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Metabolic syndrome and lung function in Korean children and adolescents: A cross-sectional study

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This study aimed to investigate whether obesity and metabolic syndrome (MetS) are associated with pulmonary function in Korean children and adolescents. Data from the 2009–2011 Korea National Health and Nutrition Examination Survey which is cross-sectional, nationwide, and representative survey were used. Adjusted regression analysis was performed to evaluate the association of obesity and MetS with lung function in children and adolescents. A total of 763 children and adolescents aged 10–18 years were evaluated. We found no significant difference in FEV₁% predicted, FVC% predicted, and FEV₁/FVC ratio among the obesity groups. Subjects with MetS showed a significantly lower FEV₁ predicted ($91.54 \pm 0.74\%$ vs $94.64 \pm 0.73\%$, $P = 0.004$), lower FVC% predicted ($91.86 \pm 0.63\%$ vs $95.20 \pm 0.63\%$, $P < 0.001$), and lower FEV₁/FVC ratio ($76.76 \pm 0.43\%$ vs $80.13 \pm 0.43\%$, $P < 0.001$) than those without MetS. Elevated waist circumference (WC), systolic blood pressure, fasting glucose, and lower high-density lipoprotein cholesterol (HDL-C) were independently associated with lower FEV₁/FVC ratio (all $P < 0.05$, respectively). Among MetS components, increased WC was the most important factor influencing lower FEV₁/FVC ratio. In conclusion, lung function in MetS patients was significantly lower, and the MetS component was independently associated.

Obesity is a worldwide public health issue with increasing incidence¹. In the US, approximately 35% of adults and 17% of children and adolescents are obese². The prevalence of overweight or obesity in Korean adolescents has significantly increased from 16.4% in 1998 to 24.2% in 2005³. Metabolic syndrome (MetS) is a common metabolic disorder that can result from obesity⁴. MetS is defined as abdominal obesity, hypertension, dyslipidemia, and glucose intolerance⁵. In the US, roughly more than 20% of the population and 60% of obese people have MetS⁶. In Korea, MetS is prevalent in 5.7% of adolescents and in 30.5% of adults^{7,8}. Research interest to MetS-related diseases has been increasing owing to the increasing incidence of obesity and MetS.

Overweight and obesity are associated with lower lung function in adults, but whether such association also exists in children is unclear^{9,10}. Studies have reported that obesity in children and adolescents is associated with a high forced expiratory volume in the 1st second (FEV₁) and forced vital capacity (FVC) and a lower FEV₁/FVC¹⁰. However, one study reported that obese non-asthma children showed lower residual capacity, residual volume, and expiratory reserve volume than their non-obese counterparts¹¹. Further, other studies have reported no significant association between obesity and pulmonary function¹².

The association between MetS and pulmonary function is also controversial. One cross-sectional study in France reported that MetS is associated with lower FEV₁ or FVC¹³, and another study reported that MetS is associated with significant restrictive pattern of lung function¹⁴. Although increasing evidence indicates that MetS may be associated with lung disease, the mechanisms behind this association are complex and are yet to be clearly understood. Moreover, although the respiratory system of children is different from that of adults, studies about the association between lung function and MetS in children and adolescent are scarce.

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	Total	Normal weight	Overweight	Obesity	P
	(n = 763)	(n = 304)	(n = 235)	(n = 224)	
Male (%)	414 (54.3%)	197 (64.8%)	134 (57.0%)	83 (37.1%)	<0.001
Age (years)	13.61 ± 0.09	14.61 ± 0.13	13.51 ± 0.15	12.36 ± 0.14	<0.001
Height SDS	0.88 ± 0.08	0.10 ± 0.11	1.03 ± 0.13	1.79 ± 0.13	<0.001
Weight SDS	1.28 ± 0.04	0.33 ± 0.06	1.48 ± 0.05	2.36 ± 0.05	<0.001
BMI SDS	1.18 ± 0.03	0.43 ± 0.03	1.33 ± 0.01	2.05 ± 0.02	<0.001
WC SDS	1.27 ± 0.03	0.59 ± 0.04	1.43 ± 0.03	2.04 ± 0.03	<0.001
SBP (mmHg)	123.5 ± 0.61	120.67 ± 0.96	123.28 ± 1.08	127.58 ± 1.11	<0.001
DBP (mmHg)	78.82 ± 0.38	76.70 ± 0.60	79.23 ± 0.65	81.26 ± 0.69	<0.001
Glucose (mg/dL)	99.25 ± 0.78	96.84 ± 1.12	100.66 ± 1.72	101.03 ± 1.22	0.043
T-C (mg/dL)	191.77 ± 1.36	185.88 ± 1.98	193.34 ± 2.44	198.13 ± 2.71	0.001
HDL-C (mg/dL)	47.96 ± 0.43	49.94 ± 0.71	47.66 ± 0.77	45.59 ± 0.74	<0.001
TG (mg/dL)	141.74 ± 3.89	128.28 ± 6.98	144.96 ± 6.68	156.62 ± 5.88	0.009
LDL-C (mg/dL)	116.69 ± 1.21	111.77 ± 1.73	117.77 ± 2.20	122.26 ± 2.46	0.001
Alcohol drinking (%)	321 (42.1%)	119 (39.1%)	108 (44.7%)	97 (43.3%)	0.394
Smoking (%)	141 (18.5%)	58 (19.1%)	40 (17.0%)	43 (19.2%)	0.786
Physical activity (%)	381 (49.9%)	139 (45.7%)	127 (54.0%)	115 (51.3%)	0.141
Household income (≤lowest quartile, %)	101 (13.2%)	48 (15.8%)	27 (11.5%)	6 (11.6%)	0.238
Residence (rural, %)	117 (15.3%)	48 (15.8%)	38 (16.2%)	31 (13.8%)	0.756
Hypertension (%)	199 (26.1%)	52 (17.1%)	62 (26.4%)	85 (37.9%)	<0.001
Dyslipidaemia (%)	101 (13.2%)	26 (8.6%)	37 (15.7%)	38 (17.0%)	0.007
Diabetes (%)	60 (7.9%)	19 (6.3%)	22 (9.4%)	19 (8.5%)	0.379
Asthma (%)	22 (2.9%)	5 (1.6%)	7 (3.0%)	10 (4.5%)	0.159
Atopic dermatitis (%)	13 (1.7%)	5 (1.6%)	2 (0.9%)	6 (2.7%)	0.317
FEV ₁ (%)	93.10 ± 0.51	91.71 ± 0.85	93.96 ± 0.85	94.06 ± 0.91	0.029
FVC (%)	93.54 ± 0.43	94.09 ± 0.71	94.49 ± 0.70	91.79 ± 0.81	0.084
FEV ₁ /FVC (%)	78.73 ± 8.18	78.33 ± 9.30	78.04 ± 7.62	78.98 ± 7.04	0.439

Table 1. Clinical characteristics of the study population according to the obesity in Korean boys and girls aged 10–18 years (n = 763). SDS, standard deviation score; BMI, body mass index; WC, waist circumference; SBP, systolic blood pressure; DBP, diastolic blood pressure; T-C, total cholesterol; HDL-C, high-density lipoprotein cholesterol; TG, triglyceride; LDL-C, low-density lipoprotein cholesterol; FEV₁, forced expiratory volume in one second; FVC, forced vital capacity; FVC forced vital capacity. Statistical significance was determined using a one-way ANOVA for continuous variables and a chi-square test for categorical variables (P < 0.05).

Therefore, the purpose of this study was to analyze the association of obesity and MetS with pulmonary function to help understand the mechanism by which obesity or MetS influences pulmonary function in children and adolescents and provide a basis for establishing related health policies in the future.

Results

Clinical characteristics of the study participants. Of the 1,958 subjects aged 10–18 years identified, those who had no data for anthropometrical information (n = 160), BMI and blood pressure (n = 317), and pulmonary function test (n = 717) were excluded. Thus, 763 children and adolescents aged 10–18 years (414 males and 349 females) were included in this study. The clinical characteristics of the study population are summarized in Table 1. The mean age was 13.61 ± 0.09 years. In total, 235 (30.8%) and 224 (29.4%) participants were overweight and obese, respectively. Compared with the normal weight group, the overweight and obesity groups were younger (P < 0.001), more likely to be female (P < 0.001), and taller (P < 0.001). Blood pressure (P < 0.001), serum glucose (P = 0.043), total cholesterol (P = 0.001), TG (P = 0.009), and LDL-C (P = 0.001) were significantly different between the three groups, whereas no significant differences in alcohol drinking, smoking, physical activity, household income, the prevalence of diabetes, atopic dermatitis, and asthma were noted.

With respect to pulmonary function test, FEV₁% predicted was significantly lower in the normal weight group than that in the obesity group, while FVC% predicted and FEV₁/FVC ratio was not significantly different between these two groups.

The clinical characteristics of the study population according to the presence of MetS are summarized in Table 2. The overall prevalence of MetS was 49.8% (n = 380). Patients with the MetS were significantly younger (P < 0.001) and were less often male (P = 0.019) compared to participants without MetS. Metabolic components such as systolic blood pressure (SBP) (P < 0.001), diastolic blood pressure (DBP) (P < 0.001), waist circumference (WC) (P < 0.001), serum fasting glucose (P < 0.001), and serum triglyceride (TG) (P < 0.001) were significantly higher while HDL-C (P < 0.001) was significantly lower in participants with MetS than in those without MetS. Meanwhile, there was no significant difference in alcohol drinking, smoking, physical activity, household income, the presence of atopic dermatitis, and asthma between subjects with and without MetS. With respect

	Total	No MetS	MetS	P
	(n = 763)	(n = 383)	(n = 380)	
Male (%)	414	224 (58.5%)	190 (150.0%)	0.019
Age (years)	13.61 ± 0.09	13.85 ± 0.12	13.37 ± 0.13	<0.001
Height SDS	0.88 ± 0.08	0.53 ± 0.10	1.24 ± 0.11	<0.001
Weight SDS	1.28 ± 0.04	0.88 ± 0.06	1.69 ± 0.06	<0.001
BMI SDS	1.18 ± 0.03	0.87 ± 0.04	1.50 ± 0.03	<0.001
WC SDS	1.27 ± 0.03	0.85 ± 0.04	1.70 ± 0.03	<0.001
SBP (mmHg)	123.5 ± 0.61	117.84 ± 0.81	129.21 ± 0.82	<0.001
DBP (mmHg)	78.82 ± 0.38	76.11 ± 0.54	81.55 ± 0.48	<0.001
Glucose (mg/dL)	99.25 ± 0.78	92.90 ± 0.62	105.64 ± 1.37	<0.001
T-C (mg/dL)	191.77 ± 1.36	187.48 ± 1.73	196.09 ± 2.08	0.002
HDL-C (mg/dL)	47.96 ± 0.43	52.62 ± 0.58	43.26 ± 0.54	<0.001
TG (mg/dL)	141.74 ± 3.89	100.22 ± 3.21	183.58 ± 6.42	<0.001
LDL-C (mg/dL)	116.69 ± 1.21	115.10 ± 1.57	118.34 ± 1.86	0.182
Alcohol drinking (%)	321 (42.1%)	154 (40.2%)	167 (43.9%)	0.296
Smoking (%)	141 (18.5%)	66 (17.2%)	75 (19.7%)	0.373
Physical activity (%)	381 (49.9%)	185 (48.3%)	196 (51.6%)	0.366
Household income (≤lowest quartile, %)	101 (13.2%)	56 (14.6%)	45 (11.8%)	0.257
Residence (rural, %)	117 (15.3%)	59 (15.4%)	58 (13.3%)	0.957
Hypertension (%)	199 (26.1%)	48 (12.5%)	151 (39.7%)	<0.001
Dyslipidaemia (%)	101 (13.2%)	6 (1.6%)	95 (25.0%)	<0.001
Diabetes (%)	60 (7.9%)	7 (1.8%)	53 (13.9%)	<0.001
Asthma (%)	22 (2.9%)	9 (2.3%)	13 (3.4%)	0.377
Atopic dermatitis (%)	13 (1.7%)	6 (1.6%)	7 (1.8%)	0.769
FEV ₁ (%)	93.10 ± 0.51	95.33 ± 0.57	91.73 ± 0.63	<0.001
FVC (%)	93.54 ± 0.43	94.06 ± 0.68	92.12 ± 0.75	0.055
FEV ₁ /FVC (%)	78.43 ± 0.29	80.07 ± 0.45	76.83 ± 0.45	<0.001

Table 2. Clinical characteristics of the study population according to the presence of metabolic syndrome (MetS) in Korean boys and girls aged 10–18 years ($n = 763$). The data are shown as the means ± SEs (standard errors). MetS, metabolic syndrome; SDS, standard deviation score; BMI, body mass index; WC, waist circumference; SBP, systolic blood pressure; DBP, diastolic blood pressure; T-C, total cholesterol; HDL-C, high-density lipoprotein cholesterol; TG, triglyceride; LDL-C, low-density lipoprotein cholesterol; FEV₁, forced expiratory volume in one second; FVC, forced vital capacity. Statistical significance was determined using independent *t*-test for continuous variables and a chi-square test for categorical variables ($P < 0.05$).

to pulmonary function test, FEV₁% predicted (91.73 ± 0.63 vs. 95.33 ± 0.57 , $P < 0.001$) and FEV₁/FVC ratio (76.83 ± 0.45 vs. 80.07 ± 0.45 , $P < 0.001$) was significantly lower in those with MetS than those without MetS. Further, FVC% predicted tended to be lower in those with MetS (92.12 ± 0.75 vs. 94.06 ± 0.68 , $P = 0.055$).

Obesity and pulmonary function tests. After adjustment for age, sex, square of height (m^2), household income, alcohol drinking, smoking, physical activity, and atopic dermatitis, there were no significant differences in FEV₁ predicted ($93.40 \pm 1.21\%$ vs. $93.77 \pm 0.90\%$, $91.97 \pm 1.47\%$, $P = 0.529$), FVC% predicted ($94.36 \pm 1.04\%$ vs. $94.42 \pm 0.77\%$, $91.51 \pm 1.26\%$, $P = 0.125$), and FEV₁/FVC ratio ($78.51 \pm 0.72\%$ vs $78.06 \pm 0.54\%$, $78.80 \pm 0.88\%$, $P = 0.654$) between the normal weight group, the overweight group, and the obesity group (Table 3). In obese patients with asthma, FEV₁% predicted ($66.03 \pm 10.30\%$), FVC% predicted ($82.13 \pm 8.11\%$), and FEV₁/FVC ratio ($62.42 \pm 7.70\%$) were lower than those of normal weight patients with asthma, but the difference was not statistically significant.

Metabolic syndrome and pulmonary function tests. After adjustment for age, sex, square of height (m^2), weight (kg), household income, alcohol drinking, smoking, physical activity, and diagnosis of atopic dermatitis, subjects with MetS showed a significantly lower FEV₁ predicted ($91.54 \pm 0.74\%$ vs $94.64 \pm 0.73\%$, $P = 0.004$), FVC% predicted ($91.86 \pm 0.63\%$ vs $95.20 \pm 0.63\%$, $P < 0.001$), and lower FEV₁/FVC ratio ($76.76 \pm 0.43\%$ vs $80.13 \pm 0.43\%$, $P < 0.001$) than those without MetS (Table 4). In the no-asthma group, subjects with MetS had significantly lower FEV₁% predicted ($92.02 \pm 0.73\%$ vs $94.71 \pm 0.73\%$, $P = 0.013$), lower FVC% predicted ($92.01 \pm 0.64\%$ vs $95.18 \pm 0.63\%$, $P = 0.001$), and lower FEV₁/FVC ratio ($77.03 \pm 0.43\%$ vs $80.23 \pm 0.43\%$, $P < 0.001$) than those without MetS. Among subjects with or without MetS, those with self-reported asthma showed lower FEV₁ predicted ($77.12 \pm 5.34\%$ vs $92.96 \pm 6.76\%$, $P = 0.130$), FVC% predicted ($87.95 \pm 3.98\%$ vs $95.83 \pm 5.04\%$, $P = 0.299$), and FEV₁/FVC ratio ($69.03 \pm 12.74\%$ vs $76.25 \pm 9.81\%$, $P = 0.277$), but there were no statistically significant difference (Table 4).

	Normal weight	Overweight	Obesity	P
All Participants	<i>n</i> = 304	<i>n</i> = 235	<i>n</i> = 224	
FEV ₁ (%)	93.40 ± 1.21	93.77 ± 0.90	91.97 ± 1.47	0.529
FVC (%)	94.36 ± 1.04	94.42 ± 0.77	91.51 ± 1.26	0.125
FEV ₁ /FVC (%)	78.51 ± 0.72	78.06 ± 0.54	78.80 ± 0.88	0.654
No asthma	<i>n</i> = 299	<i>n</i> = 228	<i>n</i> = 214	
FEV ₁ (%)	93.52 ± 1.21	94.05 ± 0.90	92.46 ± 1.49	0.575
FVC (%)	94.39 ± 1.05	94.38 ± 0.79	91.69 ± 1.30	0.181
FEV ₁ /FVC (%)	78.60 ± 0.72	78.33 ± 0.53	79.04 ± 0.89	0.727
Asthma	<i>n</i> = 5	<i>n</i> = 7	<i>n</i> = 10	
FEV ₁ (%)	107.69 ± 11.97	91.48 ± 8.92	66.03 ± 10.30	0.156
FVC (%)	101.02 ± 9.43	97.06 ± 7.03	82.13 ± 8.11	0.511
FEV ₁ /FVC (%)	86.77 ± 8.95	75.10 ± 6.67	62.42 ± 7.70	0.261

Table 3. Adjusted means of forced expiratory volume in one second (FEV₁), forced vital capacity (FVC), and FEV₁/FVC according to the obesity in Korean boys and girls aged 10–18 years (*n* = 763). The data are shown as the means ± SEs (standard errors). MetS, metabolic syndrome; FEV₁, forced expiratory volume in one second; FVC, forced vital capacity. FEV₁, FVC, and FEV₁/FVC were adjusted for age, gender, square of height (m²), household income, alcohol drinking, smoking, residence, physical activity and atopic dermatitis. Statistical significance was determined using an analysis of covariance (ANCOVA).

	No MetS	MetS	P
All Participants	<i>n</i> = 383	<i>n</i> = 380	
FEV ₁ (%)	94.64 ± 0.73	91.54 ± 0.74	0.004
FVC (%)	95.20 ± 0.63	91.86 ± 0.63	<0.001
FEV ₁ /FVC (%)	80.13 ± 0.43	76.76 ± 0.43	<0.001
No asthma	<i>n</i> = 374	<i>n</i> = 367	
FEV ₁ (%)	94.71 ± 0.73	92.02 ± 0.73	0.013
FVC (%)	95.18 ± 0.63	92.01 ± 0.64	0.001
FEV ₁ /FVC (%)	80.23 ± 0.43	77.03 ± 0.43	<0.001
Asthma	<i>n</i> = 9	<i>n</i> = 13	
FEV ₁ (%)	92.96 ± 6.76	77.12 ± 5.34	0.130
FVC (%)	95.83 ± 5.04	87.95 ± 3.98	0.299
FEV ₁ /FVC (%)	76.25 ± 9.81	69.03 ± 12.74	0.277

Table 4. Adjusted means of forced expiratory volume in one second (FEV₁), forced vital capacity (FVC), and FEV₁/FVC according to the presence of metabolic syndrome (MetS) in Korean boys and girls aged 10–18 years (*n* = 763). The data are shown as the means ± SEs (standard errors). MetS, metabolic syndrome; FEV₁, forced expiratory volume in one second; FVC, forced vital capacity. FEV₁, FVC, and FEV₁/FVC were adjusted for age, gender, square of height (m²), weight (kg), household income, alcohol drinking, smoking, residence, physical activity and atopic dermatitis. Statistical significance was determined using an analysis of covariance (ANCOVA).

Metabolic syndrome components and FEV₁/FVC ratio. The results on the association between MetS components and FEV₁/FVC ratio are presented in Table 5. MetS components including elevated WC, elevated SBP, elevated fasting glucose, and low HDL-C were independently associated with lower FEV₁/FVC ratio (β coefficient; -0.243 , -0.160 , -0.111 , and -0.088 , respectively $P < 0.05$) after adjusting for age, sex, square of height (m²), weight (kg), household income, alcohol drinking, smoking, residence, physical activity, and atopic dermatitis. The direction and significance of all results for the non-asthmatic subjects remained the same with those of the overall cohort, whereas asthmatic subjects (*n* = 22) showed only elevated WC, and this was significantly related with lower FEV₁/FVC ratio (β coefficient; -0.602 , $P = 0.047$). In the normal weight group, MetS components including elevated WC, elevated SBP, and elevated fasting glucose were independently associated with lower FEV₁/FVC ratio (β coefficient; -0.230 , -0.196 , and -0.142 , respectively, $P < 0.05$) after adjusting for age, sex, square of height (m²), household income, alcohol drinking, smoking, residence, physical activity, and atopic dermatitis. The direction and significance of all results for the overweight/obese subjects were similar with those of normal weight subjects.

Discussion

This study showed that obesity was not significantly associated with pulmonary function but having MetS was significantly related with lower pulmonary function in a nationally representative population of children and adolescents in Korea. MetS was associated with lower lung function, regardless of obesity status, even in non-asthmatics. Among MetS components, WC was the most significant factor, and high SBP, high fasting glucose, and low HDL-C were significantly associated with lower FEV₁/FVC ratio.

	Elevated WC	P	Elevated BP	P	Elevated glucose	P	Elevated TG	P	Reduced HDL-C	P	MetS	P
All participants (<i>n</i> = 763)	−0.243	<0.001	−0.160	<0.001	−0.111	0.002	−0.033	0.370	−0.088	0.018	−0.205	<0.001
The presence of Asthma												
No-asthmatics (<i>n</i> = 741)	−0.238	<0.001	−0.160	<0.001	−0.090	0.015	−0.040	0.295	−0.102	0.006	−0.199	<0.001
Asthmatics (<i>n</i> = 22)	−0.602	0.047	−0.102	0.701	−0.552	0.038	0.146	0.604	0.603	0.098	−0.350	0.277
BMI criteria												
Normal weight (<i>n</i> = 304)	−0.230	<0.001	−0.196	0.001	−0.142	0.015	0.042	0.479	−0.082	0.169	−0.168	0.006
Overweight/obese (<i>n</i> = 459)	−0.191	<0.001	−0.112	0.017	−0.098	0.035	−0.086	0.067	−0.087	0.066	−0.210	<0.001

Table 5. Relationship between metabolic syndrome and its component and FEV₁/FVC in Korean boys and girls aged 10–18 years according to asthma status and obesity (*n* = 763). Statistical significance was determined using an analysis of multivariate linear regression analyses after adjustment for age, gender, square of height (m²), weight (kg), household income, alcohol drinking, smoking, residence, physical activity and atopic dermatitis. WC, waist circumference; BP, blood pressure; TG, triglyceride; HDL-C, high-density lipoprotein cholesterol; MetS, metabolic syndrome.

The relationship between obesity and pulmonary function in children and adolescents is controversial. In our study, there were no significant differences in FEV₁, FVC, and FEV₁/FVC ratio between the normal, the overweight, and the obesity groups. Some studies also demonstrated no difference in FEV₁, FVC, and FEV₁/FVC ratio between obese/overweight and normal weight children^{12,15}. However, in majority of studies, the lung functions of overweight/obese children were significantly associated with at least one of the spirometric variables, but the results are inconsistent^{10,11,16}. A recent meta-analysis found more pronounced FEV₁/FVC ratio deficit with unchanged FEV₁ or FVC in obese children and lower FEV₁, FVC, and total lung capacity in obese adults¹⁶. They reported that among obese subjects those with lower FEV₁/FVC ratio showed greater lung capacity than those with relatively higher FEV₁ and FVC, but the airway diameter has not grown proportionally^{17–19}. Pulmonary function is lower in obese asthmatics^{20,21}, but our study did not show any statistical relationship between obesity and pulmonary function. However, the FEV₁ was considerably lower in obese asthmatic patients, and they showed obstructive lung pattern. Future research is needed to further clarify these findings.

There are few studies on the association between lung function and MetS in school-aged children, and the results are unclear in adults. In a Taiwanese study, restrictive lung function was significantly associated with MetS after adjusting for age, sex, BMI, alcohol use, smoking, and physical activity¹⁴. In a study of adolescents in the USA, MetS was related with lower FEV₁/FVC ratio, and such association was more pronounced among asthma patients²². In our study, patients with MetS showed lower FEV₁, FVC, and FEV₁/FVC ratio regardless of obesity and asthma status. Meanwhile, although asthma patients with MetS did not show any statistical significance, they showed substantially lower FEV₁ and obstructive pattern of lung function. By contrast, a previous study reported an inverse correlation between MetS and lung function in asthma patients²². This discrepancy might be due to the limited number of asthmatic subjects in this study and the use of self-reported asthma diagnosis. Further studies should be conducted to investigate the relationship between pulmonary function and MetS in subjects with asthma.

MetS is a complex disorder that includes chronic inflammation characterized by abdominal obesity, hyperglycemia, hypertension, and dyslipidemia. Previous studies have investigated the relationship between individual components of MetS and pulmonary function, but the influence of each factor seems to vary between each study group. For example, lower HDL-C was the major predictor for impaired pulmonary function in an Italian population²³. Meanwhile, abdominal obesity and hyperglycemia were reported to be significantly associated with pulmonary function impairment and MetS in a Japanese male population²⁴. Another study that included obese patients in the Netherlands reported that only hypertension was the significant MetS component associated with lower FEV₁/FVC ratio²⁵. In our study, which was conducted in Korean children and adolescents, increased WC, BP, fasting glucose, and low HDL-C were significantly associated with lower FEV₁/FVC ratio.

Previous studies suggested several potential hypotheses explain the relationship between MetS and impaired pulmonary function. One is that systemic inflammations caused by MetS are associated with altered pulmonary immune and oxidative stress reactions^{26–28}. Another is that insulin resistance alters protein metabolism and results in epithelial damage²⁹. Interestingly, MetS was also associated with lower pulmonary function in the normal weight group and the non-asthmatics. These findings provide additional evidence to support the hypothesis that aside from the classic atopic airway inflammation, other mechanisms are involved in lower pulmonary function in asthma patients. The range to which these mechanisms mediated the consequence of metabolic anomalies on pulmonary function needs further research. Moreover, future intervention studies will be needed to determine if treatment of MetS can prevent lower lung function in subjects with MetS.

This study has several limitations. First, this was a cross-sectional study that measured pulmonary function and MetS components at a single period rather than doing long-term repeated measurements. Therefore, prospective longitudinal studies are needed to identify the definite pathophysiologic mechanism by which MetS influences pulmonary function. Second, the sample designed for KNHANES was selected, but this study showed higher proportion of MetS than that previously reported^{7,8}, indicating that there may have been a higher number of high-risk patients who are obese or have abnormal blood tests that participated in the pulmonary function tests. However, this was the first study in Korea to investigate the association between MetS and pulmonary

function in a representative population of children and adolescents. The results will help to elucidate the pathogenesis of MetS and lung-related diseases.

Conclusion

Pulmonary function was not significantly different according to obesity status among Korean children and adolescents. However, patients with MetS had significantly lower lung functions, and MetS components were independently associated with pulmonary function. Physicians should be aware of the adverse effects of MetS on lung function.

Methods

Study population. This study was conducted using data obtained from the 2009–2011 Korea National Health and Nutrition Examination Survey (KNHANES). The KNHANES is a cross-sectional, nationwide, and representative survey regularly conducted by the Chronic Disease Surveillance Department, Korean Centers for Disease Control and Prevention. The KNHANES enrolls approximately 10,000 people annually as a survey sample and collects information through health interviews, health examinations, and nutrition surveys. To capture a representative population, multi-stage stratified statistical design is applied in this survey³⁰. All participants in the study provided written consent form. And the researcher obtained informed consent from a parent and/or legal guardian for study participation. This survey received institutional review board approval from the Korean Centers for Disease Control and Prevention (approval no: 2009-01CON-03-2C, 2010-02CON-21-C, 2011-02CON-06-C). Of the 17,720 individuals included in the KNHANES, we identified children and adolescents aged 10–18 years as potential candidates for this study. For users and researchers who promise to follow the research ethics throughout the world, micro-data (in the form of SAS and SPSS files) can be downloaded by e-mail and the details of KNHANES can be accessed on the KNHANES website in English version (<http://knhanes.cdc.go.kr>). All methods were performed in accordance with the relevant guidelines and regulations

Measurements. Anthropometric measurements were obtained for all participants by trained staff. Height was measured to the nearest 0.1 cm with a portable stadiometer (Seca, Hamburg, Germany), while weight was measured to the nearest 0.1 kg on a medical balance scale (GL-6000-20; CAS, Seoul, Korea). The BMI was calculated as weight (kg) divided by height squared (m^2). Height, weight, and BMI standard deviation score (SDS) was determined using the 2007 Korean reference data³¹. Waist circumference (WC) was measured at the midpoint between the lowest margin of the rib and the uppermost lateral border of the iliac crest during expiration using a flexible tape (Seca 225; Hamburg, Germany). The mean and standard deviation of anthropometric and body composition values (height, weight, BMI, and WC) were calculated. Age- and gender-specific percentiles were calculated by using the Lambda-MuSigma (LMS) method (LMS Chartmaker Pro, version 2.5, Medical Research Council, Cambridge, UK) to estimate the skewness (L), median (M), and coefficient of variation (S). The blood pressure (BP, mmHg) was measured from the right upper arm, after the subject had rested for 5 minutes, in a seated position using calibrated sphygmomanometer (Baumanometer Desk model 0320, Baum, NY, USA) and an appropriately sized cuff. Systolic blood pressure (SBP) and diastolic blood pressure (DBP) were measured three times, and the second and third measurements were averaged and used for the analysis.

A blood sample was collected from each participant after overnight fasting. The samples were analyzed using an auto-analyzer (Hitachi automatic analyzer 7600, Hitachi, Tokyo, Japan) to determine the serum levels of glucose, total cholesterol, triglyceride (TG), and high-density lipoprotein cholesterol (HDL-C). The level of low-density lipoprotein cholesterol (LDL-C) was calculated with Friedewald's equation³². Pulmonary function was measured using a spirometer (model 2130; SensorMedics, CA, USA); all spirometric measurements were pre-bronchodilators. The FVC and FEV₁ defined according to the American Thoracic Society guidelines, were recorded³³. Spirometry is simple, noninvasive method used to monitor clinically important changes in lung functions. FVC is the maximum volume of air exhaled with maximum forced expiration effort as quickly as possible. FVC typically is decreased in restrictive pulmonary diseases. FEV₁ is total volume of air exhaled during the first seconds with maximal effort. FEV₁ is decreased in obstructive disorders. FEV₁/FVC ratio is the percentage of the FVC expired in one second. If the FEV₁/FVC ratio decreased, it suggests an obstructive defect. The FVC, FEV₁, and FEV₁/FVC ratio were measured and are expressed as both absolute values (L) and predicted values (%) calculated from large Korean healthy population³⁴.

Definition. Obesity was defined using the 2007 Pediatric Adolescent Standard Growth Chart from the Center for Disease Control and the Association of Korean Pediatrics³¹. Weight classifications according to the BMI diagnostic criteria were defined as normal weight (<85th percentile by sex and age; overweight (≥ 85 th percentile and <95th percentile); and obesity (≥ 95 th percentile or BMI ≥ 25 kg/m²)^{3,35}. MetS was defined as the presence of at least three of the following five criteria in the modified NCEP-ATP III⁵: (1) elevated WC (i.e., ≥ 90 th percentile for age and sex); (2) elevated BP (i.e., SBP or DBP ≥ 90 th percentile for age and sex and height according to 2007 Korean reference data)³¹; (3) glucose intolerance (i.e., fasting glucose concentrations ≥ 110 mg/dL); (4) elevated TG (i.e., serum TG concentrations ≥ 110 mg/dL); and (5) low HDL-C (i.e., levels of serum HDL-C < 40 mg/dL). Asthma was defined as a self-assessment diagnosis in a health interview survey. The survey included questions about the use of asthma medication (including inhalers, aerosols, or tablets), experience of wheezing in the last 12 months, and asthma diagnosed by a doctor.

Statistical analysis. Statistical analyses were performed using SPSS software for Windows (SPSS version 23.0, IBM SPSS Inc., Chicago, IL, USA). Normally distributed variables are presented as means \pm standard errors (SE), while categorical variables are presented as percentages (%). Because height, weight, BMI, and WC were not

evenly distributed among the different age groups, the SDS of these measures were determined using the LMS method according to the 2007 Korean National Growth Charts³¹. Statistical significance was determined for continuous variables using analysis of variance according to obesity or independent t-test according to the presence of MetS. Meanwhile, a chi-square test was used for categorical variables. Analysis of covariance was used to evaluate pulmonary function according to obesity or presence of MetS after adjusting for possible confounding factors, such as age, sex, square of height (m²), weight, household income, alcohol drinking, smoking, residence, physical activity, and atopic dermatitis. The data were presented as the adjusted means \pm SE. Additional analysis was also performed depending on the presence or absence of asthma. To investigate the associations between pulmonary function and MetS and its components, multiple linear regression analyses were conducted after adjustment for age, sex, square of height (m²), weight, household income, alcohol drinking, smoking, residence, physical activity, and atopic dermatitis among all participants. Additionally, subgroup analysis was performed because the relationship could change depending on the patient's characteristics. Therefore, subgroups were analyzed by the presence of asthma and normal weight or overweight/obesity. Corresponding standardized regression coefficients (β) were determined, and *P* values of < 0.05 were considered statistically significant.

Data availability

All the data generated and/or analyzed during the current study are included in this article and are available from the corresponding author on reasonable request.

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References

- Ogden, C. L. *et al.* Prevalence of overweight and obesity in the United States, 1999–2004. *Jama* **295**, 1549–1555 (2006).
- Ogden, C. L., Carroll, M. D., Kit, B. K. & Flegal, K. M. Prevalence of childhood and adult obesity in the United States, 2011–2012. *Jama* **311**, 806–814 (2014).
- Park, M. J., Boston, B. A., Oh, M. & Jee, S. H. Prevalence and trends of metabolic syndrome among Korean adolescents: from the Korean NHANES survey, 1998–2005. *The Journal of pediatrics* **155**, 529–534 (2009).
- Weiss, R. *et al.* Obesity and the metabolic syndrome in children and adolescents. *The New England journal of medicine* **350**, 2362–2374 (2004).
- Cook, S., Weitzman, M., Auinger, P., Nguyen, M. & Dietz, W. H. Prevalence of a metabolic syndrome phenotype in adolescents: findings from the third National Health and Nutrition Examination Survey, 1988–1994. *Archives of pediatrics & adolescent medicine* **157**, 821–827 (2003).
- Beltran-Sanchez, H., Harhay, M. O., Harhay, M. M. & McElligott, S. Prevalence and trends of metabolic syndrome in the adult U.S. population, 1999–2010. *Journal of the American College of Cardiology* **62**, 697–703 (2013).
- Kim, S. & So, W.-Y. Prevalence of Metabolic Syndrome among Korean Adolescents According to the National Cholesterol Education Program, Adult Treatment Panel III and International Diabetes Federation. *Nutrients* **8**, 588 (2016).
- Lee, S. E. *et al.* Trends in the prevalence of metabolic syndrome and its components in South Korea: Findings from the Korean National Health Insurance Service Database (2009–2013). *PLoS one* **13**, e0194490–e0194490 (2018).
- Jones, R. L. & Nzekwu, M. M. The effects of body mass index on lung volumes. *Chest* **130**, 827–833 (2006).
- Peters, U., Dixon, A. E. & Forno, E. Obesity and asthma. *The Journal of allergy and clinical immunology* **141**, 1169–1179 (2018).
- Rastogi, D., Bhalani, K., Hall, C. B. & Isasi, C. R. Association of pulmonary function with adiposity and metabolic abnormalities in urban minority adolescents. *Annals of the American Thoracic Society* **11**, 744–752 (2014).
- Li, A. M. *et al.* The effects of obesity on pulmonary function. *Archives of disease in childhood* **88**, 361–363 (2003).
- Leone, N. *et al.* Lung function impairment and metabolic syndrome: the critical role of abdominal obesity. *American journal of respiratory and critical care medicine* **179**, 509–516 (2009).
- Lin, W. Y., Yao, C. A., Wang, H. C. & Huang, K. C. Impaired lung function is associated with obesity and metabolic syndrome in adults. *Obesity (Silver Spring, Md.)* **14**, 1654–1661 (2006).
- Liyanage, G., Jayamanne, B. D., Aaqiff, M. & Sriwardhana, D. Effect of body mass index on pulmonary function in children. *The Ceylon medical journal* **61**, 163–166 (2016).
- Forno, E., Han, Y. Y., Mullen, J. & Celedon, J. C. Overweight, Obesity, and Lung Function in Children and Adults—A Meta-analysis. *The journal of allergy and clinical immunology. In practice* **6**, 570–581.e510 (2018).
- Cibella, F. *et al.* An elevated body mass index increases lung volume but reduces airflow in Italian schoolchildren. *PLoS One* **10**, e0127154 (2015).
- Yao, T. C. *et al.* Obesity disproportionately impacts lung volumes, airflow and exhaled nitric oxide in children. *PLoS One* **12**, e0174691 (2017).
- Costa Junior, D. *et al.* Influence of Body Composition on Lung Function and Respiratory Muscle Strength in Children With Obesity. *Journal of clinical medicine research* **8**, 105–110 (2016).
- Jones, M. H. *et al.* Asthma and Obesity in Children Are Independently Associated with Airway Dysanapsis. *Frontiers in pediatrics* **5**, 270 (2017).
- Mafori, T. T., Rufino, R., Costa, C. H. & Lopes, A. J. Obesity: systemic and pulmonary complications, biochemical abnormalities, and impairment of lung function. *Multidisciplinary respiratory medicine* **11**, 28 (2016).
- Forno, E., Han, Y. Y., Muzumdar, R. H. & Celedon, J. C. Insulin resistance, metabolic syndrome, and lung function in US adolescents with and without asthma. *The Journal of allergy and clinical immunology* **136**, 304–311.e308 (2015).
- Rogliani, P. *et al.* Metabolic syndrome and risk of pulmonary involvement. *Respiratory medicine* **104**, 47–51 (2010).
- Yoshimura, C. *et al.* Relationships of decreased lung function with metabolic syndrome and obstructive sleep apnea in Japanese males. *Internal medicine (Tokyo, Japan)* **51**, 2291–2297 (2012).
- van Huisstede, A. *et al.* Systemic inflammation and lung function impairment in morbidly obese subjects with the metabolic syndrome. *Journal of obesity* **2013**, 131349 (2013).
- Thijis, W. *et al.* Association of lung function measurements and visceral fat in men with metabolic syndrome. *Respiratory medicine* **108**, 351–357 (2014).
- Lewis, G. F. & Rader, D. J. New insights into the regulation of HDL metabolism and reverse cholesterol transport. *Circulation research* **96**, 1221–1232 (2005).
- Gowdy, K. M. & Fessler, M. B. Emerging roles for cholesterol and lipoproteins in lung disease. *Pulmonary pharmacology & therapeutics* **26**, 430–437 (2013).

29. Agrawal, A., Mabalirajan, U., Ahmad, T. & Ghosh, B. Emerging interface between metabolic syndrome and asthma. *American journal of respiratory cell and molecular biology* **44**, 270–275 (2011).
30. Kweon, S. *et al.* Data resource profile: the Korea National Health and Nutrition Examination Survey (KNHANES). *International journal of epidemiology* **43**, 69–77 (2014).
31. Moon, J. S. *et al.* 2007 Korean National Growth Charts: review of developmental process and an outlook. *Korean J Pediatr* **51**, 1–25 (2008).
32. Friedewald, W. T., Levy, R. I. & Fredrickson, D. S. Estimation of the concentration of low-density lipoprotein cholesterol in plasma, without use of the preparative ultracentrifuge. *Clinical chemistry* **18**, 499–502 (1972).
33. Standardization of Spirometry, 1994 Update. American Thoracic Society. *American journal of respiratory and critical care medicine* **152**, 1107–1136 (1995).
34. Hyue Park, C. *et al.* *Predicted normal values of pulmonary function tests in normal Korean children*. Vol. 2 (2014).
35. de Onis, M. *et al.* Development of a WHO growth reference for school-aged children and adolescents. *Bulletin of the World Health Organization* **85**, 660–667 (2007).

Author contributions

Minji Kim designed the study, drafted the initial manuscript, and analyzed the publicly available data set. Seoheui Choi, Soo-Han Choi, Seon-Hee Shin, and Sung Koo Kim reviewed and revised the manuscript and provided important intellectual content, including conceptualization of the study design. Young Suk Shim and You Hoon Jeon supervised all aspects of manuscript preparation and assisted with the study formulation, data analysis, manuscript writing, and interpretation of the findings. All authors approved the final manuscript as submitted and agree to be accountable for all aspects of the work.

Competing interests

The authors declare no competing interests.

Additional information

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