to the Chest Department, Kasr Alainy Hospital, Faculty of Medicine, Cairo University. The study participants were divided into three groups: *group 1* nonsmoker healthy control, *group 2* smoker non-COPD, and *group 3* smoker COPD which further divided according to GOLD 2023 into mild, moderate, and severe COPD. The smoking status, exhaled CO, and spirometry test including FEV1/FVC and FEV1 were measured for each patient.

Results Exhaled CO was significantly increased in the smoker group (mean 9.69, *SD* 3.11) compared to the non-smoker group (mean 2.19, *SD* 0.98) with p-value < 0.001. Exhaled CO was also statistically significantly higher in the smoker COPD group (mean 10.45, *SD* 3.03) compared to the smoker non-COPD group (mean 7.05, *SD* 1.56) with p-value < 0.001. Although exhaled CO was increased in the severe COPD group compared to the mild and moderate group, there is no statistically significant difference between them.

Conclusion Exhaled CO is a fast, sensitive, noninvasive, and well-established method test that can be used to identify smokers from nonsmokers with 98.9% sensitivity at 4.5 cutoff value. Also, exhaled CO levels in COPD patients vary with different degrees of airway obstruction.

Keywords Exhaled CO, COPD, Smokers

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Introduction

COPD is the third most frequently occurring disease that leads to death worldwide [1]. Also, COPD is considered the most frequent cause of chronic disability and mortality throughout the world [2]. Post-bronchodilator spirometry is the most effective way to measure airflow dynamics. Post-bronchodilator forced expiratory volume in 1 s (FEV1) is the cornerstone of classification of degrees of severity of COPD, and it is used to predict mortality from COPD [3]. Smoking is the main environmental risk factor for COPD. Smokers are more prone for developing pulmonary complications and pulmonary function abnormalities, a higher rate of decrease in FEV1 per year, and higher COPD death rates than nonsmokers [4]. Inflammation of the airways is a major feature of COPD, and it affects both the small and large air passages. Airway and systemic inflammation in COPD are responsible for progressive nature of the disease [5]. Estimation of exhaled carbon monoxide is a fast, less invasive, and well-established test used to distinguish smokers from nonsmokers [6]. Smokers with high risk of developing COPD may benefit from using exhaled carbon monoxide to diagnose the disease earlier even before the clinical and functional affection appear [7]. This could achieve a remarkable improvement in COPD management.

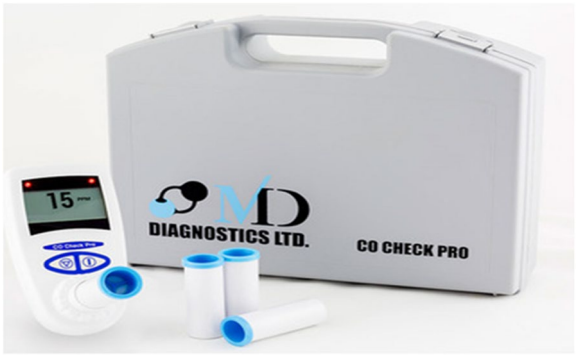

Fig. 1 CO Check Pro device

Aim of the work

Evaluate the role of exhaled CO in the assessment of COPD severity.

Patients and methods

Study design

This cross-sectional study was carried out between December 2022 and December 2023, and it included 132 individuals who visited the outpatient clinic or were admitted to the Chest Department, Kasr Alainy Hospital, Faculty of Medicine, Cairo University. Our study patients were divided into three groups: group 1 nonsmoker healthy control, group 2 smoker non-COPD, and group 3 smoker COPD which further divided according to GOLD 2023 into mild, moderate, and severe COPD and the

Table 1 Demographics of the study participants

			Count			%
Sex		**Male**	132			100.0%
Smoking status		**Yes**	96			72.7%
		No	36			27.3%
Diagnosis		**Control**	36			27.3%
		Non-COPD smokers	21			15.9%
		Mild COPD smokers	24			18.2%
		Moderate COPD smokers	26			19.7%
		Severe COPD smokers	25			18.9%
Comorbidities		**Obesity**	1			0.8%
		DM	10			7.6%
		HTN	20			15.2%
		HTN–DM	4			3.0%
		DM–obesity	1			0.8%
		No	96			72.7%
		COPD		**Control**		
		Count	**%**	**Count**	**%**	***p*-value**
Comorbidities	**Yes**	24	32.0%	12	21.1%	0.162
	No	51	68.0%	45	78.9%	

DM diabetes mellitus, *HTN* hypertension, *COPD* chronic obstructive airway disease

Table 2 Comparison between exhaled CO in the smoker and the nonsmoker groups

	Smokers		Nonsmokers		
	Mean	Standard deviation	Mean	Standard deviation	*p*-value
Exhaled CO	9.69	3.11	2.19	0.98	< 0.001

Unpaired *t*-test

Table 3 Comparison between exhaled CO in the smoker COPD and smoker non-COPD groups

	Non-COPD smokers		COPD smokers		
	Mean	Standard deviation	Mean	Standard deviation	*p*-value
Exhaled CO	7.05	1.56	10.45	3.03	< 0.001

Unpaired *t*-test

more severe group which were excluded from the study as they cannot perform the exhaled CO test.

Patients meeting the following inclusion criteria were enrolled: Patients with COPD seeking medical advice at Kasr Alainy Chest Department.

Patients with bronchial asthma, pneumonia, bronchogenic carcinoma, liver diseases, renal diseases, interstitial fibrosis, heart failure, and vascular diseases were excluded from the study.

Clinical information

- Full history and clinical examination including age, gender, assessment of smoking status, and chest X-ray
- Exhaled CO by CO Check Pro device: A portable device designed for handheld use can measure the concentration of carbon monoxide CO (ppm) in exhaled breath based on an electrochemical fuel cell sensor. The individuals were asked to breath out completely to empty their lungs, fully inspire, and then hold their breath for as long as they can. After holding of breath for at least 10 s, they were asked to expire slowly into the CO Check Pro device and were encouraged to exhale fully to sample the exhaled air. The device displays the concentration of exhaled CO in ppm and can convert it to percent carboxyhemoglobin (%COHb) using the mathematical relationships described by *Jarvis* et al. *(1986)* [8] for concentrations below 90 ppm and by *Stewart* et al. *(1976)* [9] for higher levels (Fig. 1).
- Post-bronchodilator pulmonary function test (FEV1and FVC) by MasterScreen PFT 2012, CareFusion 234 GmbH, Germany (V-781267-057 version 03.00).

Statistical methods

To present quantitative data, we used mean and standard deviation, as well as frequencies. The use of an unpaired *t* test to compare 2 groups and an ANOVA test when comparing more than 2 groups (Chan, 2003a). We utilized the Pearson correlation coefficient to establish correlations between quantitative variables. ROC curve was constructed with area under curve analysis performed to detect best cutoff value of exhaled CO for detection of smokers. Statistical significance is considered when *p*-values are less than 0.05.

Results

Demographics of the study participants

This study was carried out at Kasr Alainy Faculty of Medicine, Cairo University, and included 132 individuals. They were divided into three groups: group 1 nonsmoker healthy control, group 2 smoker non-COPD, and group 3 smoker COPD which further divided according to GOLD 2023 into mild, moderate, and severe COPD. All of them were men with mean age 51.94 ± 12.66 years. Ninety-six were smokers, while 36 nonsmokers (Table 1).

Comparison between exhaled CO in the smoker and the nonsmoker groups

Exhaled CO was statistically significantly increased in the smoker group (mean 9.69 ± 3.11) in comparison to the non-smoker group (mean 2.19 ± 0.98) with *p*-value < 0.001 (Table 2).

Table 4 Comparison between exhaled CO in the mild, moderate, and severe COPD groups

	Mild COPD smokers		Moderate COPD smokers		Severe COPD smokers		
	Mean	Standard deviation	Mean	Standard deviation	Mean	Standard deviation	*p*-value
Exhaled CO	9.54	3.32	10.44	2.43	11.32	3.15	0.122

ANOVA test

Table 5 Correlation between exhaled CO and FEV1 and FEV1/FVC in COPD patients

		Exhaled CO
FEV1/FVC	**r**	-0.083-
	***p*-value**	0.482
	N	74
FEV1	**r**	-0.239-
	***p*-value**	0.040
	N	74
Age	**r**	-0.137-
	***p*-value**	0.246
	N	74

Comparison between exhaled CO in the smoker COPD and smoker non-COPD groups

Exhaled CO was statistically significantly greater in the smoker COPD group (mean 10.45 ± 3.03) than the smoker non-COPD group (mean 7.05 ± 1.56) with p-value < 0.001 (Table 3).

Comparison between exhaled CO in the mild, moderate, and severe COPD groups

Exhaled CO was increased in the severe COPD group (mean 11.32 ± 3.15) more than mild (9.54 ± 3.32) and moderate (10.44 ± 2.43) COPD but without statistically significant difference p-value 0.122 (Table 4).

There was a negative correlation between exhaled CO and FEV1 p-value 0.04 (Table 5).

Pearson correlation

Sensitivity and specificity of exhaled CO in detection of smokers

The exhaled CO test can differentiate between smokers and nonsmokers with sensitivity 98.9% and specificity 100% at cutoff point 4.5 with p-value < 0.001 (Table 6).

Discussion

Oxidative stress is an important component of airway inflammation in COPD patients. Exhaled CO is a simple and rapid method used to detect and monitor airway inflammation and oxidative stress [10].

In our study, exhaled CO was increased significantly in the smoker group (mean 9.69 ± 3.11) compared to the nonsmoker group (mean 2.19 ± 0.98) with p-value < 0.001, and this was compatible with those of the former study [11]. Minimal exposure to CO may occur during normal daily activity due to environmental pollution, passive smoking, and occupational exposure, and this explains the low level of exhaled CO among non-smokers group [12].

Our results show that cutoff value 4.5 ppm can differentiate smokers from nonsmokers with 98.9% sensitivity and 100% specificity compared to a previous study which found that exhaled CO at ≥ 7 ppm differentiated smokers from nonsmokers with sensitivity 93% and specificity 95% [13].

There is a strong relationship between the smoking habit of a given person and their blood concentration of carboxyhemoglobin (COHb) [14]. Exhaled CO is considered the mirror of COHb, and it is in dynamic equilibrium with COHb [12]. Also, exhaled CO was increased in the smoker COPD group (mean 10.45 ± 3.03) more than the smoker non-COPD group (mean 7.05 ± 1.56) with p-value < 0.001 which is similar to Montuschi et al. (2001) study [15]. This is explained by increased oxidative stress in the COPD group. In our study, exhaled CO was higher in the severe COPD group (mean 11.32 ± 3.15) compared to between the mild (9.54 ± 3.32) and the moderate (10.44 ± 2.43) COPD but without statistically significant difference with p-value 0.122, and there was a negative correlation between exhaled CO and FEV1 with p-value 0.04 which is similar to results of Sivagnaname (2014) study [16], but our results were different from Montuschi et al. (2001) study [15] that found no negative correlation between exhaled CO levels and pulmonary function.

Our study had some limitation including small sample size and single-center location, and so we need further studies in other centers to prove these results.

In conclusion, exhaled CO is a fast, sensitive, noninvasive, and well-established method test that can be used to identify smokers from nonsmokers with 98.9% sensitivity at 4.5 cutoff value. Also, exhaled CO levels in COPD patients vary with different degrees of airway obstruction.

Table 6 Sensitivity and specificity of exhaled CO in detection of smokers

Area under the curve	*p*-value	95% confidence interval		Cut off	Sensitivity %	Specificity %	PPV %	NPV %	Accuracy
		Lower bound	Upper bound						
0.999	< 0.001	0.998	1.001	4.5	98.9	100	100	97.30	99.24

ROC curve for prediction of smokers using CO

Abbreviations

COPD	Chronic obstructive pulmonary disease
FEV1	Forced expiratory volume in 1 s
FVC	Forced vital capacity
Exhaled CO	Carbon monoxide
GOLD	Global Initiative for Chronic Obstructive Lung Diseases

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Authors' contributions
HF, contributed to the conception and the design of the work, drafted the work, and revised it. MH, shared in the acquisition and analysis of data, shared in writing the manuscript, drafted the work, and revised it. MG, shared in writing the manuscript and the design of the work. All authors read and approved the final manuscript.

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Availability of data and materials
The datasets used and/or analyzed during the current study are available from the corresponding author upon reasonable request.

Declarations

Ethics approval and consent to participate
The Ethics Committee of Faculty of Medicine Cairo University approved the study protocol (N-221-2023). The written informed consent was obtained from all the participants.

Consent for publication
Not applicable.

Competing interests
The authors declare that they have no competing interests.

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References

1. Meghji J, Mortimer K, Agusti A et al (2021) Improving lung health in low-income and middle-income countries: from challenges to solutions. Lancet 397(10277):928–940
2. Mathers CD, Loncar D (2006) Projections of global mortality and burden of disease from 2002 to 2030. PLoS Med 3(11):e442
3. Jenkins C, Rodríguez-Roisin R (2009) Quality of life, stage severity and COPD. Eur Respir J 33:953–955
4. Kohansal R, Martinez-Camblor P et al (2009) The natural history of chronic airflow obstruction revisited: an analysis of the Framingham offspring cohort. Am J Respir Crit Care Med 180(1):3–10
5. Vogelmeier CF, Criner GJ, Martinez FJ et al (2017) Global strategy for the diagnosis, management, and prevention of chronic obstructive lung disease 2017 report: GOLD executive summary. Eur Respir J 49:1700214
6. Sato S, Nishimura K, Koyama H et al (2003) Optimal cutoff level of breath carbon monoxide for assessing smoking status in patients with asthma and COPD. Chest 124:1749–1754
7. O'Reilly P, Bailey W (2007) Clinical use of exhaled biomarkers in COPD. Int J Chron Obstruct Pulmon Dis 2:403–408
8. Jarvis MJ, Belcher M, Vesey C, Hutchison DCS (1986) Low cost carbon monoxide monitors in smoking assessment. Thorax 41:886–887
9. Stewart RD, Stewart RS, Stamm W, Seelen RP (1976) Rapid estimation of carbon monoxide level in fire fighters. J Am Med Assoc 235:390–392
10. Repine JE, Bast A, Lankhorst I (1997) Oxidative stress in chronic obstructive pulmonary disease. Oxidative Stress Study Group. Am J Respir Crit Care Med 156:341–357
11 Middleton ET, Morice AH (2000) Breath carbon monoxide as an indication of smoking habit. Chest. 117:758–763
12. Jarvis MJ, Tunstall-Pedoe H, Feyerabend C, Vesey C, Salloojee Y (1984) Biochemical markers of smoke absorption and self-reported exposure to passive smoking. J Epidemiol Commun Health. 38:335–339
13. Nakayama T, Yamamoto A, Ichimura T et al (1998) An optimal cutoff point of expired-air carbon monoxide levels for detecting current smoking: in the case of a Japanese male population whose smoking prevalence was sixty percent. J Epidemiol 8:140–145
14. Jones RH, Ellicott MF, Cadigan JB et al (1958) The relationship between alveolar and blood carbon monoxide concentrations during breath-holding. J Lab Clin Med 51:553–564
15. Montuschi P, Kharitonov SA, Barnes PJ (2001) Exhaled carbon monoxide and nitric oxide in COPD. Chest 120:496–501
16 Sivagnaname Y (2014) Utility of measuring exhaled carbon monoxide (ECO) level in addition to pulmonary function test (spirometry) in the monitoring of chronic obstructive pulmonary disease (COPD). Int J Med Sci Public Health. 3:289–94

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