The impact of metabolic syndrome on ventilatory pulmonary functions

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Background A relationship between metabolic syndrome (MS) and lung disease has been observed in several cross-sectional and longitudinal studies. This syndrome has been identified as an independent risk factor for worsening respiratory symptoms and higher lung function impairment.

Aim The aim of this study was to analyze the effect of MS on ventilatory pulmonary functions.

Patients and methods This study included 60 participants. They were divided to two groups – group A included 45 patients with MS, and group B included 15 apparently healthy participants as a control group. All of them were subjected to the following: complete history taking and physical examination (blood pressure, BMI, and waist circumference), laboratory investigations for fasting blood glucose, lipid profile (triglyceride and high-density lipoprotein), C-reactive protein, and HbA1C, and spirometry [forced vital capacity (FVC), forced expiratory volume in first second (FEV_1), and FEV_1/FVC].

Results Among MS participants (n=45), 28 (63%) had the restrictive ventilatory pattern, three (6%) had the obstructive pattern, nine (20%) were normal, and five (11%) had a mixed pattern. Pulmonary functions were impaired more among MS cases. FVC% predicted of group A was 61.49±17.56%, whereas in group B it was 85.73±5.24%. FEV_1% predicted of group A was 66.22±18.7%, whereas in group B it was 87.73 ±7.98%. The differences were statistically highly significant. Pulmonary function impairment was more prominent among males than among females. After examining the association between metabolic components and both FVC% predicted and FEV_1% predicted, the results revealed that there was a strong linear decrease in FVC% predicted and FEV_1% predicted as the number of components of MS increased. The β coefficients of FVC% predicted for those with 1, 2, 3, 4, and 5 features of MS were 0.011, –0.018, –0.023, –0.035, and –0.048 in men and 0.020, –0.029, –0.035, –0.047, and –0.068 in women, respectively. The β coefficients of FEV_1% predicted for those with 1, 2, 3, 4, and 5 features of MS were 0.009, –0.015, –0.026, –0.041, and –0.051 in men and 0.004, –0.009, –0.017, –0.029, and –0.038 in women, respectively.

Conclusion Pulmonary function impairment (mainly restrictive pattern) is commonly associated with MS. FVC and FEV_1 are inversely associated with the accumulation of elements of MS and also associated independently with each element of MS, especially waist circumference.

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Keywords: forced expiratory volume in the first second, forced vital capacity, metabolic syndrome, spirometry, waist circumference

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Introduction

Metabolic syndrome (MS) is a complex disorder with high socioeconomic costs, and is defined by a cluster of interconnected factors that directly increase the risk of coronary heart disease, other forms of cardiovascular atherosclerotic diseases, and diabetes mellitus type 2 [1].

Its main components are dyslipidemia [elevated triglycerides (TGs) and apolipoprotein B containing lipoproteins and low high-density lipoproteins (HDL)], elevation of arterial blood pressure, and dysregulated glucose homeostasis, whereas abdominal obesity and/or insulin resistance (IR) have gained increasing attention as the core manifestations of the syndrome [1].

In a number of recent studies, it has been reported that among the changes in pulmonary function, pulmonary function deterioration is related to hypertension, type 2 diabetes, low-density lipoprotein cholesterol (LDL-c), overall obesity, abdominal obesity, and IR [2]. Among the above-listed factors, hypertension, diabetes, and abdominal obesity are included as diagnostic criteria for MS; hence, it can be inferred that identifying the relationship between MS and pulmonary function deterioration is meaningful.

The presence of obstructive or restrictive lung diseases as assessed by spirometry is associated with a higher risk of death [3]. In addition, lung function impairment is also associated with IR [4], type 2 diabetes [5], and cardiovascular diseases [6]. Therefore, lung function test may be commonly used as a tool for general health assessment.

Aim

We aimed to study the effect of MS on ventilatory pulmonary function.

Patients and methods

This cross-sectional study included 60 participants admitted to the Chest and Internal Medicine Departments at Benha University hospitals from August 2014 to November 2015. They were classified into two groups:

(1) Group A included 45 patients with MS.
(2) Group B included 15 apparently healthy participants.

All the participants were subjected to the following: complete history taking and physical examination (blood pressure and waist circumference), laboratory investigations for fasting blood glucose (FBG), lipid profile (TG and HDL), C-reactive protein, and HbA1C, and spirometry [forced vital capacity (FVC), forced expiratory volume in first second (FEV_1), and FEV_1/FVC].

Metabolic syndrome

MS was defined according to the American Heart Association/National Heart, Lung, and Blood Institute [7]. This definition is satisfied if at least three of the following five criteria are met:

(1) Large waist circumference (>102 cm in men and >88 cm in women).
(2) High TGs (>150 mg/dl) or lipid-specific treatment.
(3) Low high-density lipoprotein cholesterol (HDL-C) (men <40 and women <50 mg/dl) or lipid-specific treatment.
(4) High fasting glucose (>100 mg/dl) or diabetes treatment.
(5) High systolic blood pressure (>130 mmHg) or diastolic blood pressure (>85 mmHg) or use of antihypertensive therapy.

Pulmonary functions

The lung function test was performed in all participants by using an automated flow-sensing spirometer (Spirolab III, version 4.3 SN 311860; Italy) based on the American Thoracic Society (ATS)/European Respiratory Society, 2005 recommendations [8]. If at all possible, at least three forced expiratory maneuvers were performed in an effort to meet the ATS standards. The predicted value, actual value, and the percentage predicted value for the individuals were measured, and these values were based on height, age, sex, and ethnicity of the participants. The recoded data included FVC, FEV_1, and FEV_1/FVC ratio.

Lung function impairment

It was defined as FEV_1 or FVC less than the lower limit of normal. The definitions of lung function parameters with reference to the ATS/European Respiratory Society Guidelines [9] are as follows:

(1) Obstructive lung impairment was defined as an FEV_1-to-FVC ratio less than 70% and an FVC greater than 80% of the predicted value.
(2) Restrictive lung impairment was defined as an FVC less than 80% of the predicted value and an FEV_1-to-FVC ratio greater than 70%.
(3) Mixed lung impairment was defined as an FEV_1-to-FVC ratio less than 70% and FVC less than 80% of the predicted value. Values apart from these were defined as normal lung function [10].

Data management

The clinical data were recorded on a report form. These data were tabulated and analyzed using the computer program statistical package for the social sciences version 16 (SPSS; SPSS Inc., Chicago, Illinois, USA).

Descriptive data

Descriptive statistics were calculated as follows:

(1) Mean±SD for quantitative data.
(2) Frequency and distribution for qualitative data.

Analytical statistics

For statistical comparison between the different groups, the significance of difference was tested using one of the following tests:

(1) Student's t-test was used to compare mean of two groups of quantitative data:

$$t = \frac{\overline{x}_1 - \overline{x}_2}{\sqrt{\frac{SD_1^2}{n_1} + \frac{SD_2^2}{n_2}}}.$$

(2) Intergroup comparison of categorical data was performed by using the χ^2-test

$$\chi^2 = \frac{\sum(\text{observed} - \text{expected})^2}{\text{expected}}.$$

$$\text{Expected} = \frac{\text{column total} \times \text{row total}}{\text{grand total}}.$$

(3) The regression coefficient was calculated to evaluate linear association between variables.

A P value less than 0.05 was considered statistically significant, whereas a P value greater than 0.05 was considered statistically insignificant. A P value less than 0.005 was considered highly significant in all analyses.

Results

In this study, group A included 16 men and 29 women with an average age of 54.29±7.61 years, and group B included four men and 11 women with an average age 53.3±6.62 years. As for BMI, the mean value of group A was 45.62±4.85 and of group B 28.4±4.58. The sex distribution of MS was 64.4% female and 35.6% male (Table 1). Among MS patients (n=45), 28 (63%) had the restrictive ventilatory pattern, three (6%) had the obstructive pattern, nine (20%) were normal, and five (11%) had the mixed pattern (Table 2).

Pulmonary functions were impaired to a greater extent among MS cases. The FVC% of group A was 61.49± 17.56%, whereas in group B it was 85.73±5.24%. The FEV_1 of group A was 66.22±18.7, whereas in group B it was 87.73±7.98; the differences were statistically highly significant (Table 3).

In group A, the results revealed that pulmonary function impairment was more prominent among males than among females, as FVC% of males was 61.44±17.7, whereas in females it was 61.52±18.12, with a range of 22–93. FEV_1% for males was 64.38± 17.9, whereas for females it was 67.24±19.36. All these differences were statistically not significant (Table 4).

By comparing the metabolic components between the subgroups of ventilatory patterns (normal, restrictive, obstructive, and mixed), we found significant differences in waist circumference, and it was larger in the restrictive pattern subgroup, whereas no statistically significant differences were observed in FBG, blood pressure, TGs, and HDL-C among the four subgroups (Table 5).

After examining the association between metabolic components and FVC% predicted values, our results revealed that there was a strong linear decrease in FVC % predicted as the number of components of MS increased. The β coefficients of FVC% predicted (%) for those with 1, 2, 3, 4, and 5 features of MS were 0.011, −0.018, −0.023, −0.035, and −0.048 in men and 0.020, −0.029, −0.035, −0.047, and −0.068 in women, respectively ($P_{trend}<0.005$). In males and females, abdominal obesity, elevated blood pressure, high TGs, FBG, and low HDL-C were significantly associated with lower FVC% predicted in the fully adjusted model (most of the parameters, $P<0.005$) (Table 6).

On examining the association between metabolic components and FEV_1% predicted, our results revealed that there was a significant adverse relationship between the number of components present and pulmonary function. The β coefficients of FEV_1% predicted for those with 1, 2, 3, 4, and 5 features of MS were 0.009, −0.015, −0.026, −0.041, and −0.051 in males and 0.004, −0.009, −0.017, −0.029, and– 0.038 in females, respectively ($P_{trend}<0.001$). In both men and women, abdominal obesity, high blood pressure, increased TGs, and low HDL-C were significantly associated with lower FEV_1% predicted in the fully adjusted model (most of the parameters, $P<0.005$) (Table 7).

Discussion

MS or IR syndrome predicts diabetes and cardiovascular disease, but the definition and the clinical usefulness of MS are controversial [11].

MS as a clustering of inter-related metabolic risk factors may evolve through adipose tissue disease [12], and may not only be restricted to a risk factor for diabetes and cardiovascular disease but also be related to many other systemic disorders such as chronic kidney disease [13], chronic lung disease [14], and fatty liver disease [15].

Decreased lung function, as measured by FVC or FEV_1, is known to be associated with increased

Table 1 Comparison between group A and group B regarding age, sex, and BMI

Variables	Groups (mean±SD)		Student's t-test	P value
	Group A (n=45)	Group B (n=15)		
Age (years)	54.29±7.61	53.3±6.62	0.434	>0.05
Sex				
Male	16 (35.6)	4 (26.7)	χ^2=0.40	>0.05
Female	29 (64.4)	11 (73.3)		
BMI (kg/m^2)	45.62±4.85	28.4±4.58	12.07	<0.005

prevalence of and mortality associated with cardiovascular diseases [16].

Many studies have concluded that pulmonary function drops among obese people [17]. Previously, studies have used BMI, waist circumference, waist/hip circumference ratio, abdominal thickness (height), and skin thickness tests as markers of obesity [18]. However, recent studies focus on abdominal obesity as an indicator of overall obesity. As such, this study tried to examine waist circumference, which demonstrates abdominal obesity, as well as the relationship between MS components that are easily found among obese people and effects of these factors on pulmonary function.

The results of this study revealed no significant differences between the two studied groups with regard to age and sex, and thus both these groups were comparable, but there was a statistically significant difference regarding BMI, which was higher in group A, as obesity is one of the parameters of MS.

Sex distribution among MS patients in this study revealed that it was more common in females (64.4%) than in males (35.6%). These results are in agreement with Chen *et al.* [19] who examined the association between MS and lung function in 8602 participants – 26.85% of them had MS. Most of the MS patients were females (61.5%) [19]. Similar results were also obtained by Choudhary and Jani Rameshchandra [20] who assessed pulmonary functions in 200 patients with MS and most of them were females (55.5%).

In this study, the results revealed that the prevalence of the restrictive pattern among MS groups was 63%. The results of this study are similar to those reported by Choudhary and Jani Rameshchandra [20] who observed that the prevalence of ventilatory patterns was 50% and restrictive pattern represented the highest value of 66%. Another study by Lim *et al.* [21] who assessed MS, IR, and systemic inflammation as risk factors for reduced lung function in Korean nonsmoking males found that MS was more significantly related with the restrictive pattern (64.7%).

In the present study, pulmonary functions such as FEV_1% predicted and FVC_1% predicted were significantly decreased among those with MS in comparison with those without the syndrome

Table 2 Prevalence of ventilatory patterns in group A

Ventilatory patterns	*n*=45 [*n* (%)]
Normal	9 (20)
Restrictive	28 (63)
Obstructive	3 (6)
Mixed	5 (11)

Table 3 Comparison between group A and group B regarding pulmonary functions

PFT	Groups (mean±SD)		Student's *t*-test	*P* value
	Group A	Group B		
FVC%	61.49±17.56	85.73±5.24	5.24	<0.005
FEV_1%	66.22±18.7	87.73±7.98	4.31	<0.005
FEV_1/FVC	91.53±9.87	84.67±5.79	2.54	<0.05

FEV_1, forced expiratory volume in first second; FVC, forced vital capacity; PFT, pulmonary function test.

Table 4 Differences between males and females regarding pulmonary functions in group A

PFT	Groups (mean±SD)			
	Male group (*n*=16)	Female group (*n*=29)	Student's *t*-test	*P* value
FVC%	61.44±17.07	61.52±18.12	0.014	>0.05
FEV_1%	64.38±17.9	67.24±19.36	0.488	>0.05
FEV_1/FVC	89.87±11.23	92.44±9.11	0.834	>0.05

FEV_1, forced expiratory volume in first second; FVC, forced vital capacity; PFT, pulmonary function test.

Table 5 Comparison of the components of metabolic syndrome among ventilatory pattern subgroups

Variables	Patterns				*F* test	*P* value
	Normal	Restrictive	Obstructive	Mixed		
BMI (kg/m^2)	44.56±1.25	46.93±3.63	45.5±5.58	44.83±3.39	0.28	<0.005
WC (cm)	96.38±2.77	98.1±4.55	92.67±3.51	95.0±6.71	3.74	<0.005
SBP (mmHg)	133.75±11.9	137.24±12.8	140.0±10.0	134.0±11.4	0.314	>0.05
DBP (mmHg)	83.75±7.44	87.59±9.12	90.0±0.0	82.0±4.47	1.14	>0.05
FBS (mg/dl)	186.25±29.9	227.55±66.3	244.0±69.2	219.2±37.1	2.18	>0.05
TG (mg/dl)	198.62±36.6	198.38±29.0	180.0±20.0	181.0±33.2	0.749	>0.05
HDL (mg/dl)	43.0±9.17	39.41±8.41	40.33±9.5	42.6±8.14	0.482	>0.05

DBP, diastolic blood pressure; FBS, fasting blood sugar; FEV_1, forced expiratory volume in first second; FVC, forced vital capacity; HDL, high-density lipoprotein; SBP, systolic blood pressure; TG, triglycerides; WC, waist circumference.

Table 6 Regression coefficients of the components of metabolic syndrome for forced vital capacity percent predicted

Variables	Groups					
	Male			Female		
	β	*P* value	95% CI	β	*P* value	95% CI
Presence of MS	−0.028	<0.005	−0.040, −0.017	−0.028	<0.005	−0.042, −0.018
Number of MS components						
1	0.011	>0.05	−0.013, 0.022	0.020	>0.05	−0.031, 0.017
2	−0.018	>0.05	−0.029, 0.016	−0.029	>0.05	−0.044, 0.019
3	−0.023	<0.05	−0.038, 0.009	−0.035	<0.005	−0.050, −0.025
4	−0.035	<0.05	−0.048, −0.020	−0.047	<0.005	−0.064, −0.023
5	−0.048	<0.005	−0.063, −0.032	−0.068	<0.005	−0.085, −0.036
BMI (kg/m^2)	−0.036	<0.005	−0.044, −0.027	−0.032	<0.005	−0.041, −0.029
WC (cm)	−0.042	<0.005	−0.051, −0.038	−0.026	<0.005	−0.037, −0.020
SBP (mmHg)	−0.026	<0.005	−0.037, −0.042	−0.028	<0.005	−0.035, −0.022
DBP (mmHg)	−0.021	<0.05	−0.029, −0.014	−0.022	<0.05	−0.031, −0.019
FBS (mg/dl)	−0.015	<0.005	−0.025, −0.009	−0.038	<0.005	−0.044, −0.029
TG (mg/dl)	−0.023	<0.05	−0.027, −0.014	−0.017	<0.005	−0.026, −0.009
HDL (mg/dl)	−0.018	<0.005	−0.028, −0.010	−0.018	<0.05	−0.028, −0.011

DBP, diastolic blood pressure; FBS, fasting blood sugar; FEV_1, forced expiratory volume in first second; FVC, forced vital capacity; HDL, high-density lipoprotein; MS, metabolic syndrome; SBP, systolic blood pressure; TG, triglycerides; WC, waist circumference.

Table 7 Regression coefficients of the components of metabolic syndrome for forced expiratory volume in first second percent predicted

Variables	Groups					
	Male			Female		
	β	*P* value	95% CI	β	*P* value	95% CI
Presence of MS	−0.024	<0.005	−0.039, −0.014	−0.033	<0.005	−0.049, −0.021
Number of MS components						
1	0.009	>0.05	−0.023, 0.020	0.004	>0.05	−0.027, 0.020
2	−0.015	>0.05	−0.030, 0.014	−0.009	>0.05	−0.038, 0.024
3	−0.026	<0.05	−0.035, −0.012	−0.017	>0.05	−0.047, 0.014
4	−0.041	<0.005	−0.058, −0.019	−0.029	<0.05	−0.048, −0.019
5	−0.051	<0.005	−0.076, −0.028	−0.038	<0.005	−0.065, −0.010
BMI(kg/m^2)	−0.046	<0.005	−0.055, −0.038	−0.037	<0.005	−0.045, −0.027
WC (cm)	−0.031	<0.005	−0.043, −0.027	−0.031	<0.005	−0.040, 0.022
SBP (mmHg)	−0.025	<0.005	−0.035, −0.015	−0.026	<0.005	−0.036, −0.018
DBP (mmHg)	−0.023	<0.05	−0.033, −0.017	−0.018	<0.005	−0.028, −0.008
FBS (mg/dl)	−0.028	<0.05	−0036, −0.019	−0.023	<0.05	−0.029, −0.017
TG (mg/dl)	−0.015	<0.005	−0.023, −0.009	−0.021	<0.05	−0.031, −0.013
HDL (mg/dl)	−0.019	<0.005	−0.28, −0.012	−0.020	<0.05	−0.027, −0.009

DBP, diastolic blood pressure; FBS, fasting blood sugar; FEV_1, forced expiratory volume in first second; FVC, forced vital capacity; HDL, high-density lipoprotein; MS, metabolic syndrome; SBP, systolic blood pressure; TG, triglycerides; WC, waist circumference.

($P<0.005$), and the FEV_1/FVC ratio was significantly higher among those with MS compared with those without the syndrome. These results are in agreement with Chen *et al.* [19] who found that FEV_1% predicted and FVC_1% predicted were significantly lower among those with MS compared with those without the syndrome (for all the parameters, $P<0.001$), but the FEV_1/FVC ratio showed a statistically nonsignificant difference between those with and without MS in both men and women ($P=0.588$ and 0.079, respectively) [19]. Another study showed that pulmonary function variables such as FVC% predicted and FEV_1% predicted were significantly lower in participants with MS than nonmetabolic participants [20]. In addition, another study demonstrated that there was a small but statistically significant difference in the FEV_1/FVC ratio between metabolic and nonmetabolic participants [22].

Impairment of pulmonary function among those with MS is due to abdominal obesity, which is considered the core of the pathophysiology of MS [23]. One possible explanation is that increased abdominal obesity directly affects thoracic and diaphragm compliance, which impairs lung function [24].

In the present study, comparison of metabolic components between ventilatory patterns (normal,

restrictive, obstructive, and mixed) revealed that there were statistically significant differences regarding waist circumference, which was higher in the restrictive pattern group among the subgroups of ventilatory patterns ($P<0.005$), but the other components showed no statistically significant differences. In agreement with this observation, a study conducted on 300 participants (200 of them had MS) found that there were significant differences in BMI ($P<0.05$) and waist circumference ($P<0.001$) between the four subgroups [20].

The results of this study revealed that both FVC% and FEV_1% predicted significantly declined when the sum of MS diagnostic factors increased. All diagnostic factors such as abdominal obesity, elevated blood pressure, high FBS, high TGs, and low HDL-C were significantly linked with reduced FVC% predicted and FEV_1% in males and females.

These observations are in agreement with Chen *et al.* [19] who examined the association between MS and lung function in 8602 participants, and 26.85% of them had MS. They showed a significant linear decrease in FVC% and FEV_1 predicted as the number of components of MS increased. In both males and females, abdominal obesity, high blood pressure, high TGs, and low HDL-C were significantly associated with lower FVC% predicted and FEV_1% predicted in fully adjusted models (for all the parameters, $P<0.05$), but high glucose was significantly associated with lower FVC% predicted in both males and females and with lower FEV_1% predicted in females in fully adjusted models [19].

In a study by Myoung-Sook *et al.* [25], there was a reverse correlation between diagnostic criteria of MS and pulmonary function. Among males, although there were significant differences in FVC according to whether or not there were any diagnostics components for MS, there were no FVC differences found among females. However, for both males and females, pulmonary function differed significantly according to waist circumference. For males, there was a significant statistical difference in FVC and FEV_1/FVC [25].

In a study conducted by Leone *et al.* [26] both males and females showed reverse correlation between all diagnostic criteria of MS and pulmonary function. As in this study, abdominal obesity was reported as the most potent predictor of poor pulmonary function [26]. In addition, Chen *et al.* [19] found out that both males and females showed negative correlation between FEV_1/FVC and waist circumference even after age, height, weight, workload, energy consumption, and smoking were factored. Thus, the larger the waist circumference, the greater its effect on pulmonary function, eventually having partial impact on the movements of the diaphragm and chest [19].

In Australia, Lazarus *et al.* [27] showed that FVC has a negative correlation with waist circumference in males. This study included about 2744 men and studied the association between body composition and lung function [27]. Furthermore, Ochs-Balcom *et al.* [28] also demonstrated that FEV_1 and FVC in males and females showed negative correlation with waist circumference. Moreover, Harik-Khan *et al.* [29] demonstrated that the correlation between FVC and FEV_1 and waist circumference was negative among men, whereas in women only FVC was correlated and FEV_1 was not correlated. They explained such sex differences by fat distribution that could affect diaphragm and thoracic movement in women more than men.

The results of this study revealed that low HDL-C was correlated positively with impaired pulmonary function (FEV_1% and FVC%). This observation was in agreement with the study by Rogliani *et al.* [30] who examined 237 patients and found that serum HDL-C had an inverse relationship with lower FEV_1 and FVC. Similar results were demonstrated by Chen *et al.* [19] who examined the association between MS and lung function and showed that low HDL-C was correlated with decreased pulmonary function. The pathophysiology underlying this association remains vague. Lower HDL-C levels are linked to the development of coronary heart disease due to the function of HDL-C in reverse cholesterol transport and anti-inflammation. It is tempting to speculate that serum HDL-C acts as a predictor for the decline of lung function, mainly due to its pleiotropic properties including antioxidative function, inhibition of cytokine-induced expression of endothelial cell adhesion molecules, and suppression of the chemotactic activity of monocytes and lymphocytes [31].

There are several explanations for the relationship between reduced lung function and MetS. MetS is a cluster of diseases comprised of multiple cardiovascular risk factors such as IR, dyslipidemia, glucose intolerance, and hypertension, most of which could stem from one cause – visceral obesity [32].

Obesity has long been shown to cause physiological impairments in the respiratory system [33]: airflow limitation with reduction of both FEV_1 and FVC, reduction in lung volumes, especially expiratory reserve volume, and functional residual capacity, which 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 hyper-responsiveness. Taken together, the decrease in retractive forces of the lung parenchyma on the airways at low lung volume in obese people lead to reduced airway caliber and increased airway hyper-responsiveness, potentially causing a detrimental effect on lung function. The association of obstructive lung function with MetS could be explained by obesity and subsequent systemic inflammation and by the role of adipokines [34].

Conclusion

(1) Pulmonary function impairment (mainly restrictive pattern) is commonly associated with MS.
(2) FVC and FEV_1 are inversely associated with the accumulation of elements of the MS and are also associated independently with each element of the MS, especially waist circumference.

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form the patient(s) has/have given his/her/their consent for his/her/their images and other clinical information to be reported in the journal. The patients understand that their names and initials will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

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Conflicts of interest

There are no conflicts of interest.

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