

# Perspiration During Exercise in Patients With Stable Chronic Obstructive Pulmonary Disease

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## Research article

**Keywords:** COPD pathophysiology, pulmonary physiology, perspiration physiology

**Posted Date:** August 25th, 2020

**DOI:** <https://doi.org/10.21203/rs.3.rs-49970/v1>

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# Abstract

**Background:** Chronic obstructive pulmonary disease (COPD) is a common progressive respiratory condition. Chills in the back region with excessive sweating are common symptoms in COPD patients. The aim of our study was to identify factors associated with increased rates of perspiration in COPD patients.

**Methods:** We performed a prospective cohort study over the course of one year by recruiting 120 COPD patients and 32 healthy controls. All patients underwent pulmonary function testing (PFT) and cardiopulmonary exercise testing (CPET). The rate of perspiration was determined during CPET through sweat collection. The relationship between perspiration rate and multiple clinical and physiologic variables was explored through correlative analyses. Logistic regression analysis was used to reveal the multifactorial influence on the risk of acute COPD exacerbations.

**Results:** Results showed that COPD patients were found to have a higher rate of perspiration during CPET than healthy individuals. We observed a direct relationship between perspiration rate and clinical measures of disease severity such as air flow limitations and the number of acute COPD exacerbations. The rate of perspiration was also found to be correlated with several clinical (i.e. number of hospitalizations) as well as physiologic variables (i.e. PFT and CPET parameters). Lastly, we generated a logistic regression model which predicted the likelihood of acute COPD exacerbations with an accuracy of 87.4%. Thus, elevated perspiration rates during exercise are observed in COPD patients, which is also directly correlated with the degree of dyspnea and disease progression.

**Conclusions:** perspiration may be used as a biomarker for disease state with prognostic value.

## 1. Background

Chronic obstructive pulmonary disease (COPD) is a common progressive respiratory condition [1]. With poorly established pathogenesis, treatments cannot prevent progressive decline in pulmonary function and ultimately lead to poor health outcomes with long-lasting economic impact [2]. Two common, but often disregarded, symptoms frequently reported by COPD patients are chills in the back region with excessive sweating [3]. These findings are supported by reports showing that COPD patients have lower skin temperature than healthy individuals[3]. While the primary function of perspiration is to regulate body temperature, additional roles include the maintenance of metabolic stability, protection from the external environment, and the removal of toxins [4]. In this way, alterations in perspiration may be involved in the pathophysiology of body temperature dysregulation and in the altered sweating in COPD patients. To elucidate the relationship between perspiration and possible associated factors, we performed pulmonary function testing (PFT) and cardiopulmonary exercise testing (CPET) while simultaneously collecting sweat from COPD patients. Alterations in perspiration rates were compared between COPD patients and healthy individuals. We also identified clinical and physiologic variables correlated with perspiration rate in COPD patients. Using perspiration as an objective measure, we

explored autonomic involvement in pulmonary pathophysiology and provide new hypotheses for the pathogenesis of COPD.

## 2. Methods

### 2.1. Patients

As part of this prospective cohort study, we enrolled 120 patients with stable COPD and 32 healthy individuals between May 2015 and May 2016 at the outpatient clinic of the Fourth Affiliated Hospital of Xinjiang Medical University. Healthy individuals were recruited from the community and underwent baseline physical examination performed at our institution.

This study was approved by the ethics committee of Traditional Chinese Medicine Hospital of Xinjiang Uygur Autonomous Region. The ethics committee approval number was 2015XE0113-1. Informed consent was obtained from each subject in writing before any study-specific procedures were conducted.

Inclusion criteria were as follows:

- (1) Meet GOLD2013 COPD diagnostic criteria and COPD stability criteria;
- (2) Age between 45 and 75;
- (3) Capacity to understand the purpose of the study and sign an informed consent form and the will and desire to do so.

Exclusion criteria were as follows:

- (1) Pneumothorax, pleural effusion, lung cancer, active pulmonary tuberculosis, or other serious lung disease;
- (2) Severe cardiovascular, cerebrovascular, hepatorenal, or hematopoietic disease;
- (3) Metabolic disease such as thyroid disease, diabetes, liver, or kidney insufficiency, or adrenal diseases;
- (4) Mental illness;
- (5) Pregnancy or lactation;
- (6) Tumors or congenital or acquired immune deficiency;
- (7) Participation in other clinical trials in the past 1 month;
- (8) Declined to participate;
- (9) Global Initiative for Chronic Obstructive Lung Disease (GOLD) grade of 4.

## 2.2. General information

The following clinical information was recorded from each subject and included in our analysis: age, gender, ethnicity, occupation, height, weight, tobacco and alcohol use, duration of disease, number of acute exacerbation events within the past year, number of hospitalizations within the past year, comorbidities, COPD Assessment Test (CAT) score, Modified Medical Research Council (mMRC) scores, and the GOLD criteria where a numbered grading system (ranging from 1 to 4) was used to quantify the severity of dyspnea and a lettered staging system (ranging from A to D) represented the normalized risk of mortality.

## 2.3. Pulmonary function testing

Spirometry was performed in all subjects using a MasterScreen Pulmonary Function Test (PFT) Breathing Airflow-Flow Rate Meter (Jaeger; CareFusion, Germany). Measurements included in this study are forced expiratory volume in 1 second (FEV1), forced vital capacity (FVC), and FEV1/FVC ratio (FEV1%).

## 2.4. Cardiopulmonary exercise testing

We used the Medgraphics Ultima PFX® pulmonary function/stress testing system with gas exchange to perform CPET. Calibrations of gas, flow, and capacity were performed over approximately ½ hour before the testing. Patients were encouraged to perform maximum tolerable exercise. Exercise stress increments were selected based on patient height, weight, age, baseline fitness, and static lung function.

Physiological variables include in this study are peak work rate, peak O<sub>2</sub> uptake (VO<sub>2peak</sub>), anaerobic threshold (AT), peak heart rate (peak HR), ventilatory equivalent for CO<sub>2</sub> (VE/VCO<sub>2</sub>), VE/VCO<sub>2</sub> slope, oxygen pulse (O<sub>2pulse</sub>), O<sub>2pulse</sub> as a percentage of predicted value (O<sub>2pulse</sub>%pred), and respiratory exchange ratio (RER).

## 2.5. Collection of perspiration

Collection of perspiration was performed as described by Verde et al. using cotton gauze sponges [5]. First, 70% isopropyl alcohol was used to clean the surface of the skin of the patients' backs. Next, sterile tweezers were used to spread the sterile sponge onto the skin from which sweat would be collected. Finally, we covered the gauze with a sterilized plastic pad to prevent the moisture from escaping. Temporary bonding was then applied at the perimeter of the plastic cover to prevent loosening. The gauze was weighed both before and after CPET to determine the rate of perspiration (scale model: SI-203, Denver Instruments, d = 0.001 g). Our method was less subject to contamination by sweat from adjacent regions than other methods are. The location from which sweat was collected was selected based on a previous study [6]. CPET was performed at an ambient temperature of 25 °C, relative humidity of 50%, and wind speed of less than 2 meters per second. The maximum sweating rate in the upper, middle, and lower back reached 1197, 1145, and 856 g/(m<sup>2</sup>•h), respectively. The upper back collection site was 10 cm across the midline beginning superiorly at the seventh cervical vertebra and extends 20 cm inferiorly (Fig. 1).

## 2.6. Measurement of the rate of perspiration

Perspiration rates were calculated using previously reported methods [7]. The rate of perspiration was measured as the mass of water per unit area per unit time  $w_s = (w_{\text{post}} - w_{\text{pre}}) / (t \times s)$ . Through cardiopulmonary exercise testing, we were able to calculate the total work (Joules) performed by the subject during exercise. As a result, the rate of perspiration may be determined for every unit of work ( $\text{g}/(\text{m}^2 \cdot \text{J})$ ) as calculated by the weight gain of the sweat-absorbent gauze divided by work. Our formula achieves greater accuracy in estimating perspiration per unit of work than previously reported formulas.

## 2.7. Statistical methods

We used the Excel software package to establish a database of COPD patients and healthy individuals. All data were subsequently entered into the SPSS 19.0 statistical software (IBM Corp., Armonk, New York, US) for analysis. All statistical values are expressed as mean  $\pm$  standard deviation. Inter-group comparisons were made using the T-test or one-way analysis of variance (ANOVA). Pearson and Spearman's coefficients were calculated for correlation analyses. Logistic regression was used to model the probability of developing an acute exacerbation using clinical and physiologic variables. Statistical significance is defined as  $P < 0.05$ .

## 3. Results

### 3.1. Patients

Our study enrolled a total of 120 COPD patients (80 male, 40 female) with a mean age of  $60.72 \pm 7.88$  years and body mass index (BMI) of  $26.16 \pm 3.31 \text{ kg}/\text{m}^2$ . No differences were observed when the COPD group was compared to the control group of 32 healthy control patients (18 male, 14 female,  $P = 0.187$ ) with a mean age of  $57.72 \pm 9.65$  years ( $P = 0.071$ ) and BMI of  $25.25 \pm 3.12 \text{ kg}/\text{m}^2$  ( $P = 0.165$ , Table 1).

Table 1  
Patient demographics

Variable	COPD group	Health controls	Summary statistic	<i>P</i>	
Gender	Male	80	18	$\chi^2 = 1.197$	0.274
	Female	40	14		
Age (years)	$60.72 \pm 7.88$	$57.72 \pm 9.65$	$t = -1.821$	0.071	
BMI ( $\text{kg}/\text{m}^2$ )	$26.16 \pm 3.31$	$25.25 \pm 3.12$	$t = -1.395$	0.165	
COPD = Chronic obstructive pulmonary disease; BMI = body mass index.					

We first compared the rate of perspiration across all patient groups. The perspiration rate of COPD patients exceeded that control patients ( $P < 0.001$ , Table 2, Fig. 2). The COPD patients were stratified based on the degree of airflow limitation (GOLD grades, Table 3)[8] and inter-group differences in perspiration were compared. No differences were observed between patients with mild airflow limitations (GOLD 1) and healthy controls ( $P = 0.496$ ). The perspiration rate of GOLD 2 patients exceeded those of healthy controls ( $P < 0.001$ ) but was lower than those of GOLD 3 patients ( $P < 0.001$ ), whose perspiration rates were higher than those of GOLD 1 patients ( $P < 0.001$ , Table 3). Furthermore, after stratifying COPD patients by GOLD grades (scaled from A to D), which predicts mortality risk, we found significantly elevated perspiration during exercise in COPD patients with GOLD grades C and D (Table 4). These observations suggest a direct correlation between perspiration rate and airflow limitation across our patient population.

Table 2  
Comparison of perspiration rates

Patient group	<i>n</i> =	Perspiration rate (g/m <sup>2</sup> ·J)	<i>t</i>	<i>P</i>
COPD group	117	3.29 ± 2.04	-5.721	0.000
Control group	31	1.89 ± 0.88		
COPD = Chronic obstructive pulmonary disease.				

Table 3  
Perspiration rates in COPD patients stratified by airflow limitation

Grade of airflow limitation	<i>n</i> =	Perspiration rate	<i>F</i>	<i>P</i>
Health controls	31	1.89 ± 0.88#	21.55	0.000
GOLD1	45	2.34 ± 1.53#		
GOLD2	50	3.28 ± 1.59**#		
GOLD3	22	4.69 ± 1.09**		
**Comparison to healthy controls ( $P < 0.01$ ), #Comparison to GOLD 3 patients ( $P < 0.01$ ). COPD = Chronic obstructive pulmonary disease; GOLD = Global Initiative for Chronic Obstructive Lung Disease.				

Table 4

Perspiration rates in COPD patients stratified by severity of symptoms and acute exacerbations

GOLD stage	n=	Perspiration rate	F	P
Healthy controls	31	1.89 ± 0.88	10.831	0.000
A	16	1.71 ± 1.17		
B	14	2.73 ± 1.45		
C	25	3.27 ± 1.66**#		
D	62	3.65 ± 1.67**##		
** Comparison to healthy controls ( $P < 0.01$ )				
# Comparison to GOLD stage A group ( $P < 0.05$ )				
## Comparison to GOLD stage A group ( $P < 0.01$ )				
Patients were stratified based on the 2017 Global Initiative for Chronic Obstructive Lung Disease guidelines. COPD patients were divided into four groups: A, B, C, and D. Perspiration rates were assessed across groups and in healthy patients. GOLD C and D patients showed significantly higher perspiration rates ( $P = 0.006$ and $P = 0.000$ ) than healthy controls and GOLD A patients ( $P = 0.011$ and $P = 0.000$ ). COPD = Chronic obstructive pulmonary disease; GOLD = Global Initiative for Chronic Obstructive Lung Disease.				

## 3.2. Clinical and physiologic variables related to the rate of perspiration

To assess correlations between the rate of sweating and disease severity in COPD patients, we determined the relationship between the rate of perspiration and various clinical and physiologic variables such as smoking index, disease course, mMRC score, CAT score, pulmonary function (FEV1%, FVC%, and FEV1/FVC), and CPET variables. In terms of clinical variables, positive correlations were observed between perspiration rate and the mMRC score ( $r = 0.331$ ,  $P < 0.001$ ), number of acute COPD exacerbations ( $r = 0.207$ ,  $P = 0.029$ ), number of hospitalizations within the past year ( $r = 0.395$ ,  $P = 0.000$ ). PFT variables such as FEV1% ( $r = -0.410$ ,  $P < 0.001$ ), FVC% ( $r = -0.375$ ,  $P < 0.001$ ), and FEV1/FVC ( $r = -0.378$ ,  $P < 0.001$ ) were negatively correlated with perspiration rate. While such CPET variables as peak work rate ( $r = -0.462$ ,  $P < 0.001$ ), maximum ventilatory flow ( $r = -0.188$ ,  $P = 0.048$ ), and peak oxygen uptake per kilogram of body weight ( $r = -0.258$ ,  $P = 0.006$ ) were negatively correlated, ventilatory CO<sub>2</sub> equivalent ( $r = 0.198$ ,  $P = 0.038$ ) and physiological dead space ( $r = 0.279$ ,  $P = 0.003$ ) were positively correlated with perspiration rate (Table 5).

Table 5  
Correlation between perspiration rate and relevant factors in COPD patients

Factor	<i>r</i>	<i>P</i>
Disease course	0.104	0.280
Smoking index	0.091	0.343
Number of acute exacerbations within the past one year	0.207	0.029*
Number of hospitalizations within the past one year	0.395	0.000**
mMRC (Modified Medical Research Council) Dyspnea Scale	0.331	0.000**
CAT (COPD Assessment Test)	0.010	0.916
<b>Pulmonary function test (PFT)</b>		
Forced expiratory volume in 1 second (FEV1)	-0.410	0.000**
Forced vital capacity (FVC)	-0.375	0.000**
FEV1/FVC (FEV1%)	-0.378	0.000**
<b>Cardiopulmonary exercise function (CPET)</b>		
Peak work rate	-0.462	0.000**
Peak tidal volume	0.066	0.489
Maximum voluntary ventilation	-0.188	0.048*
Peak oxygen uptake per kilogram of body weight	-0.258	0.006**
Peak oxygen uptake (VO <sub>2</sub> )	-0.186	0.050
Anaerobic threshold	0.099	0.303
Peak oxygen pulse	-0.127	0.184
Ventilatory equivalent for carbon dioxide (VEqCO <sub>2</sub> )	0.198	0.038*
Ventilatory equivalent for oxygen (VEqO <sub>2</sub> )	0.117	0.223
Expiratory reserve volume	0.168	0.079
Heart rate reserve	0.145	0.129
Physiological dead space	0.279	0.003**
* <i>P</i> < 0.05, ** <i>P</i> < 0.01. COPD = Chronic obstructive pulmonary disease; <i>r</i> = Modified Medical Research Council (mMRC) scores.		

### 3.3. Risk of acute COPD exacerbations

We used logistic regression analysis to model the risk of acute exacerbations (Y) based on multiple independent variables (X) including age, BMI, smoking index, disease course, mMRC, CAT, PFT variables, and perspiration rate (Table 6). The resulting model, in which *R* is the rate of perspiration, can predict the rate likelihood of acute COPD exacerbations with an accuracy of 87.4%.

Table 6  
Logistic regression model of acute exacerbation risk in COPD patients

Influencing factor	B	SE	Wals	P	OR	95% CI	
						Upper limit	Lower limit
Constant	0.482	0.595	0.656	0.418	1.619		
Perspiration rate	0.550	0.234	5.557	0.018	1.734	1.097	2.740

COPD = Chronic obstructive pulmonary disease.

## 4. Discussion

The primary function of perspiration is regulation of body temperature mediated by sympathetic drive, which also leads to vasodilation and tachypnea, resulting in rapid heat dissipation to maintain homeostasis [9]. Other roles of perspiration include the excretion of toxins [10], maintenance of electrolyte balance, and control of microbial growth through antibacterial peptides [11]. Our study investigates excessive perspiration, an often-neglected symptom of COPD, through objective measures and we explored its association to varying severities of COPD pulmonary dysfunction. While the causal relationship between COPD and perspiration remains unclear, we offer multiple explanations that might provide insight into their correlation.

In this study, we found there to be significantly more perspiration during exercise in COPD patients than in healthy individuals. Furthermore, perspiration rates increased with worsening ventilatory dysfunction. One possible mechanism involves elevated sympathetic excitability, which is an autonomic response driven by hypoxia and/or CO<sub>2</sub> retention [12, 13]. Basal metabolism may also contribute to altered perspiration as evidenced by the high correlation between the basal metabolic rate and perspiration rate [7]. The basal metabolic rate in COPD patients is significantly elevated, an observation attributed to catabolic/anabolic imbalance through catabolic hyperactivity [14]. The basal metabolic rate in COPD patients is approximately 10% higher than that of healthy individuals [15]. As airway resistance increases in COPD, oxygen consumption will be further elevated due to respiratory muscle load and so result in higher levels of metabolic demand at rest and during exercise [16, 17].

COPD patients expend more energy during exercise than healthy individuals [18], and this may contribute to increased perspiration. CPET measurements reflect both cardiopulmonary physiology and metabolic consumption [19, 20], which are inferred from such variables as peak per-kilogram O<sub>2</sub> uptake, CO<sub>2</sub> ventilation, and metabolic equivalents. We propose perspiration may serve as a proxy for metabolism.

This is supported by the observation that increased severity of COPD is associated with higher levels of perspiration.

Some common medications indicated for COPD can significantly increase resting oxygen consumption, resulting in an elevated basal metabolic rate [21]. Theophylline and  $\beta$ 2-receptor agonists may synergistically increase oxygen consumption, resulting in increased metabolic rates [21]. However, these bronchodilators also reduce airway resistance, leading to a reduction in resting oxygen consumption. The long-term effects of these COPD medications on basal metabolism have yet to be reconciled [22, 23].

In this study, we found perspiration rate in COPD patients to be closely correlated with multiple CPET variables such as peak work rate, maximum voluntary ventilation, peak  $O_2$  uptake,  $CO_2$  ventilatory equivalent, and physiological dead space. The peak work rate reflects the patient's exercise tolerance, the maximum voluntary ventilation reflects a patient's ventilation capacity, and the  $CO_2$  ventilatory equivalent is a normalized indicator of a patient's ventilatory ability. When combined, these parameters can be used to assess pulmonary function with high reproducibility and accuracy and so facilitate objective comparisons between subjects [24, 25]. Based on previous reports,  $CO_2$  ventilatory equivalent is an indicator for early mortality assessment in patients with COPD [26–28]. For these reasons, the rate of perspiration in COPD patients may even have prognostic value.

While perspiration rate has been found to be correlated with age and BMI [29], we did not here observe such a correlation. Our results instead show the severity of dyspnea (mMRC) and ventilation dysfunction to be correlated with increased rates of perspiration in COPD patients. Additionally, the increased perspiration rate in COPD patients may be a marker of worsening lung function, increasing the severity of clinical symptoms and decreasing quality of life. The increased perspiration rate in patients with COPD may not only be a manifestation of clinical symptoms, but also can be served as an indicator of disease progression.

Our study has several limitations. The site of perspiration measurement was well-defined and placed consistently across subjects. However, all parts of the body perspire during exercise and regional contributions may differ from those produced by the back. Collecting sweat from other body parts of the body may further support our claim that altered perspiration is related to systemic autonomic dysfunction. While our perspiration measurements were made during exercise, evaluating perspiration at rest can exclude the possibility that perspiration dysfunction is linked to levels of physical activity. This may be performed through a clinical symptom survey or through measurement of perspiration during recovery phases after exercise testing. Lastly, our claims relating perspiration to severity of COPD are made from correlation, not causation. While multiple theories have been proposed, elucidating these mechanisms will require well-designed studies at the clinical and experimental levels.

## 5. Conclusion

In this prospective cohort study, we measured perspiration during exercise using well-controlled measures for sweat collection and cardiopulmonary testing. We found the rate of perspiration to be significantly higher in COPD patients than in healthy individuals. Additionally, the degree of elevation of perspiration is directly correlated with the degree of dyspnea and the severity of disease. Furthermore, by combining multiple parameters measured in this study, we were able to predict the risk of future COPD acute exacerbations with high accuracy. While the precise mechanism underlying the increased perspiration in COPD is unknown, and objective characterization of perspiration may be used as a low-cost, clinically relevant indicator of prognosis and a biomarker of disease progression.

## Abbreviations

analysis of variance (ANOVA)

anaerobic threshold (AT)

body mass index (BMI)

Chronic obstructive pulmonary disease (COPD)

cardiopulmonary exercise testing (CPET)

COPD Assessment Test (CAT)

forced expiratory volume in 1 second (FEV1)

FEV1/FVC ratio (FEV1%)

forced vital capacity (FVC)

Global Initiative for Chronic Obstructive Lung Disease (GOLD)

Modified Medical Research Council (mMRC)

oxygen pulse (O<sub>2</sub>pulse)

O<sub>2</sub>pulse as a percentage of predicted value (O<sub>2</sub>pulse%pred)

peak heart rate (peak HR)

pulmonary function testing (PFT)

respiratory exchange ratio (RER)

ventilatory equivalent for CO<sub>2</sub> (VE/VCO<sub>2</sub>)

peak O<sub>2</sub> uptake (VO<sub>2</sub>peak)

# Declarations

## Ethics approval and consent to participate

This study was approved by the ethics committee of Traditional Chinese Medicine Hospital of Xinjiang Uygur Autonomous Region. The ethics committee approval number was 2015XE0113-1. Informed consent was obtained from each subject in writing before any study-specific procedures were conducted.

## Consent for publication

Informed consent was obtained from each subject in writing before any study-specific procedures were conducted.

## Availability of data and materials

The datasets used and/or analyzed during the current study are available from the corresponding author on reasonable request.

## Competing interests

The authors declare that they have no competing interests.

## Funding

This study was funded by Natural Science Foundation of China (Grand No. 81660739), Special Scientific Research Project of National Clinical Research Base of Traditional Chinese Medicine (Grand No. JDZX2015239) and Project of Capacity for the Prevention and Treatment of Major Difficult Diseases of Traditional Chinese Medicine (Grand No. 201502).

## Authors' contributions

All authors made substantial contributions to conception and design, or acquisition of data, or analysis and interpretation of data; Zheng Li and Yanxin Zhang involved in drafting the manuscript and revising it critically for important intellectual content; Fengsen Li gave final approval to the version to be published. All authors read and approved the final manuscript.

## Acknowledgements

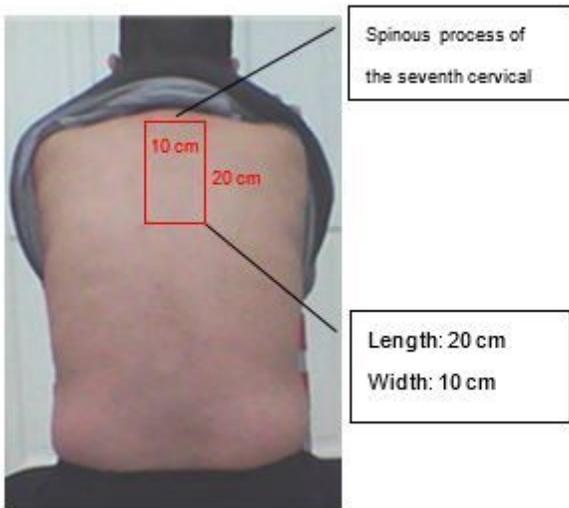
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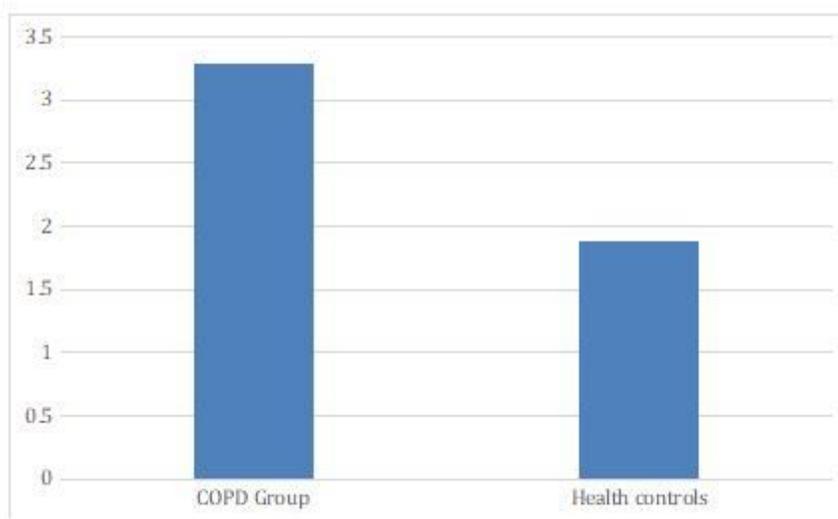
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## Figures



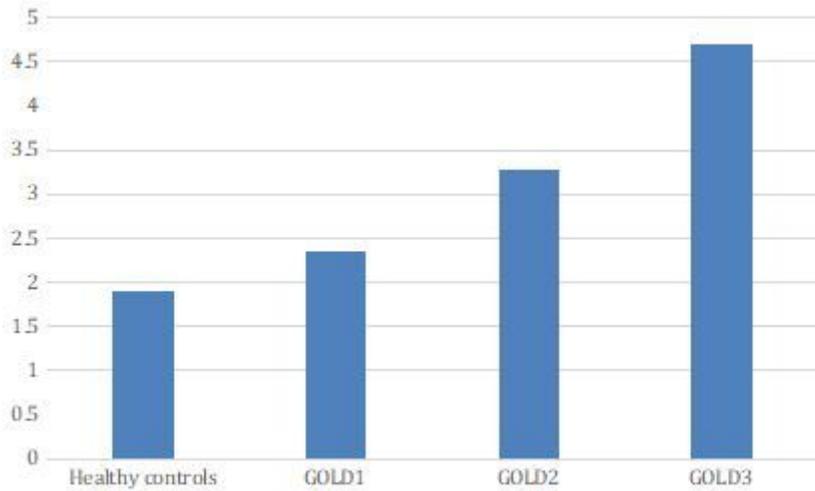
**Figure 1**

Area of skin surface from which perspiration is collected.



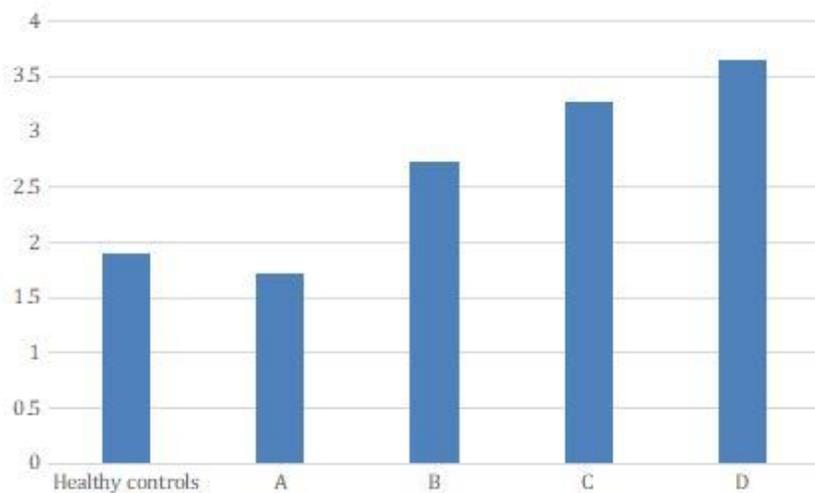
**Figure 2**

Comparison of the rate of perspiration between COPD patients and healthy controls.



**Figure 3**

Comparison of sweating rates among COPD patients stratified by airflow limitations.



**Figure 4**

Comparison of sweating rates among COPD patients stratified by severity of symptoms and acute exacerbations.

## Supplementary Files

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