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## Original Article

## Metabolic syndrome impact on pulmonary function of women

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## ABSTRACT

**Background:** The presence of metabolic syndrome (MetS) and its components may induce structural and physiological changes that exacerbate the impairment of the respiratory function. The aim of the study is to evaluate the impact of metabolic syndrome and its components on lung function in women.

**Methods:** This is cross-sectional study. A total of 121 women aged 20–75 years were assisted in two primary health centers of Brazil. These women were divided into two groups according to the presence of metabolic syndrome. Waist circumference and blood pressure measurements, high density low-cholesterol (HDL-c) and triglycerides analysis and pulmonary function tests by spirometry were performed.

**Results:** Metabolic syndrome prevalence was 46.3%. Systemic arterial pressure (BP) and waist circumference (WC) were identified with higher eigenvalues in the main components explaining 26.78% of the variance. The multiple regression analysis showed an inverse relationship between forced expiratory volume in the first second predicted (FEV<sub>1</sub>) ( $\beta = -6.0$ ,  $p = 0.03$ ) and predicted forced vital capacity (FVC %) ( $\beta = -7.02$ ,  $p = 0.004$ ) with the presence of MetS. PA ( $\beta = -8.50$ ,  $p = 0.003$ ) and WC ( $\beta = -0.24$ ,  $p = 0.001$ ) it presented an inverse relationship with FVC% when was adjusted for age, smoking history, menopausal BMI.

**Conclusions:** WC and PA were considered the parameters most related to MetS by principals components analysis. The diagnosis of MetS presented an inverse relation with the spirometrics parameters. Elevation of BP and WC were the predictors of the CFV% reduction.

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## 1. Introduction

Metabolic syndrome comprises a set of associated cardiovascular risk factors, involving obesity, elevated systemic blood pressure, hyperglycemia and dyslipidemia [1]. Obesity is considered the main factor to contribute to the inflammatory response barrier offers meconium for respiration, lipid deposition and smooth muscle hyperplasia of the airways, this can culminate in reduced functional capacity [2,3]. In women, the presence of the metabolic syndrome is influenced by the number of pregnancies, gestational diabetes, pre-eclampsia and menopause [4]. Low income, too, this factor has a link with this clinical condition [5]. There is evidence

that intravascular atherosclerotic obstruction occurring in metabolic syndrome is related to the components of it [6].

The damage occurs in pulmonary function, both obstructive and restrictive, it is associated with several clinical conditions such as chronic lung disease, obesity, diarrhea, hypertension, heart disease and menopausal in women [7,8]. The mechanisms of dysfunction have not yet been clarified, however, obesity seems to be the risk factor that triggers the changes, because of the inflammatory response activation [9,10] and arterial hypertension influences the respiratory function by remodeling the left ventricle which suffers and may interfere with vascular flow for pulmonary gas exchange, especially in women [7].

In pulmonary function, the damages associated with metabolic syndrome occur due to by bronchial hyperreactivity [11,12] leading to airflow obstruction, reduction of functional residual capacity (FRC) and, consequently, changes in ventilation perfusion (V/Q)

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ratio, with the reduction of tidal volume in the pulmonary base predisposing to alveolar collapse and reduction of tissue oxygenation [9]. The mechanical changes caused by obesity contribute to the restrictive pattern and are related to reduction in the amplitude of the diaphragm during respiration and because of the decline in the amount and type of fibers recruited. The clinical consequences are reduction of strength and respiratory muscle endurance generating muscle fatigue [13] and in extreme conditions acute respiratory failure.

The metabolic syndrome components may influence lung function, but there are issues to be clarified, such as the type of ventilatory disorder that occurs most frequently and the pathways in which the changes in lung function happen. Thus, the present study aimed to evaluate the impact of metabolic syndrome and its components on the pulmonary function of women.

## 2. Materials and methods

### 2.1. Sample

The cross-sectional study was carried out in Goiânia city, Goiás, Brazil from January to November 2015 with women. They were assisted in two units of the Family Health Strategy (FHS), the primary health care center. 131 women aged 20–75 years, recruited by convenience, accepted to participate and 121 women were evaluated at all stages. They all were older than 18 years and were enrolled in FHS (Fig. 1). Participants with cardiovascular disease (infarct in the last six months, unstable angina, cardiac arrhythmia and history of stroke), clinical diagnosis of chronic pulmonary disease (chronic obstructive pulmonary disease, asthma, bronchiectasis) and who were unable to communicate in a comprehensible form.

The sample calculation was based on GPower software (version 3.0, Dusseldorf, Germany), considering a sample power of 80%, alpha of 5%, mean the prevalence of airflow obstruction or restrictive pattern found in the literature between 23 and 45% [14–16], requiring 119 women. They signed the consent form approved by the Ethics and Research Committee on Humans of the Federal University of Goiás. Protocol number is 784.446/2014.

### 2.2. Study design

The data were collected every morning in the two health posts of the FHS. The participants were interviewed for eligibility, signing informed consent, and for lifestyle information (history of smoking, comorbidities, drug use) and socio-demographic characteristics. After inclusion, blood samples were performed for fasting blood glucose and lipid profile measurements. The anthropometric (body mass, height and waist circumference) and blood pressure measurements (systolic blood pressure and diastolic blood pressure) were performed in a reserved room. The spirometrics tests (forced vital capacity - FVC, forced expiratory volume in the first second - FEV<sub>1</sub> and FEV<sub>1</sub>/FCV) were previously scheduled according to the availability of the women since their execution depends on the learning, sometimes lasting for an average of 35 min.

### 2.3. Blood sample

Venous blood samples (approximately 5 mL) for serum low-density lipoprotein cholesterol (HDL-c), triglycerides, and fasting glycemia were collected in the first morning by laboratory technicians responsible for the analysis following biosafety procedures after 8 h of fasting. The blood was centrifuged at 3000 g for 10 min

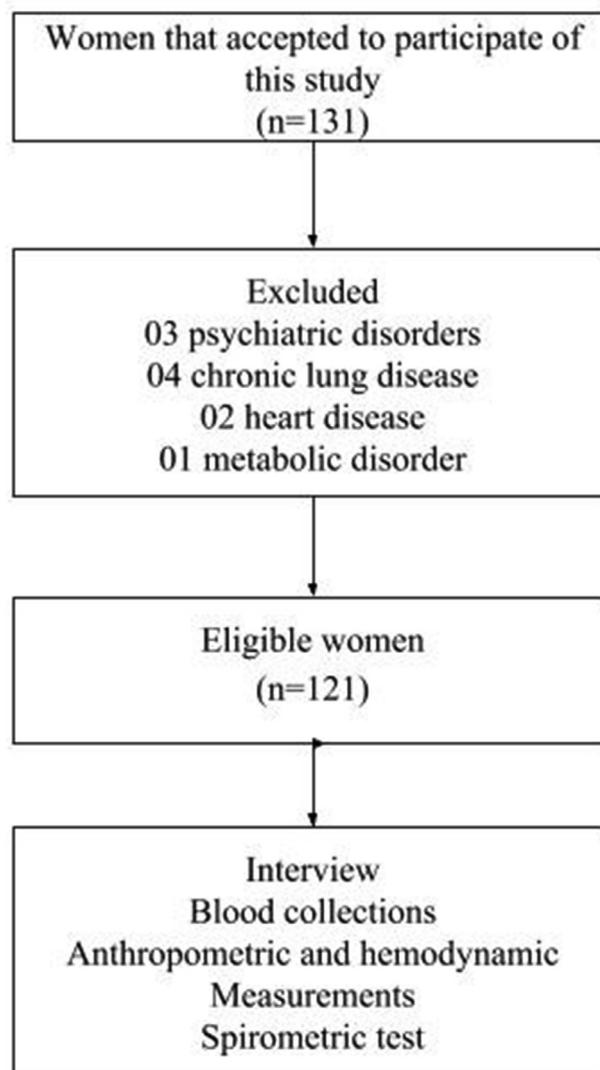


Fig. 1. Selection of women for inclusion in the study.

and the analysis was performed until 1 h after the collection by an autoanalyzer (Cobas Integra 400, Roche Diagnostics) by the enzymatic-calorimetric method.

### 2.4. Anthropometry measurements

The body mass was obtained in electronic scale (Toledo, model 2096PP) with automatic calibration and capacity of up to 150 kg (kg). The women remained barefoot and dressed in light clothing. The stature was recorded in centimeters (cm) by means of a stadiometer (Sanny, Caprice model, São Paulo, Brazil) the precision scale was 35–200 cm. Participants remained in the upright position and with upper limbs peddling along the body. Subsequently, the body mass index (BMI) was calculated by the ratio between body mass (kg) and height squared (m<sup>2</sup>). Waist circumflex (WC) was measured in centimeters with an inextensible tape measure (Seca, model 201, São Paulo, Brazil) at the midpoint between the last rib (12th rib) and the iliac crest.

## 2.5. Blood pressure

Systemic blood pressure was measured using an automatic arm monitor (Omron, model HEM-7113, São Paulo, Brazil). The women remained seated with their legs uncrossed, feet resting on the ground, backs remembered in the chair and relaxed for 5 min in a quiet environment. The upper limb remained propped up, with the palm of the hand facing up and the elbow slightly flexed. The cuff was positioned 2–3 cm above the cubital fossa without leaving clearances. Three measurements were taken at 5-min intervals and the mean was used for analysis [17].

## 2.6. Pulmonary function

Spirometry was performed with a portable spirometer (Cosmed, Micro Quark model, Roam, Italy) according to the guidelines of the American Thoracic Society/European Respiratory Society [18]. The FVC was performed with seated and clipped women, from maximum inspiration to total lung capacity (TLC) followed by an inspiratory pause and forced expiration lasting at least 6 s. Each participant performed up to eight maneuvers and two acceptable and reproducible ones were considered for analysis. The results of the tests were reproducible if the differences between the maneuvers were less than 5% or 0.15 L for FVC and FEV<sub>1</sub>. The relationship between FEV<sub>1</sub> and FVC were calculated. The losses in pulmonary function were defined when FEV<sub>1</sub> and FVC had values below the lower limit (LL) of 70% [19]. Ventilatory patterns were defined taking into account the obstructive component FEV<sub>1</sub> and FEV<sub>1</sub>/FVC < LL and the restrictive component with FVC < LL. When the two changes were present it was classified as mixed ventilatory disorder. The reference values for the Brazilian population were obtained by the equations below [20]:

$$\begin{aligned} \text{FVC} &= \text{height (m)} * 0.0433 - \text{age (years)} * 0.0164 - 2.967 \\ \text{FEV}_1 &= \text{height (m)} * 0.0338 - \text{age (years)} * 0.0210 - 1.782 \end{aligned}$$

## 2.7. Diagnosis of metabolic syndrome

For the diagnosis of metabolic syndrome, the harmonization document published by the International Diabetes Federation (IDF) and American Heart Association/National Heart, Lung and Blood Institute (AHA/NHLBI) [1], including the presence of three of the five risk factors. Elevated waist circumference ( $\geq 90$  mg/dL or under treatment), increase in serum triglyceride concentration ( $\geq 150$  mg/dL), reduction of high-density lipoprotein cholesterol (HDL-c) ( $< 50$  mg/dL or under treatment), high systemic blood pressure (systolic blood pressure  $\geq 130$  mmHg and/or diastolic blood pressure  $\geq 85$  mmHg or under treatment) and high fasting glycemia ( $\geq 100$  mg/dL or under treatment) [1]. To analyze were classified two groups: with and without metabolic syndrome.

## 2.8. Data analysis

Data were expressed as mean, standard deviation and confidence intervals. The Kolmogorov-Smirnov or Shapiro-Wilk test were used to verify the distribution of the data. To compare the groups, t-student test was used for independent samples and calculated the effect size of Cohen (d). Principal components analysis was used to identify the variable or group of metabolic syndrome variables that could be used in prediction models and the load considered was  $\geq 0.40$ . The multiple linear regression models, stepwise method, were used to establish the relationship between spirometric parameters, %FEV<sub>1</sub> and %FVC (dependent variables) with the presence of metabolic syndrome and its components

(independent variables). The value considered for p was  $< 0.05$ . Data were analyzed in Statistical Package Social Science (SPSS, version 21.0).

## 3. Results

### 3.1. Prevalence of metabolic syndrome and socio-demographic profile

The prevalence of metabolic syndrome was 46.3% (56 with and 65 without metabolic syndrome) and the baseline characteristics are presented in Table 1. Of the total number of women evaluated with MetS, 55 (98.2%) had WC measurements above predicted to be overweight/obese, 33 (58.9%) dyslipidemias characterized by increased triglycerides and HDL-c below predicted in 52 (92.9%). In the group without MetS, the most prevalent components were elevated WC in 46 (70.8%) and low HDL-c in 45 (69.2%) of the women. The HR (d = 0.99) and the BP (d = 0.80) had the largest effect size, whereas, for respiratory function, the parameters FEV<sub>1</sub>, FVC and %FVC predicted had a mean effect size (0.40–0.70) (Table 1).

The chi-square test showed an association between the presence of metabolic syndrome and ventilatory disorders (p = 0.02). In the MetS group, 24 (42.9%) women with obstructive component, 07 (12.5%) mixed component, and 25 (44.6%) normal spirometry. In the group without metabolic syndrome, 23 (35.4%) were characterized with obstruction, 01 (1.5%) mixed, and 41 (63.1%) spirometry within the predicted for age.

### 3.2. Predictors of principals components of metabolic syndrome

The principal components analysis identified two factors and their respective loads (Table 2). Factor 1 included glycemia, triglycerides, and low HDL-c, while factor 2 included both WC and blood pressure. No variables were loaded in more than one factor and the two together explained 56.77% of the variance.

### 3.3. Components of metabolic syndrome as predictor of pulmonary function

Multiple regression analysis showed an inverse relationship between %FEV<sub>1</sub> (p = 0.03) and %FVC (p = 0.004) with the presence of MetS. PA (p = 0.003) and WC (p = 0.001) when adjusted only for age presented an inverse relation with %FVC. It also occurred when the history of smoking, the presence of menopause and BMI were added to the regression models (Table 3).

## 4. Discussion

The results from this study support that almost half of the women had a diagnosis of metabolic syndrome. In the categorical evaluation without the presence of adjustment variables obstructive ventilatory disorder was common in women. In the logistic regression models, the presence of metabolic syndrome and components, waist circumference and elevated systemic blood pressure were the components that indicated the reduction of forced vital capacity in the women evaluated. The loss of lung function has been associated with the metabolic syndrome and its components, mainly with obese obesity, it is the factor for triggering other clinical conditions that lead to an increase in the risk of cardiac event and mortality rate [21–23].

The mechanisms by which the metabolic syndrome induces the reduction of lung function are still not well understood since there are studies wherein the disorders manifest themselves as an obstructive component [14,15] and others including the prevalence

**Table 1**  
Baseline characteristics and women lung function according to the presence of the metabolic syndrome (MetS).

Baseline characteristics	Total (n = 121)	Without MetS (n = 65)	With MetS (n = 56)	d	p-value <sup>a</sup>
Age (years)	47.90 (12.90)	45.12 (13.80)	51.11 (10.90)	0.48	0.01
Body mass index (kg/m <sup>2</sup> )	32.40 (6.80)	29.74 (4.80)	35.46 (7.50)	0.92	<0.001
Diabetes Mellitus (n, %)	32 (26.40)	02 (3.10)	30 (53.60)	–	<0.001
Hypertension (n, %)	28 (23.10)	04 (6.20)	24 (42.90)	–	<0.001
Ex-smoker (n, %)	34 (28.10)	19 (29.20)	15 (26.80)	–	0.77
Menopause (n, %)	57 (47.10)	23 (35.40)	34 (60.70)	–	0.005
Waist circumference (cm)	96.40 (16.60)	89.40 (12.90)	104.00 (16.70)	0.99	<0.001
Systolic blood pressure (mmHg)	119.60 (18.10)	114.30 (10.00)	125.80 (22.90)	0.67	0.001
Diastolic blood pressure (mmHg)	78.00 (11.40)	74.10 (9.10)	82.60 (12.20)	0.80	<0.001
HDL-c (mg/dL)	43.50 (10.30)	45.50 (10.00)	41.10 (10.30)	0.44	0.02
Triglycerides (mg/dL)	137.10 (64.50)	107.90 (44.90)	170.90 (67.50)	1.11	<0.001
Glycemia (mg/dL)	100.50 (54.00)	86.70 (37.90)	116.50 (64.90)	0.57	0.003
Pulmonary function					
FEV <sub>1</sub> (L)	2.40 (0.50)	2.50 (0.50)	2.20 (0.50)	0.52	0.006
FEV <sub>1</sub> (% of predicted)	91.30 (115.80)	97.00 (17.30)	94.00 (15.10)	0.19	0.28
FVC (L)	2.90 (0.50)	3.10 (0.50)	2.70 (0.50)	0.66	<0.001
FVC (% of predicted)	91.90 (13.30)	98.60 (13.20)	93.20 (14.20)	0.40	0.03
FEV <sub>1</sub> /FVC (%)	81.80 (12.30)	81.50 (9.00)	82.60 (8.00)	0.12	0.50

Note. Data presented as mean (standard deviation) or frequency (%). d effect size - Cohen's test; FEV<sub>1</sub>, forced expiratory volume in the first second; FVC, forced vital capacity. Data to p < 0.05.

**Table 2**  
The main components analysis of metabolic syndrome factors (n = 121).

	Factor 1 <sup>a</sup> (HDL-c, Triglycerides, glycemia)	Factor 2 (WC e BP)
High Waist Circumference	0.27	0.74
High blood pressure	–0.21	0.84
HDL-c low	0.58	0.07
High triglycerides	0.67	0.29
Elevated glycemia	0.77	–0.03
Eigenvalues	1.50	1.34
Total variance (%)	29.99	26.78
Cumulative variance (%)	29.99	56.77

HDL-c, high density lipoprotein-cholesterol; WC, waist circumference; BP, systemic blood pressure. <sup>a</sup>Considered factor load  $\geq 0.4$ .

**Table 3**  
Multiple linear regression coefficients of the metabolic syndrome and individual components according to the percentage of predicted FVC and FEV<sub>1</sub> (n = 121).

		FEV <sub>1</sub> predicted (%)		FVC predicted (%)	
		$\beta$ (IC 95%)	<sup>a</sup> p-value	$\beta$ (IC 95%)	<sup>a</sup> p-value
Syndrome Metabolic	M1	–6.6 (–11.90, –0.50)	0.03	–7.04 (–11.74, –2.34)	0.004
	M2	–6.0 (–11.80, –0.22)	0.04	–7.02 (–11.78, –2.26)	0.004
Waist circumference	M1	–0.14 (–0.31, 0.03)	0.12	–0.24 (–0.37, –0.10)	0.001
	M2	–0.13 (–0.30, 0.04)	0.13	–0.24 (–0.37, –0.10)	0.001
Triglycerides	M1	–0.04 (–0.08, 0.01)	0.08	–0.03 (–0.06, 0.01)	0.17
	M2	–0.04 (–0.08, 0.01)	0.08	–0.03 (–0.06, 0.01)	0.17
HDL-c	M1	0.10 (–0.21, 0.35)	0.64	0.12 (–0.08, 0.37)	0.25
	M2	0.08 (–0.20, 0.36)	0.58	0.14 (–0.09, 0.38)	0.23
Blood pressure	M1	–6.45 (–13.10, 0.16)	0.06	–8.40 (–13.81, –3.00)	0.003
	M2	–6.29 (–13.00, 0.42)	0.07	–8.50 (–13.96, –3.03)	0.003
Fasting glycemia	M1	–0.03 (–0.09, 0.02)	0.22	–0.03 (–0.07, 0.02)	0.26
	M2	–0.03 (0.09, 0.02)	0.24	–0.03 (–0.08, 0.02)	0.22

FEV<sub>1</sub>, expired forced expiratory in the first second; FVC, forced vital capacity. Model 1 (M1): adjusted for age; Model 2 (M2): adjusted for model 1, smoking, menopause and BMI (except WC). Data to p < 0.05.

is the restrictive disorders [24]. The results of the present study are similar wherein studying French and Chinese people that showed prevalence of obstructive ventilatory disorder and the relationship of these with abdominal obesity [14,15]. The presence of obstructive ventilatory districts that is characterized by the reduction of FEV<sub>1</sub>, can be explained by the presence of bronchial hyper-responsiveness, due to the chronic inflammatory state that obesity triggers [12]. This fact was verified in a study where was found high C-reactive protein levels in women with MetS when compared to

women without MetS [12]. WC and BP were the components evaluated in the current research and presented an inverse relation with forced vital capacity predicted. The existence of pulmonary alterations in the presence of metabolic syndrome and its components may be triggered by obesity, and also leads to restrictive breathing patterns through the conformational and morphological changes occurring in the individual's thoracic cavity with local losses in the pulmonary parenchyma [25].

The main change due to obesity would be the reduction in

diaphragm amplitude during respiration. decrease in the amount of fibers recruited and respiratory muscle strength [25]. In addition, changes in the ventilation/perfusion ratio (V/Q), increased ventilation in the upper zones (areas of higher ventilation and reduced perfusion) and reduction in the inferior ones, culminating in a decrease in lung base volume predisposing to alveolar collapse, response inflammatory and tissue oxygenation reduction [9] may reduce the functional residual capacity (FRC) of these women. The inverse relationship found in %FVC with hypertension is related to left ventricular (LV) changes, nevertheless, according to the literature the antihypertensive treatment minimizes the effects of ventricular overload on pulmonary function [7,26]. Mendes et al. [7] found that the reduction in FVC and FEV<sub>6</sub> were associated with an increase in left ventricular mass, while the reduction in obstruction. FEV<sub>1</sub>/FVC and FEV<sub>6</sub>/FVC were associated with a higher left atrial volume index in women. The FEV<sub>1</sub>/FVC ratio was similar between the groups with and without MetS. There are reports in the literature of the association of this maker of respiratory function with components, hypertension and waist circumference [11,14]. There are speculations that the presence of menopause may promote these manifestations since the action of hormones in women in this period, such as androgens can lead to cardiac cell hypertrophy and stimulate airway hyperresponsiveness, while estrogen that are concentrated reduce LV structural changes and promote bronchodilation [27–29].

Among the strengths of the our research are the indication of BP and WC as a factor that best explains the presence of MetS by principal component analysis. Thus, it becomes possible to use them in larger samples, since the collection and the blood dosage of the biochemical parameters require a greater logistics and cost. This study took into account the presence of menopause for the construction of regression models, in detriment to the literature consulted. It is known that menopause is associated with a decline in lung function being more evident in the reduction of %FVC and that the change in hormone metabolism that occurs during this period contributes significantly. Regarding ventilatory disorders, even if the prevalence of obstructive component was higher in women with MetS, when the relationship was analyzed with each of the components and adjusted with the variables age, BMI and the presence of menopause, the inverse relationship was verified, only the FVC with the PA and WC components. Some limitations should be scored, Spirometry does not offer measures of physical fitness, but rather the ability of the respiratory system to deliver the volume required for tissue oxygenation. Thus, can be used as a marker of functional capacity since if there are changes in conductive pathways (airways) or flow-generating (respiratory muscles), probably daily activities are hampered by the lack of oxygen uptake for peripheral functions.

## 5. Conclusion

Metabolic syndrome was present in almost half of the women evaluated. The parameters of spirometry, %FEV<sub>1</sub> and %FVC were reduced when compared to women in Metabolic syndrome. When the components were analyzed by analysis of primary components, WC and BP were the factors with the highest eigenvalues. In the regression models, WC and PA had an inverse relationship with % FVC, supporting the general concept that abdominal obesity could induce restriction of pulmonary parenchyma expansibility by mechanical barrier and elevated blood pressure, probably through left ventricular remodeling could cause damage in pulmonary volumes and capacity in women with metabolic syndrome. Metabolic syndrome is a multicausal clinical condition, and it is composed of factors which contribute to structural and physiological changes that can lead to reduced functional capacity. This condition

generates a need for a multidisciplinary team and rehabilitation programs involving important aspects for the human being as a physical condition, emotional and social coexistence.

## Disclosure statement

No conflict of interest.

## Declarations

### *Ethics approval and consent to participate*

This study was approved by Research Ethics Committees on Human Beings of the Federal University of Goiás under the number 784.446/2014. The opinion image was attached below for the purposes of proving the information.

### *Consent for publication*

If it requested, the volunteers will be available to give the consent for publication.

### *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 interest*

The authors declare that they have no competing interests.

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## Appendix A. Supplementary data

Supplementary data to this article can be found online at <https://doi.org/10.1016/j.dsx.2018.11.044>.

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## List of abbreviations

MetS: Metabolic syndrome  
 FRC: functional residual capacity  
 V/Q: ventilation-perfusion ratio  
 FHS: family health strategy  
 WC: waist circumference  
 BMI: body mass index  
 FVC: forced vital capacity  
 TLC: total lung capacity  
 FEV<sub>1</sub>: forced expiratory volume in 1 s  
 LL: lower limit  
 BP: blood pressure