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Original Article

Study of pulmonary functions in patients with metabolic syndrome

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Abstract

Introduction: Metabolic syndrome (MetS) and impaired lung functions have been associated with an increased risk for coronary heart disease. The aim of this study was to investigate the pulmonary functions in patients with MetS.

Methods: This cross-sectional study included 200 subjects with MetS in the study group and 100 subjects without MetS in the control group. Participants were examined at M.P. Shah Medical College, Jamnagar, India between 2013 to 2016. MetS was assessed according to the National Cholesterol Education Program's-Adult Treatment Panel III Criteria. Pulmonary function, fasting glucose, insulin and lipid profile levels were measured and homeostatic model assessment was used to assess insulin resistance. Pulmonary function and components of MetS were examined using independent Student's t-test, analysis of variance and chi-square test.

Results: The overall prevalence of pulmonary functions impairment in patients with MetS was 50% with high prevalence of restrictive ventilatory patterns (33%). Insulin resistance was significantly (P<0.001) higher in the study group than in control group, while pulmonary functions variables of study group were significantly (P<0.001) lower than those of control group. There were significant differences in the body mass index, waist circumference, blood glucose, and insulin resistance (P<0.05) between ventilatory pattern of subgroups.

Conclusion: We found that components of MetS and insulin resistance were significantly related to the impairment of pulmonary function. Therefore present study suggests that increased components of MetS and insulin resistance are risk factors for decline pulmonary functions in subjects with MetS.

Keywords:
Metabolic syndrome;
Pulmonary functions;
Insulin resistance;
Prevalence

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Introduction

The metabolic syndrome (syndrome X or insulin resistance syndrome) is one of the major public health issues of this century. It is a constellation of physical conditions and metabolic abnormalities which include central obesity, hyperglycemia plus insulin resistance (IR), hypertension, dyslipidemia and proinflammatory conditions, usually occurring together that increases an individual's risk for development of type 2 diabetes mellitus and cardiovascular disease (Pandey et al., 2009). Impaired lung function, as measured by forced vital capacity (FVC) or forced expiratory volume in one second (FEV1) and it is known to be associated with

increased prevalence and mortality of cardiovascular diseases (Lim et al., 2010). Several large prospective studies have shown that lung function impairment was predictive of increased cardiovascular morbidity and mortality, independent of smoking. Positive associations with lung function impairment have been reported for major cardiovascular risk factors such as hypertension, type II diabetes mellitus, LDL cholesterol, insulin resistance, and overall obesity. Therefore, metabolic syndrome (MetS) and impaired lung function have been associated with an increased risk of coronary heart disease in middle-aged subjects. The mechanisms underlying the relationship between impaired lung function and cardiovascular risk are unclear (Leone et al., 2009). However, scanty data are available on the relationship between lungs function impairment and MetS, while not a single study still performed in Indian population in best of my knowledge. Therefore, the present study aimed to investigate the impact of MetS on lung function impairment.

Materials and methods

Study design and participants

This cross-sectional study was conducted as a part of Ph.D. research program for duration of three years (from July 2013 to June 2016) at the Department of Physiology, M.P. Shah Medical College, Jamnagar, Gujarat, India. The patients aged between 25-65 years, were randomly selected from the outpatient clinic and diabetes center of Department of General Medicine, M.P. Shah Medical College and associate hospital. 200 patients (mean age= 52.34±8.56), with MetS who fulfilled the National Cholesterol, Education Program, Adult Treatment Panel-III (NCEP ATP-III, 2001) criteria were included in the study group (MetS group). Age and sex matched 100 healthy volunteers (mean age= 48.62 ± 10.48) who had no features of MetS were included in the control group (Non-MetS). Patients with history of respiratory disease, malignancy, smokers, alcoholics, congestive cardiac failure, pregnant women, and liver disease, were excluded from this study. Trained interviewers, using a structured questionnaire, interviewed all the participants to obtain the information on socio-demographic characteristics, physical activity, smoking, alcohol drinking habits, dietary characteristics, personal and family history of diseases, and hospitalization. Anthropometric measurements and blood pressure measurements were obtained after complete physical examination. Blood pressure (BP) was measured using a mercury sphygmomanometer with over the right arm with the patient lying supine. Weight and height were measured using a daily calibrated digital scale and stadimeter with subject wearing light clothing and no shoes and body mass index (BMI) was also calculated by using Quetlet index (MacKay, 2010) (weight/height^2- kg/m^2). Waist circumference (WC) was measured on bare skin during mid respiration at the narrowest indentation between the 10th rib and iliac crest to the nearest 0.1cm while the patient was standing. Informed consent was obtained from all the participants prior to start the study. The study protocol was approved by institutional ethics committee and research development council of Saurashtra University, Rajkot (CUSMC/IEC (HR)/ APPRO-1/6412/2014).

Definition of metabolic syndrome (MetS)

The MetS was diagnosed according to the National Cholesterol Education Program's Adult Treatment Panel-III (NCEP ATP-III) criteria when more than three of the following five components were present: waist circumference (WC) > 102 cms in men and 88 cms in women, blood pressure (BP) >130/85 mmHg or on antihypertensive medications, fasting plasma glucose (FBG) > 110 mg/dL or on anti-diabetic medications, fasting triglycerides (TG) > 150 mg/dl, HDL-C < 40 mg/dL in males and <50 mg/dL in females.

Pulmonary functions test

Lung function test was performed in all participants by using an automated flow-sensing spirometer (Helios 401' Recorders & Medicare Systems Pvt. Ltd Chandigarh, India) based on American Thoracic Society/European Respiratory Society, 2005 recommendations (ATS/ERS) (Miller et al., 2005) with all subjects in a sitting position. If at all possible, at least three and up to a maximum of eight forced expiratory maneuvers were performed in an effort to meet the American Thoracic Society standards. The predicted value, actual value and the percentage predicted value for the individuals were measured and these values were based on height, age, gender, and ethnicity of the subjects. Variables used in this study were the forced vital capacity (FVC %

Predicted Pretest), forced expiratory volume in 1 second, (FEV_1% Predicted Pretest), FEV_1-to-FVC % predicted Pretest ratio, and Mean % predicted Forced Expiratory Flow during the middle of the FVC (FEF 25%-75%). The highest FVC and FEV_1 values of the three or more tests with acceptable curves were used in the analysis. According to a modified classification of the Global Initiative for Chronic Obstructive Lung Disease (GOLD), obstructive lung impairment was defined as an FEV_1-to-FVC ratio < 70% and an FVC > 80% of the % predicted value. Restrictive lung impairment was defined as an FVC < 80% of the % predicted value and an FEV_1-to-FVC ratio >70%. Mixed lung impairment was defined as a FEV_1-to-FVC ratio < 70% and FVC < 80% of the % predicted value. The normal lung function was defined as FVC >80% and FEV_1/FVC > 70% (Sagun et al., 2015).

Serum sampling and biochemical analysis

Blood samples were obtained following 12 hours of fasting were immediately centrifuged (3000 rpm) for 10 minute; the sera were separated and frozen at -8°C until analysis. Fasting blood glucose (FBG), total cholesterol, triglycerides (TG), and high density lipoprotein cholesterol (HDL-C) levels were determined by enzymatic method using commercial available diagnostic kit on fully automated biochemical analyzer. Low density lipoproteins cholesterol (LDL-C) was determined by using Friedewald formula (Friendewald et al., 1972). Fasting serum insulin was measured by enzyme linked immunosorbent assay (ELISA) using commercially available diagnostic kit (LDN Labor Diagnostic Nord, Elisa Kit, Gmbh & Co. Kg). Homeostatic Model Assessment of Insulin Resistance (HOMA-IR) was calculated using following formula: HOMA-IR=Fasting glucose (mg/dL) x Fasting Insulin (µU/mL) / 405. HOMA-IR cut-off value used was 2.7 (>2.7 was considered insulin resistant and <2.7 was considered insulin sensitive) (Rutter et al., 2005).

Statistical analysis

Baseline characteristics of the participants were expressed in mean ± SD. Independent Student independent *t*-test was used to compare differences in baseline characteristics between the study group and the control group. Analysis of variance (ANOVA) with post hoc analysis according to Tukey (HSD) was used to compare data among ventilatory pattern subgroups. Chi-square test and Fischer's exact chi Square test were used for the comparison of qualitative data. P< 0.05 were considered statistically significant. Statistical analysis was performed using SPSS 20.0 software (SPSS Inc., Chicago, Illinois).

Results

Subjects and prevalence of ventilatory pattern

Demographic characteristics are presented in Table 1. The totals of 300 subjects were included in this study. Study group (MetS group) included 200 subjects (111 female, 89 male, mean age 52.34 ± 8.56) and control group (Non-MetS) included 100 subjects (37 female and 63 male, mean age 48.62 ± 10.48). The two groups were not significantly different with respect to dietary habits and life style (P> 0.05) while significantly greater number of subjects in the metabolic group had sex, education level, and ventilatory pattern (P< 0.001). Among 200 metabolic subjects, 66 (33%) had mild restrictive ventilatory pattern, 26 (13%) had mild obstructive pattern, 8 (4%) had mixed ventilatory pattern, and 100 (50%) were normal. The pattern of pulmonary functions in patients with MetS was shown in Figure 1. Therefore, the overall prevalence of the pulmonary functions impairment was 100 (50 %) in the study group. In the healthy non metabolic group, only 3 (3%) had restrictive pattern and 97 (97%) showed normal respiratory pattern. The overall prevalence of pulmonary functions impairment was 3% among non-metabolic subjects.

Anthropometric, MetS and others parameters

The base line characteristics of the study population were shown in Table 2. Differences between anthropometric and components of MetS between subjects with MetS and healthy non metabolic, were tested by Student independent *t*-test. Mean value for age (P<0.01), body mass index (P<0.001), waist circumference (P< 0.001), systolic and diastolic blood pressure (SBP/DBP) (P<0.001), fasting blood glucose (P< 0.001), and triglycerides (P<0.001) were significantly higher in the metabolic group compared to non-metabolic group. HDL-C levels were significantly lower in the study group compared to control group (P <0.001). In addition, patients with the MetS have a significantly higher insulin resistance

Table 1: Comparison of Socio-demographic variables between Non-Mets and MetS subjects

Socio-demographic Variables		Non-Mets control group (n=100)	Metabolic study group (n=200)	Chi Square Value	P-Value
Sex	Male	63 (63%)	89 (44.5%)	9.128*	0.003
	Female	37 (37%)	111 (55.5%)		
Dietary habits	Vegetarian	92 (92%)	183 (91.5%)	0.22	0.883
	Non-Veg.	8 (8%)	17 (8.5%)		
Life style	Sedentary	83 (83%)	180 (90%)	3.021	0.082
	Non sed.	17 (17%)	20 (10%)		
Education level	Illiterate	33 (33%)	90 (45%)	57.62*	< 0.001
	Literate	67 (67%)	110 (55%)		
Ventilatory pattern of pulmonary functions	Normal	97(97%)	100(50%)	65.513*	< 0.001
	Restrictive	3(3%)	66(33%)		
	Obstructive	0	26(13%)		
	Mixed	0	8 (4%)		

Two sided P value is > 0.05, considered not significant. The row/column association is not statistically significant and P value is < 0.05, considered significant. The row/column variables are significantly associated.

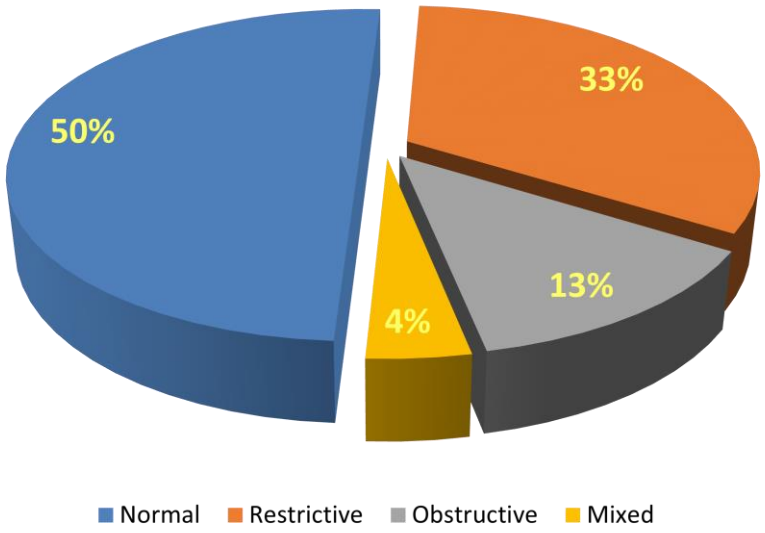

Fig.1. Prevelence of ventilatory pattern in MetS subjects Mets (n=200)

(IR) (P<0.001) compared to the patients without MetS (Table 2 & Figure 2).

MetS and pulmonary functions variables

The subjects with MetS showed significantly lower FVC % predicted (P<0.001), FEV1 % predicted (P<0.001), FEV1/FVC % predicted ratio (P< 0.001) and FEF 25%-75% percent predicted (P<0.001) compared to the group without MetS (Table-3).

Comparison of metabolic components and insulin resistance between ventilatory patterns

The metabolic components and insulin resistance between the sub groups of ventilatory patterns were compared by using one way analysis of variance with post hoc analysis according to Tukey-HSD. There were significant differences in the body mass index (P<0.05), waist circumference (P<0.001), fasting blood glucose (P<0.01) and insulin resistance (P

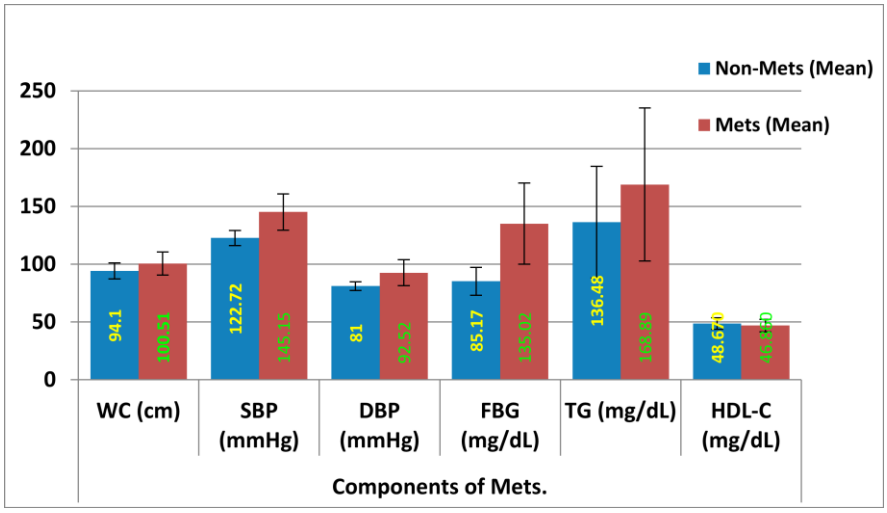

Fig.2. Components of Mets between Non-Mets and Mets groups (Mean ± 1SD)

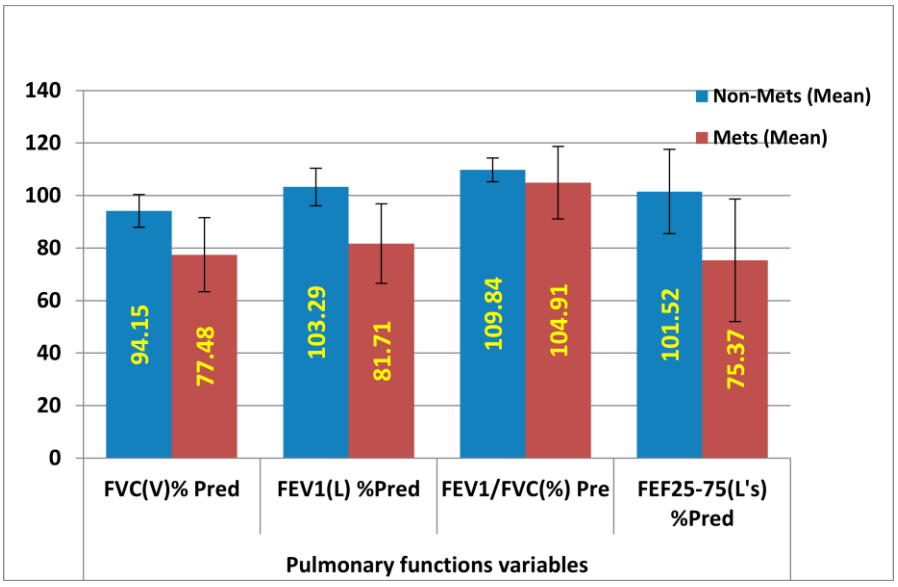

Fig.3. Pulmonary functions FVC, FEV1, FEV1/FVC & FEF25-75 of % Pred Pre Test (Mean ±1 SD)

<0.05) between four subgroups, while no differences were observed in blood pressure, triglycerides and HDL-C (Table 4).

Discussion

In this cross-sectional study, we observed that the prevalence of ventilatory patterns in the study group was 50% and its pattern showed high prevalence of mild restrictive (66%) followed by obstructive (13%) and mixed pattern (4%). The results of this study were similar to those reported from population-based studies (Lim et al., 2010; Nakajima et al., 2008). The present study showed that pulmonary function variables are significantly decreased in subject with MetS compared to non-metabolic subjects, while insulin resistance was significantly increased in patients with MetS. These finding are similar to those obtained in the studies on Korean nonsmoking males (Lim et al., 2010) and Taiwan population (Chen et al., 2014). In addition, another study shows that there was a small, but statistically significant difference in FEV_1/FVC between subjects with and without MetS (van Huisstede et al., 2013). It might support our hypothesis that the presence of MetS may influence lung function impairment. Another study showed reverse correlation between metabolic components and pulmonary functions. In addition, abdominal obesity was reported as the most powerful predictor of pulmonary function impairment (Leone et al., 2009). One potential explanation is that increased abdominal obesity directly affects thoracic and

Table 2: Comparison of base line characteristics of the study population

Anthropometry variables	Non-Mets (Mean ± SD)	Mets (Mean ± SD)	t -Value	P- Value (2-tailed)
Age (Years)	48.62 ± 10.48	52.34 ± 8.56	-3.280	<0.01
Height (CM)	164 ± 7.24	157.59 ± 9.27	6.686	< 0.001
Weight (Kg)	74 ± 8.44	76.99 ± 13.92	-1.970	<.050
BMI (Kg/Sq.M)	27.48 ± 2.56	30.74 ± 5.08	-6.037	< 0.001
WC (CM)	94.1 ± 6.99	100.51 ± 10.78	-5.746	< 0.001
HC (CM)	95.2 ± 6.97	99.52 ± 10.28	-3.783	< 0.001
Systolic BP (mmHg)	122.72±6.49	145.15±15.72	-13.684	<0.001
Diastolic BP (mmHg)	81.02±3.73	92.52±11.02	-9.940	<0.001
FBG (mg/dL)	85.17±12.19	135.02±35.102	-13.780	< 0.001
TG (mg/dL)	136.48±48.29	168.89±66.25	-4.348	< 0.001
HDL-C (mg/dL)	48.67±4.94	46.86±5.51	4.301	< 0.001
HOMA-IR	3.12 ±1.91	8.87 ±6.95	-8.101	< 0.001

All data expressed as mean ± standard deviation<0.05 is statistically significance. BMI, body mass index; WC, waist circumference; HC, hip circumference; FBG, fasting blood glucose; TG, triglycerides; HDL-C, high density lipoprotein cholesterol; HOMA-IR, homeostatic model assessment of insulin resistance.

Table 3: Comparison of pulmonary functions variables between Non-MetS and MetS groups

Pulmonary functions variables	Non-Mets (Mean ± SD)	Mets (Mean ± SD)	t -Value	P- Value (2-tailed)
FVC - % Pred Pre	94.15±6.19	77.48±14.06	11.312	< 0.001
FEV1- % Pred Pre	103.29±7.14	81.71±15.10	13.542	< 0.001
FEV_1/FVC- % Pred Pre	109.84±4.53	104.91±13.79	3.478	< 0.001
FEF 25-75 -% Pred Pre	101.52±16.04	75.37±23.32	10.77	< 0.001

All data expressed as mean ± standard deviation<0.05 is statistically significance. %Pred Pre, %Predicted Pretest; FVC, Force Vital capacity; FEV1, Force Expiratory volume in 1 second; FEV1/FVCF ratio; EF25%-75%, Middle of Force Expiratory Flow.

Table 4: Comparison of components of MetS and other trait among ventilatory pattern subgroups

Components of MetS	Normal (Mean ± SD) (n=100)	Mild Restrictive (Mean ± SD) (n=66)	Mild Obstructive (Mean ± SD) (n=26)	Mixed (Mean ± SD) (n=8)	F-Value	P -Value
BMI (Kg/M^2)	30.76 ± 4.58	31.00 ± 5.66	29.54 ± 5.90	32.25 ± 2.60	0.775	0.50
West cir (CM)	98.99±9.15	103.08±9.97	96.96±40.58	109.75±9.27	6.027	0.001
SBP(mmHg)	144.10±15.32	147.94±17.37	141.15±9.66	148.25±20.24	1.51	0.212
DBP (mmHg)	92.30±11.43	93.82±12.46	89.08±4.77	95.75±12.48	1.34	0.262
FBG(mg/dl)	130.83±37.78	132.85±31.41	148.54±30.74	161.25±23.30	3.45	0.017
TG(mg/dL)	161.97±69.11	175.74±62.74	174.38±61.55	181.00±75.62	0.745	0.527
HDL-C (mg/dL)	45.23±5.04	46.58±6.15	46.92±5.85	44.38±3.81	1.32	0.267
Homa-IR	8.45±7.35	8.44±6.45	10.65±6.81	11.75±5.70	1.23	0.29

Values are presented as mean ± standard deviation. *F* value and *P* value derived from one-way analysis of variance with post hoc analysis according to Tukey that used to evaluate in the four subgroups. SBP, systolic blood pressure; DBP, diastolic blood pressure; WC, waist circumference; FBG, fasting blood glucose; TG, triglyceride; HDL-C, high density lipoprotein cholesterol, HOMA-IR, Homeostatic Model Assessment of Insulin Resistance, BMI, Body mass index.

diaphragm compliance, which decline lung function (Salome et al., 2010). In addition, American study found a negative correlation between FEV_1/FVC and waist circumference (Chen et al., 2001). Another study from Australia showed that FVC has negative correlation with male's abdominal obesity (Lazarus et al., 1998a). In a Japanese study, lung function impairment due to hyperglycemia and abdominal obesity was suggested (Yoshimura et al., 2012). In addition, another Korean study showed that waist circumference, hypertension, hyperglycemia, and HDL-C sturdily influenced lung function (Choi et al., 2011). Fasting serum insulin levels are negatively correlated with FVC and FEV_1 (Lazarus et al., 1998 b). Furthermore, insulin resistance assessed by HOMA and prevalence of type 2 diabetes mellitus are inversely associated with FVC and FEV_1 (Lawlor et al., 2004). Our results were consistent with previous studies.

There are several explanations for the relationship between reduced lung function and MetS. MetS is a cluster of disease comprised of multiple cardiovascular risk factors such as IR, dyslipidemia, glucose intolerance, and hypertension, most of which could stem from one cause, visceral obesity. It has been shown that obesity is one of the causes of physiologic impairments in respiratory system. Obesity causes airflow limitation with reduction of both FEV1 and FVC, and reduces lung volumes, especially expiratory reserve volume (ERV), and functional residual capacity (FRC). These changes predispose toward a decrease in peripheral airway diameter, reduction in respiratory system compliance, as well as an increase in oxygen cost of breathing and airway hyperresponsiveness (AHR). Taken together, decrease in retractive forces of the lung parenchyma on the airways at low lung volume in obese people, lead to reduction in airway caliber and increased AHR, which potentially causing detrimental effect on lung function. The association of obstructive lung function with MetS could be explained by obesity and subsequent systemic inflammation and also by the role of adipokines (Lim et al., 2010).

There are few limitations in this study. First, this is a cross-sectional designed study and further longitudinal studies are needed to investigate the interactions between lung function, inflammation, IR, MetS and their relation with future cardiovascular disease. Second, analysis of the ventilatory patterns was not sufficiently adequate because the diagnosis of restrictive pattern was made without total lung capacity measurement and obstructive pattern was without post-bronchodilator assessment. The third limitation is that systemic inflammatory markers like hs-CRP, TNF-α, Eotaxin IL-1, IL-6, and leptin which might be accountable for insulin resistance, pulmonary function impairment and increase risk for cardiovascular diseases were not measured in this study.

Conclusion

In conclusion, the overall prevalence of ventilatory pattern in patients with MetS was 50% with high prevalence of restrictive pattern (33%). MetS and its components and insulin resistance significantly influence and related with the impairment of pulmonary function.

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Conflict of interest

All authors have declared no conflict of interest.

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