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Sex differences in the relationship between metabolic syndrome and pulmonary function: The 2007 Korean National Health and Nutrition Examination Survey

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Abstract. Pulmonary function impairment has a connection with abdominal obesity, type 2 diabetes, and insulin resistance. Sex differences in lifestyle factors, and pulmonary structure and function may affect pulmonary function in different manners. This study focused on sex differences in the relationship of MetS and its component with pulmonary function. Among 2,614 Korean adults (1,059 men; 1,555 women), pulmonary function was measured by the percentage of predicted forced vital capacity (FVC (%)) and a ratio between forced expiratory volume in 1 second (FEV_1)/FVC. FVC (%) and FEV_1/FVC were compared according to the presence of MetS and its components. Multiple linear regression analysis was conducted to assess the association between FVC (%), FEV_1/FVC and clinical variables. We found sex differences in the relationship of MetS and its components with pulmonary function. FVC (%) was significantly lower in subjects with MetS than in those without MetS in both men and women, and FEV_1/FVC was lower in subjects with MetS only in women. Among components of MetS, waist circumference, blood pressure and fasting plasma glucose, and HDL-cholesterol were independently related to FVC (%) in men, whereas waist circumference was significantly associated with FVC (%) in women. Blood pressure was found to be an independent factor of FEV_1/FVC in men, whereas blood pressure, fasting plasma glucose and HDL-cholesterol independently determined FEV_1/FVC in women. These findings suggest that sex-specific association between MetS and lung function measures should be considered in clinical practice.

Key words: Metabolic syndrome, Pulmonary function, Insulin resistance, Sex differences

METABOLIC syndrome (MetS) is a combination of abnormalities, including obesity, elevated blood pressure, impaired glucose metabolism, and atherogenic dyslipidemia. Subjects with MetS are more susceptible to type 2 diabetes [1] and cardiovascular disease (CVD) [2, 3]. The prevalence of MetS is increasing worldwide and becoming a global epidemic [4]. The rapid socioeconomic growth of Korea resulted in profound lifestyle changes such as the introduction of Westernized diet and sedentary behavior, which led to an increase in MetS.

Emerging evidence has shown that pulmonary function impairment is associated with all-cause and CVD mortality [5, 6]. More recent studies have shown that pulmonary function impairment has a connection with not only cigarette smoking, but also with obesity [7], type 2 diabetes [8], insulin resistance [9], conditions linked to increased oxidative stress and chronic low-grade inflammation [5, 6].

Compared with men, women tend to have smaller lung volumes and lower maximal expiratory flow rates even when corrected for sitting height [10]. Additionally, the smoking rate for women is less than 5%, which is strikingly lower than for men in Korea [11]. In the light of these novel findings, sex differences in lifestyle factors, and pulmonary structure and function may affect pulmonary function in different manners. To date, sex differences in the relationship of MetS and its component with pulmonary function have not been fully evaluated. We analyzed our data by gender using different equations for the calculation of predicted forced vital capacity (FVC) and

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forced expiratory volume in 1 second (FEV_1) for men and women.

Thus, this study aimed to investigate the association between MetS and pulmonary function, as measured by the percentage of predicted FVC (FVC (%)) and the ratio between FEV_1 and FVC (FEV_1/FVC) in Korean men and women based on the 2007 Korean National Health and Nutrition Examination Survey (KNHANES).

Materials and Methods

Study population

This study was based on the data obtained from the 2007 KNHANES which is a national cross-sectional survey conducted by the Ministry of Health and Welfare of Korea in 2007. The target population of the survey was noninstitutionalized people aged ≥ 1 year in Korea. Sampling units were households selected through a stratified, multistage, probability-sampling design based on geographic area, sex, and age group using household registries. In this study, 6,455 subjects from 2,300 households were included. One-hundred sampling frames, consisting of 2,300 households from the primary sampling units, were randomly sampled. Of these, 4,594 subjects (71.2%) were included. Weights indicating the probability of being sampled were assigned to each participant, enabling the results to represent the entire Korean population. Participants completed a questionnaire comprising four parts: health interview, health behavior, health examination, and nutrition. The survey on health examination was completed by 4,264 (65.8%) of 6,455 individuals who had taken part in the health interview survey. In this survey, pulmonary function tests were performed on individuals aged ≥ 19 years. Individuals with CVD, cancer, asthma or chronic obstructive pulmonary disease (COPD) were excluded from the study. Subjects with white blood cell count > 10,000 (cells/μL) were also excluded because of any possible undetected acute disease. As a result, a total of 2,614 subjects were included in the final analysis. This study was approved by the Institutional Review Board of Yonsei University College of Medicine in Seoul, Korea.

Data collection

When the 2007 KNHANES was conducted, candidate participants were informed that they had been randomly selected to voluntarily participate in the national representative survey conducted by the Ministry of Health and Welfare of Korea in 2007, and that they were also given the right to refuse to participate in accordance with the National Health Enhancement Act supported by the National Statistics Law of Korea. A written informed consent was obtained from the subjects. The Korea Centers for Disease Control and Prevention also obtained written informed consent to use their sera for further analysis. The health examinations in 2007 included a medical history, physical examination results, a questionnaire about health-related behavior, anthropometric measurement, and biochemical measurements. Physical examinations were performed by trained medical staff following a standardized procedure. Participants were asked about lifestyle behaviors, including cigarette smoking, alcohol consumption, and current treatment for any disease. If they were being treated for any disease, they were asked for the data of diagnosis and the list of medications being taken. Completed questionnaires were reviewed by trained staff and entered into the database. Body weight and height were measured in light indoor clothing without shoes to the nearest 0.1 kg and 0.1 cm, respectively. Body mass index was calculated as the ratio of weight (kg)/height^2 (m^2). Blood pressure was measured in the right arm using a standard mercury sphygmomanometer (Baumanometer, USA). Systolic and diastolic blood pressure readings were recorded twice with a 5-min interval and averaged for analysis. After a 12-h overnight fast, blood samples were obtained from the antecubital vein. Fasting plasma glucose, total cholesterol, triglyceride, high-density lipoprotein (HDL) cholesterol, aspartate aminotransferase (AST), alanine aminotransferase (ALT), and creatinine were measured using an ADVIA1650 autoanalyzer (Siemens Medical Solutions Diagnostics, Erlangen, Germany).

Spirometry

Pulmonary function tests were performed using a Model 1022 Spirometer (SensorMedics, USA). The same technician performed all spirometric tests to reduce inter-rater variability. Forced vital capacity (FVC) and forced expiratory volume in 1 second (FEV_1) from the best tests, as defined by the American Thoracic Society [12] were recorded. Published prediction equations were used to calculate predicted FEV_1 and FVC for each subject. Percentages of predicted FVC (FVC (%)) were calculated.

Table 1 Clinical characteristics of the study population

Variables	Men			Women		
	With MetS	Without MetS	*p* value	With MetS	Without MetS	*p* value
N	332	727		471	1084	
Age, year	53.4 ± 14.3	46.6 ± 16.4	<0.001	59.9 ± 13.6	43.4 ± 15.3	<0.001
Body mass index, kg/m^2	26.0 ± 2.8	23.0 ± 2.6	<0.001	25.8 ± 3.1	22.3 ± 2.9	<0.001
Waist circumference, cm	91.3 ± 6.8	81.7 ± 7.3	<0.001	88.2 ± 7.8	76.4 ± 8.5	<0.001
Systolic BP, mmHg	128.7 ± 15.0	116.7 ± 14.0	<0.001	127.1 ± 18.9	108.5 ± 14.4	<0.001
Diastolic BP, mmHg	82.7 ± 10.7	76.8 ± 8.6	<0.001	77.8 ± 9.5	71.0 ± 8.8	<0.001
Total cholesterol, mg/dL	192.5 ± 34.2	184.9 ± 33.4	<0.001	202.6 ± 36.3	181.9 ± 33.8	<0.001
Triglyceride, mg/dL	207.8 ± 98.2	119.1 ± 61.6	<0.001	171.4 ± 84.8	92.6 ± 42.7	<0.001
HDL cholesterol, mg/dL	35.2 ± 7.2	42.2 ± 9.8	<0.001	37.7 ± 6.9	46.6 ± 10.1	<0.001
Fasting plasma glucose, mg/dL	110.0 ± 32.4	92.4 ± 15.5	<0.001	106.6 ± 29.7	88.2 ± 9.0	<0.001
WBC, cells/μL	6929 ± 1428	6617 ± 1424	0.001	6285 ± 1494	5884 ± 1458	<0.001
AST, IU/L	30.5 ± 16.6	26.4 ± 13.1	<0.001	25.0 ± 9.3	21.6 ± 14.1	<0.001
ALT, IU/L	33.5 ± 24.5	26.0 ± 14.5	<0.001	23.8 ± 12.9	19.0 ± 12.8	<0.001
Cr, mg/dL	1.1 ± 0.2	1.1 ± 0.1	0.001	0.9 ± 0.1	0.8 ± 0.1	<0.001
Current smoker, %	125 (37.7%)	288 (39.6%)	0.543	20 (4.2%)	35 (3.2%)	0.318

All values except current smoker are expressed as mean ± SD. *p* values from t-test for continuous outcomes comparing a difference between the two study groups. BP, blood pressure; HDL, high density lipoprotein; AST, aspartate alaninetransferase; ALT, alanine aminotransferase; WBC, white blood cell; Cr, creatinine.

Men predicted FVC = 0.148 Height $_{inch}$ - 0.025 Age - 4.241
predicted FEV_1 = 0.092 Height $_{inch}$ - 0.032 Age - 1.260
Women predicted FVC = 0.115 Height $_{inch}$ - 0.024 Age - 2.852
predicted FEV_1 = 0.089 Height $_{inch}$ - 0.025 Age - 1.932

Definition of metabolic syndrome

Definitions of the MetS and its components are based on the National Cholesterol Education Program Adult Treatment Panel Ⅲ, and we used ethnicity-specific values for waist circumference based on the data from the World Health Organization and the Korean Society for the Study of Obesity [13]. Therefore, MetS was defined by the presence of 3 or more of the following risk factors: (1) central obesity (waist circumference ≥ 90 cm for men and ≥ 80 cm for women; (2) systolic BP ≥ 130 mmHg and diastolic BP ≥ 85 mmHg; (3) fasting plasma glucose, FPG ≥ 100 mg/dL; (4) triglyceride, TG ≥ 150 mg/dL; and (5) low HDL-cholesterol (≤ 40 mg/dL for men and ≤ 50 mg/dL for women). Subjects who reported taking antihypertensive or antidiabetes medications were considered to have elevated blood pressure or high fasting plasma glucose.

Statistical analysis

We separated all data by gender in all analyses because the equations used to calculate predicted FVC and FEV_1 differed by sex. The basic characteristics of the study population according to the presence of MetS were compared using independent two sample t-test for continuous variables and chi-square test for categorical variables. The FVC (%) and FEV_1/FVC were also compared using independent two sample t-test according to each component of the MetS. Pearson's correlation coefficients were determined for FVC (%) and FEV_1/FVC versus age, height, weight, waist circumference, blood pressure, BMI, glucose, cholesterol, triglyceride, and HDL cholesterol in men and women. Multivariate linear regression analyses were conducted to assess independent relationships between each component of MetS and FVC (%) and FEV_1/FVC. All analyses were conducted using SAS statistical software, version 9.1 (SAS Institute Inc, Cary, NC, USA). All statistical tests were two-sided, and a p value < 0.05 was considered significant.

Results

Table 1 shows the characteristics of 1,059 men and 1,555 women with the mean age of 48.8 ± 16.1 years for men and 48.4 ± 16.6 years for women. The mean body mass index, waist circumference, systolic and diastolic blood pressures, fasting plasma glucose, total cholesterol, triglycerides, WBC count, AST, ALT, and creatinine were higher in subjects with MetS than in subjects without MetS for both men and women. The overall prevalence of MetS according to the modified

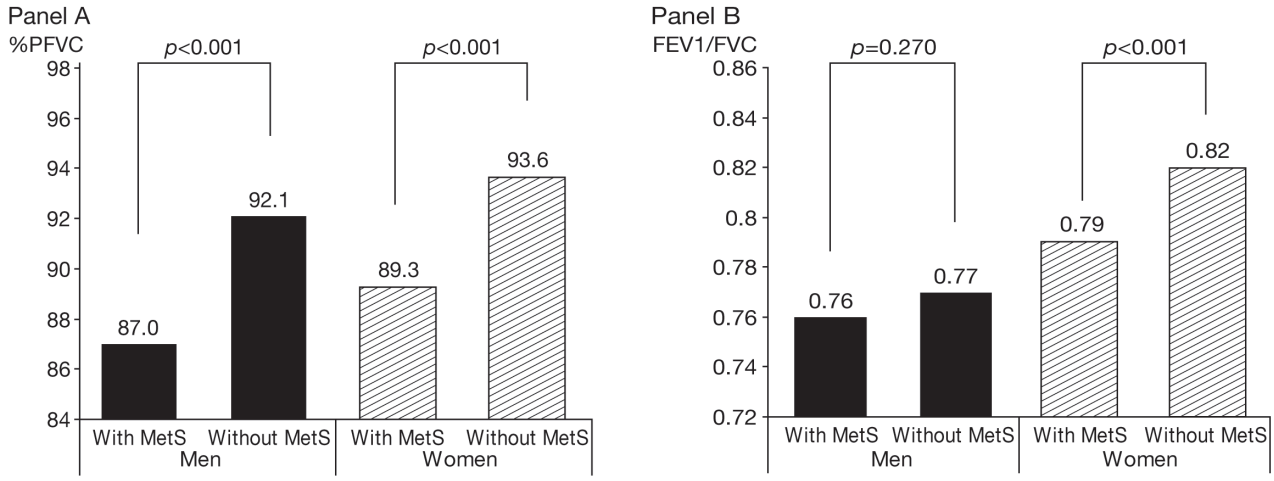

Fig. 1 Comparison of FVC (%) and FEV_1/FVC according to the diagnosis of metabolic syndrome (MetS) in men (A) and women (B).

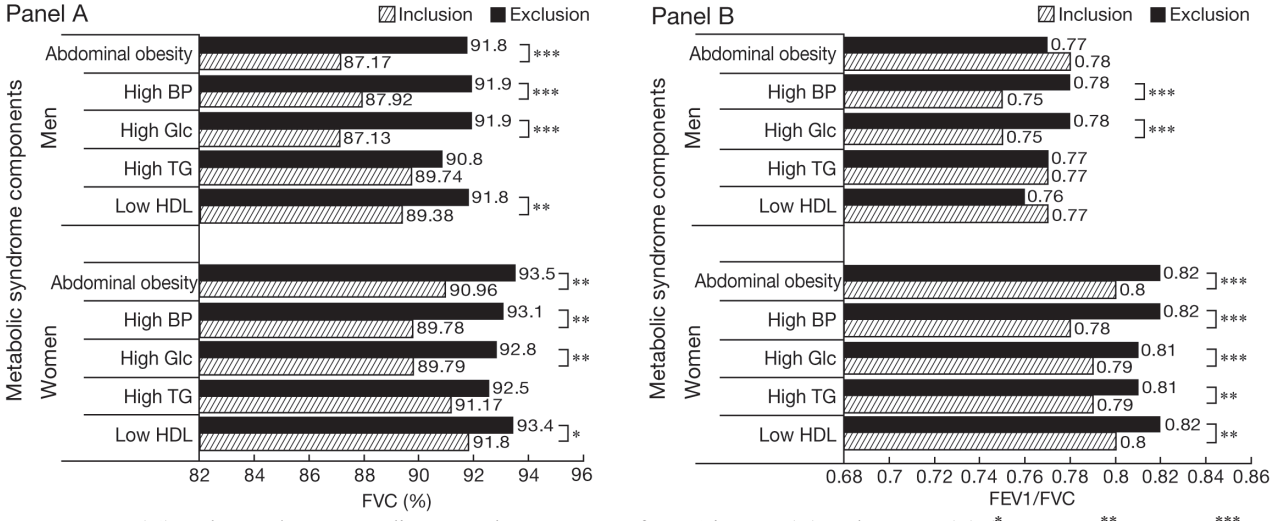

Fig. 2 FVC (%) and FEV_1/FVC according to each component of MetS in men (A) and women (B) ($^{*}p < 0.05$; $^{**}p < 0.01$; $^{***}p < 0.0001$).

NCEP-ATP Ⅲ criteria was 30.7%, which is higher in men (31.4%) than in women (30.4%) ($p < 0.001$).

Fig. 1 presents the mean values of FVC (%) and the FEV_1/FVC ratio according to the diagnosis of MetS. For both men and women, FVC (%) was significantly lower in subjects with MetS than in those without MetS ($p < 0.001$). FEV_1/FVC was significantly lower in subjects with MetS than in those without MetS only for women ($p < 0.001$).

Fig. 2 illustrates the mean values of FVC (%) and the FEV_1/FVC ratio according to each component of MetS. For both men and women, FVC (%) was significantly lower when abdominal obesity, high blood pressure, high fasting plasma blood glucose, and low-HDL cholesterol were included. FEV_1/FVC was significantly lower when high blood pressure and high fasting plasma glucose were included in men, while it was significantly lower when all MetS components were included in women.

The results of Pearson's correlation analyses are listed in Table 2. FVC (%) significantly correlated with age, height, waist circumference, body mass index, blood pressure, fasting plasma glucose, and HDL-cholesterol in both men and women. FVC (%) significantly correlated with weight only in men, and with total cholesterol only in women. FEV_1/FVC significantly correlated with age, height, body mass index, blood pressure, and fasting plasma glucose in both men and women.

Table 2 Correlation coefficients between % predicted FVC, FEV_1/FVC and other variables

Variables	FVC (%)		FEV_1/FVC	
	Men	Women	Men	Women
Age	-0.25 (p <0.001)	-0.14 (p <0.001)	-0.56 (p <0.001)	-0.49 (p <0.001)
Height	0.17 (p <0.001)	0.08 (p =0.004)	0.25 (p <0.001)	0.24 (p <0.001)
Weight	-0.01 (p <0.001)	-0.05 (p =0.09)	0.26 (p <0.001)	0.02 (p =0.56)
Waist circumference	-0.18 (p <0.001)	-0.15 (p <0.001)	0.03 (p =0.41)	-0.18 (p <0.001)
BMI	-0.13 (p <0.001)	-0.11 (p <0.001)	0.17 (p <0.001)	-0.11 (p <0.001)
Systolic BP	-0.16 (p <0.001)	-0.12 (p <0.001)	-0.22 (p <0.001)	-0.31 (p <0.001)
Fasting plasma glucose	-0.14 (p <0.001)	-0.06 (p =0.048)	-0.09 (p =0.01)	-0.16 (p <0.001)
Total cholesterol	0.01 (p =0.68)	-0.06 (p =0.04)	0.03 (p =0.46)	-0.15 (p <0.001)
Triglyceride	-0.04 (p =0.26)	-0.06 (p =0.06)	-0.01 (p =0.84)	-0.16 (p <0.001)
HDL cholesterol	0.12 (p <0.001)	0.07 (p =0.02)	-0.05 (p =0.13)	0.13 (p <0.001)

Pearson's correlation coefficients were determined for %PFVC and FEV_1/FVC ratio versus age, height, weight, waist circumference, BMI, systolic BP, fasting plasma glucose, total cholesterol, triglyceride and HDL cholesterol in men and women. BMI, body mass index; BP, blood pressure; HDL, high density lipoprotein

Table 3 Results of multiple linear regression analysis to assess independent relationships between FVC (%), FEV_1/FVC and clinical variables

Variables	FVC (%)				FEV1/FVC			
	Men		Women		Men		Women	
	β	SE	β	SE	β	SE	β	SE
Current smoking	0.77	1.14	1.67	1.15	-0.03**	0.009	-0.016*	0.007
Waist circumference	-0.17**	0.059	-0.15**	0.04	0.0007	0.0005	-0.0001	0.0002
Fasting plasma glucose	-0.056**	0.021	-0.008	0.02	-0.0003	0.0002	-0.0003*	0.0001
Systolic BP	-0.12***	0.030	-0.04	0.02	-0.001***	0.0002	-0.001***	0.0001
Total cholesterol	0.0031	0.015	-0.009	0.01	0.0001	0.0001	-0.0001*	0.00007
Triglyceride	0.0086	0.006	0.004	0.006	0.000003	0.00005	-0.000004	0.00004
HDL-cholesterol	0.14**	0.05	0.04	0.04	-0.0003	0.0004	0.0006*	0.0003

* p <0.05, ** p <0.01, *** p <0.0001. BP, blood pressure; HDL, high density lipoprotein

Meanwhile, FEV_1/FVC correlated with weight only in men and with waist circumference, total cholesterol, triglyceride and HDL-cholesterol in women.

Table 3 shows the results of multivariate linear regression analyses of the relationship between each component of MetS and pulmonary function. Among components of MetS, waist circumference, blood pressure and fasting plasma glucose, and HDL-cholesterol were independently related to FVC (%) in men, whereas waist circumference was significantly associated with FVC (%) in women. Blood pressure was found to be an independent factor of MetS in men, whereas blood pressure, fasting plasma glucose and HDL-cholesterol were independent factors of MetS in determining FEV_1 in women. Moreover, cigarette smoking was associated with lower FEV_1/FVC with the magnitude of effect being stronger in men.

Discussion

In this cross-sectional study, we investigated whether the association between MetS and pulmonary function were different by gender. FVC (%) was significantly lower in subjects with MetS than in those without MetS for men, whereas both FVC (%) and FEV_1/FVC were lower in subjects with MetS in women. In multivariate linear regression analyses, most but not all components of MetS were independently associated with FVC (%) in men and were related to FEV_1/FVC in women after adjusting for confounding factors.

In previous studies in Italy, Taiwan and Japan, MetS was independently associated with impaired

pulmonary function in a particularly restrictive pattern, measured by FVC (%) [14-16]. Moreover, abdominal obesity was a major factor that determined the association between MetS and pulmonary function impairment [17]. However, in most previous studies, sex differences were not fully considered because they did not present the data through sex-specific analyses. Our study demonstrated that the relation between MetS and its components with regard to pulmonary function were found in sex-specific manners.

Some mechanisms could explain the significant relationships between MetS and impaired pulmonary function. First, insulin resistance, a core problem of MetS, might be the reason that MetS is related to pulmonary function. Previous studies have found that MetS is associated with endothelial dysfunction as well as microangiopathy of pulmonary vessels. Microangiopathy of alveolar capillaries and pulmonary arterioles plays a substantial role in pulmonary function impairment in subjects with type 2 diabetes independently of confounding factors such as cigarette smoking and obesity [18]. Second, chronic low-grade inflammation may be another mechanism to explain the association between MetS and pulmonary function. Moreover, some prospective studies suggested that impaired pulmonary function may be a potentially novel risk factor for CVD and type 2 diabetes [19, 20], where the underlying mechanisms were closely linked to an excess of oxidative stress and chronic low-grade inflammation [21, 22]. Inflammatory markers such as C-reactive protein (CRP) have been associated with impaired pulmonary function among subjects with MetS and diabetes [23, 24]. In the present study WBC count, a marker of nonspecific systemic inflammation, was also higher in subjects with MetS than in those without MetS (Table 1).

Another noteworthy finding in our study was that FEV_1/FVC in addition to FVC was significantly lower in subjects with MetS only for women (Fig. 1). Also, all parameters of MetS were statistically different in subjects with inclusion criteria of MetS compared to subjects with exclusion criteria of MetS in women (Fig. 2). Although the reason for the sex difference in the effect of MetS on pulmonary function is unclear, some explanations may be offered. There is a marked sexual dimorphism in the structural and functional capacity of the pulmonary system. It has been suggested that sex differences in lung function can be explained by a fewer total number of alveoli and smaller airway diameter relative to lung size in women [25, 26]. Given the pulmonary structural and functional differences, women could be more susceptible to a lower FEV_1/FVC when cardiometabolic risk factors were clustered. Another possible explanation may be offered by the role of sex hormones. Estrogen may modify pulmonary function in women, which may, in turn, affect their pulmonary function. Gibbs *et al*. [27] reported that women have a decline in pulmonary function and deterioration in asthma symptoms before and during menstruation. In addition, Chandler *et al*. [28] reported that the use of oral contraceptive improved pulmonary function and symptoms in asthmatic women. Thus, the interactions between sex hormone and pulmonary function might also potentially provide a mechanism to link sex-specific association between MetS and pulmonary function.

Our study has limitations. Since it is a cross-sectional study, it cannot be concluded whether MetS is a risk factor actively involved in the development of pulmonary function impairment. Further prospective and experimental research is warranted to better understand a pathophysiologic role of MetS in the development of pulmonary impairment. Another limitation is that insulin resistance was not measured, for example, using the homeostasis model assessment of insulin resistance (HOMA-IR) index, and thus no direct relationship between insulin sensitivity and pulmonary function was demonstrated.

In conclusion, we found that there exist sex differences in the relationship between MetS and its components regarding pulmonary function. These findings suggest that sex-specific association between MetS and lung function measures should be considered in clinical practice.

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Author Disclosure Statement

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References

1. Moller DE, Kaufman KD (2005) Metabolic syndrome: a clinical and molecular perspective. *Annual Rev Med* 56: 45-62.
2. Klein BE, Klein R, Lee KE (2002) Components of the metabolic syndrome and risk of cardiovascular disease and diabetes in Beaver Dam. *Diabetes Care* 25(10): 1790-1794.
3. Isomaa B, Almgren P, Tuomi T, Forsén B, Lahti K, Nissén M, Taskinen MR, Groop L (2001) Cardiovascular morbidity and mortality associated with the metabolic syndrome. *Diabetes Care* 24(4): 683-689.
4. Cameron AJ, Shaw JE, Zimmet PZ (2004) The metabolic syndrome: prevalence in worldwide populations. *Endocrinol Metab Clin North Am* 2004;33(2): 351-375.
5. Schünemann HJ, Dorn J, Grant BJ, Winkelstein W Jr., Trevisan M (2000) Pulmonary function is a long-term predictor of mortality in the general population: 29-year follow-up of the Buffalo Health Study. *Chest* 118(3): 656-664.
6. Sin DD, Wu L, Man SF (2005) The relationship between reduced lung function and cardiovascular mortality: a population-based study and a systematic review of the literature. *Chest* 127(6): 1952-1959.
7. McClean KM, Kee F, Young IS, Elborn JS (2008) Obesity and the lung: 1. Epidemiology. *Thorax* 63(7): 649-654.
8. Yeh HC, Punjabi NM, Wang NY, Pankow JS, Duncan BB, Brancati FL (2005) Vital capacity as a predictor of incident type 2 diabetes: the Atherosclerosis Risk in Communities study. *Diabetes Care* 28(6): 1472-1479.
9. Lawlor DA, Ebrahim S, Smith GD (2004) Associations of measures of lung function with insulin resistance and type 2 diabetes: findings from the British Women's Heart and Health Study. *Diabetologia* 47(2): 195-203.
10. Crapo RO, Morris AH, Gardner RM (1982) Reference values for pulmonary tissue volume, membrane diffusing capacity, and pulmonary capillary blood volume. *Bull Eur Physiopathol Respir* 18(6): 893-899.
11. Gallop Korea. Cigarette smoking survey among adults. Seoul, South Korea: The Korea Gallup Report, 2004.
12. Standardization of Spirometry, 1994 Update. American Thoracic Society (1995) *Am J Respir Crit Care Med* 152(3): 1107-1136.
13. Lee SY, Park HS, Kim DJ, Han JH, Kim SM, Cho GJ, Kim DY, Kwon HS, Kim SR, Lee CB, Oh SJ, Park CY, Yoo HJ (2007) Appropriate waist circumference cutoff points for central obesity in Korean adults. *Diabetes Res Clin Pract* 75(1): 72-80.
14. Fimognari FL, Pasqualetti P, Moro L, Franco A, Piccirillo G, Pastorelli R, Rossini PM, Incalzi RA (2007) The association between metabolic syndrome and restrictive ventilatory dysfunction in older persons. *J Gerontol A Biol Sci Med Sci* 62(7): 760-765.
15. Lin WY, Yao CA, Wang HC, Huang KC (2006) Impaired lung function is associated with obesity and metabolic syndrome in adults. *Obesity* 14(9): 1654-1661.
16. Nakajima K, Kubouchi Y, Muneyuki T, et al (2008) A possible association between suspected restrictive pattern as assessed by ordinary pulmonary function test and the metabolic syndrome. *Chest* 134: 712-718.
17. Leone N, Courbon D, Thomas F, Ebata M, Eguchi S, Munakata H (2009) Lung function impairment and metabolic syndrome: the critical role of abdominal obesity. *Am J Respir Crit Care Med* 179(4): 509-516.
18. Klein OL, Krishnan JA, Glick S, Smith LJ (2010) Systematic review of the association between lung function and Type 2 diabetes mellitus. *Diabet Med* 27(9): 977-987.
19. Lazarus R, Sparrow D, Weiss ST (1998) Impaired ventilatory function and elevated insulin levels in nondiabetic males: the Normative Aging Study. *Eur Respir J* 12(3): 635-640.
20. Lazarus R, Sparrow D, Weiss ST (1998) Baseline ventilatory function predicts the development of higher levels of fasting insulin and fasting insulin resistance index: the Normative Aging Study. *Eur Respir J* 12(3): 641-645.
21. Nakanishi N, Yoshida H, Matsuo Y, Suzuki K, Tatara K (2002) White blood-cell count and the risk of impaired fasting glucose or Type II diabetes in middle-aged Japanese men. *Diabetologia* 45(1): 42-48.
22. Hotamisligil GS (2006) Inflammation and metabolic disorders. *Nature* 444(7121): 860-867.
23. Kony S, Zureik M, Driss F, Neukirch C, Leynaert B, Neukirch F (2004) Association of bronchial hyperresponsiveness and lung function with C-reactive protein (CRP): a population based study. *Thorax* 59(10): 892-896.
24. Mannino DM, Ford ES, Redd SC (2003) Obstructive and restrictive lung disease and markers of inflammation: data from the Third National Health and Nutrition Examination. *Am J Med* 114(9): 758-762.
25. Harms CA (2006) Does gender affect pulmonary function and exercise capacity? *Respir Physiol Neurobiol* 28: 124-131.
26. Mead J (1980) Dysanapsis in normal lungs assessed by the relationship between maximal flow, static recoil, and vital capacity. *Am Rev Respir Dis* 121(2): 339-342.
27. Gibbs CJ, Coutts II, Lock R, Finnegan OC, White RJ (1984) Premenstrual exacerbation of asthma. *Thorax* 39(11): 833-836.
28. Chandler MH, Schuldheisz S, Phillips BA, Muse KN (1997) Premenstrual asthma: the effect of estrogen on symptoms, pulmonary function, and beta 2-receptors. *Pharmacotherapy* 17(2): 224-234.