ORIGINAL ARTICLE

Abdominal adiposity intensifies the negative effects of ambient air pollution on lung function in Korean men

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BACKGROUND: Some studies have provided the possibility that adipose tissue may mediate air pollution-induced lung dysfunction. Studies using quantified fat mass data are needed to understand the biological mechanisms between adipocyte and air pollution in lung function. We aimed to investigate whether abdominal adiposity measured by computed tomography (CT) modifies the effects of air pollution on lung function in Korean men.

METHODS: A total of 1876 men who visited one of two health checkup centers were recruited for this study. Adiposity traits such as visceral adipose tissue (VAT), subcutaneous adipose tissue (SAT) and total adipose tissue (TAT) areas were measured by CT. We used the annual mean concentrations of ambient air pollutants including nitrogen dioxide (NO₂) and particulate matter with an aerodynamic diameter $\leq 10 \mu\text{m}$ (PM₁₀).

RESULTS: Interquartile range (IQR) increase in annual mean concentration of NO₂ was significantly associated with a 2.5% lower forced expiratory volume in 1 s (FEV₁) and 2.9% lower forced vital capacity (FVC) (both $P < 0.05$). The decrease in lung function was more strongly associated with adiposity traits than with body mass index. In a stratified analysis of adiposity, compared with subjects with low-VAT area (VAT $\leq 200 \text{ cm}^2$), those with high-VAT area (VAT $> 200 \text{ cm}^2$) showed a rapid decrease in FEV₁ with each IQR increase in PM₁₀ ($\beta = -0.0812$; 95% confidence interval (CI) = $-0.1590, -0.0035$) and NO₂ ($\beta = -0.0979$; 95% CI = $-0.1611, -0.0346$). In the high-VAT group, each IQR increase in NO₂ content was significantly associated with a 10.6% decrease ($\beta = -0.1056$; 95% CI = $-0.1770, -0.0343$) in FVC. SAT and TAT areas showed similar patterns.

CONCLUSIONS: We report the first finding that abdominal adiposity intensifies the inverse relationship between air pollution and lung function.

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INTRODUCTION

Ambient air pollution is one of the most important global health issues because it increases the risk of and aggravates many diseases such as asthma, lung disease, stroke and certain cancers.^{1–5} Air pollution has been shown to have negative effects on respiratory health, and acute or repeated exposure to air pollution is associated with a reduced lung function.^{6–9}

A recent genome-wide interaction study based on the SAPALDIA (Swiss Cohort Study on Air Pollution and Lung Disease in Adults) cohort reported that particulate matter with an aerodynamic diameter $\leq 10 \mu\text{m}$ (PM₁₀) was significantly associated with lung function decline by interacting with certain variants of *CDH13*.¹⁰ Our previous study also replicated this *CDH13* gene-by-PM₁₀ interaction effect on lung function in Korean men.¹¹ *CDH13* (also known as T-cadherin) is closely related to adiponectin, which is secreted exclusively from fat tissue.¹⁰ These findings indicate that there might be a potential connection between air pollution, fat tissue and lung function. In fact, several plausible hypotheses have been proposed to explain this connection, including the roles of oxidative stress and inflammation because of their shared mechanisms; that is, both obesity-induced inflammation and

oxidative stress are related to excess adipose tissue.¹² Increased adipose tissue produces predominantly proinflammatory cytokines including leptin, visfatin, resistin, tumor necrosis factor- α and interleukin-6. Activated reactive oxygen species produced by accumulated adipose tissue increases systemic oxidative stress.

Although previous reports have shown significant synergistic effects of obesity and exposure to ambient air pollutants such as nitrogen dioxide (NO₂) and PM₁₀ content on lung function using an indirect measurement of obesity including body mass index (BMI),^{6,13,14} accurate quantitative measurement of adipose tissue mass by computed tomography (CT) is needed to understand the plausible mechanisms between adipose tissue and air pollution in lung function. However, to our knowledge, no studies have investigated whether there is an additive effect of fat accumulation in adipose tissue on the relationship between ambient air pollution and lung function. In addition, most epidemiological studies regarding negative impacts of air pollution on lung function have focused mainly on children or specific populations such as Europeans, and there are few studies of these associations in Asian adults.

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This study was to investigate the chronic effects of ambient air pollutants such as PM₁₀ and NO₂ on lung function in Korean men and to identify whether these effects are mediated by abdominal adiposity in particular visceral adipose tissue (VAT), subcutaneous adipose tissue (SAT) and total adipose tissue (TAT) areas measured by CT. We provide the first evidence that adiposity may mediate the effects of air pollution on lung function in Asian adults.

SUBJECTS AND METHODS

Subjects

The participants in this study were recruited at the two health-care centers at Seoul National University Hospital from 2009 to 2014.¹¹ They visited the center to have periodic comprehensive screening health checkups. During this period, we enrolled a total of 2761 subjects, 885 of whom were excluded because they met the following exclusion criteria: (1) age ≤ 40 years; (2) lacking the necessary phenotypic information such as adiposity-related traits, lung function and smoking status; (3) lacking zip code information for estimating exposure to air pollution; or (4) missing air pollution values. Therefore, a total of 1876 subjects were included in the final analysis. This study was approved by the institutional review board of the Seoul National University Hospital Biomedical Research Institute (approval number, H-0911-010-299; C-1511-114-723).

Assessment of lung function

Pulmonary function was assessed in each subject using a 1022 digital spirometer (SensorMedics, Anaheim, CA, USA).¹⁵ After each measurement, each flow-volume curve was examined to ensure that it satisfied the acceptability and reproducibility criteria, and the same measurement process was repeated at least three times for forced expiratory volume in 1 s (FEV₁) and forced vital capacity (FVC) values. The highest absolute values for FVC and FEV₁ were chosen as the outcome variables in this study.

Adiposity-related traits assessment

The details of the methods to measure abdominal adiposity have been described in a previous study.¹⁶ Briefly, abdominal adiposity, including VAT, SAT and TAT, was measured using CT scanner (Somatom Sensation 16 CT scanner, Siemens AG, Erlangen, Germany), and the areas of the fat compartments were estimated with Rapidia 2.8 CT software (Infiniti, Seoul, Korea). To define the visceral obesity group, an optimal cut-off criterion in Korean men (VAT ≥ 136 cm²) was first considered. However, we could not observe the significant effect of visceral obesity group. Therefore, we classified into three groups according to VAT level: subjects with low-VAT level (VAT ≤ 100 cm²), subjects with moderate VAT level (100 cm² < VAT ≤ 200 cm²) and subjects with high-VAT level (VAT > 200 cm²). Similar to VAT, the subjects were categorized into three subgroups according SAT and TAT level, because of the absence of optimal cut-off criterion in Korean men for SAT or TAT.

Lifestyle and anthropometric variables

To examine the associations between adiposity, exposure to ambient air pollution and lung function, we collected data about lifestyle factors and anthropometric markers. Health-related behaviors such as smoking status and physical activity were assessed using a structured questionnaire and classified as categorical variables as follows: cigarette smoking status (current, former or never smoker) and moderate activity (yes or no). Anthropometric data including height and weight were also measured.

Assessment of air pollution exposure

To assess exposure to ambient air pollution, we obtained the monitoring data (2009–2014) for 24-h concentrations of ambient PM₁₀ and NO₂ from the Ministry of the Environment of Korea (<https://www.airkorea.or.kr>). These concentrations were measured at about 300 nationwide monitoring sites in Korea. The annual average concentrations of air pollutants at each monitoring site were calculated to identify the effects of air pollutants on lung function. Residential zip codes were used to link each subject to the annual average concentrations from the nearest monitoring site.

Statistical analysis

Correlation coefficients between air pollutants and adiposity measures were estimated using Pearson's correlational analysis. Multiple linear regression analysis was performed to evaluate the associations between ambient air pollution, adiposity traits and lung function. To identify the effects of adiposity traits on the relationship between air pollution and lung function, we performed a stratified analysis using the cut-off for the definition of high-adiposity group for each adiposity trait. The results are presented as beta coefficients and 95% confidence intervals (CIs) for lung function after adjustment for covariates such as the site of recruitment, age,² height, BMI, smoking status (never, past or current), pack years and moderate activity (yes or no). These estimates were converted by scale to the interquartile range (IQR) for each pollutant (9.2 $\mu\text{g m}^{-3}$ for PM₁₀ and 13.9 ppb for NO₂). All analyses were implemented in SAS 9.3 (SAS Institute, Cary, NC, USA).

RESULTS

The detailed characteristics of the study subjects are shown in Table 1. A total of 1876 subjects (recruitment site A, $n=1405$; recruitment site B, $n=471$) were included in the final association analyses. All subjects were men, and most were aged 50–60 years. The mean SAT area (139.8 ± 53.1 cm²) was slightly higher than the VAT area (131.4 ± 53.6 cm²). All adiposity-related traits were significantly intercorrelated ($P < 0.001$), and the correlation between VAT and TAT areas was the strongest of these correlations ($r=0.880$) (Supplementary Material; Supplementary Table S1). The percentages of former and current smokers were 42.4% ($n=796$) and 32.3% ($n=605$), respectively. The mean FEV₁ and FVC were 3.3 ± 0.5 l and 4.1 ± 0.6 l. The median PM₁₀ and NO₂

Table 1. Characteristics of study participants

Characteristics	Site A of recruitment	Site B of recruitment	Total
<i>n</i>	1405	471	1876
Age years	51.9 (5.8)	50.7 (5.3)	51.6 (5.7)
Height (cm)	169.3 (6.7)	170.7 (5.2)	169.6 (6.4)
Weight (kg)	70.4 (10.1)	72.0 (8.7)	70.8 (9.8)
<i>Adiposity measures</i>			
BMI (kg m ⁻²)	24.5 (2.8)	24.7 (2.6)	24.6 (2.7)
VAT (cm ²)	128.1 (54.5)	141.2 (49.8)	131.4 (53.6)
SAT (cm ²)	140.2 (54.4)	138.5 (49.1)	139.8 (53.1)
TAT (cm ²)	268.4 (95.3)	279.7 (89.0)	271.2 (93.8)
<i>Smoking status, n (%)</i>			
Never	372 (26.5)	103 (21.9)	475 (25.3)
Former	574 (40.9)	222 (47.1)	796 (42.4)
Current	459 (32.7)	146 (31.0)	605 (32.3)
Pack years	14.2 (18.0)	15.5 (16.9)	14.5 (17.7)
<i>Moderate activity, n (%)</i>			
Yes	614 (43.7)	263 (55.8)	877 (46.8)
No	791 (56.3)	208 (44.2)	999 (53.2)
<i>Lung function test</i>			
FEV ₁ (L)	3.3 (0.6)	3.4 (0.5)	3.3 (0.5)
FVC (L)	4.0 (0.6)	4.3 (0.6)	4.1 (0.6)
<i>Air pollutants (annual average concentration)</i>			
PM ₁₀ ($\mu\text{g m}^{-3}$)			
Mean	48.0 (7.2)	52.7 (6.7)	49.2 (7.4)
Median	47.3	52.3	49.0
IQR	9.3	6.1	9.2
NO ₂ (ppb)			
Mean	29.8 (12.5)	35.0 (13.3)	31.1 (12.9)
Median	30.0	34.4	31.5
IQR	14.6	12.4	13.9

Abbreviations: BMI, body mass index; FEV₁, forced expiratory volume in 1 s; FVC, forced vital capacity; IQR, interquartile range; NO₂, nitrogen dioxide; PM₁₀, particulate matter with aerodynamic diameter ≤ 10 μm ; SAT, subcutaneous adipose tissue; TAT, total adipose tissue; VAT, visceral adipose tissue. Data are presented as mean (s.d.) for continuous variables or n (%) for categorical variables.

Table 2. Regression results for the association between air pollution, adiposity-related traits and lung function level

Exposure	FEV ₁ (L)		FVC (L)	
	β (95% CI)	P-value	β (95% CI)	P-value
<i>Air pollution</i>				
PM ₁₀ (μg m ⁻³)	-0.0097 (-0.0335, 0.0141)	0.4259	0.0042 (-0.0222, 0.0305)	0.7556
NO ₂ (ppb)	-0.0254 (-0.0455, -0.0053)	0.0131	-0.0292 (-0.0514, -0.0070)	0.0102
<i>Adiposity measures</i>				
BMI (kg m ⁻²)	-0.0051 (-0.0118, 0.0017)	0.1430	-0.0061 (-0.0135, 0.0014)	0.1114
BMI ≥ 25 kg m ⁻²	-0.0204 (-0.0578, 0.0171)	0.2876	-0.0480 (-0.0894, -0.0067)	0.0230
VAT (cm ²)	-0.0013 (-0.0017, -0.0010)	< 0.0001	-0.0015 (-0.0019, -0.0012)	< 0.0001
SAT (cm ²)	-0.0011 (-0.0014, -0.0007)	< 0.0001	-0.0013 (-0.0017, -0.0010)	< 0.0001
TAT (cm ²)	-0.0008 (-0.0010, -0.0006)	< 0.0001	-0.0009 (-0.0011, -0.0007)	< 0.0001

Abbreviations: BMI, body mass index; CI, confidence interval; FEV₁, forced expiratory volume in 1 s; FVC, forced vital capacity; NO₂, nitrogen dioxide; PM₁₀, particulate matter with aerodynamic diameter ≤ 10 μm; SAT, subcutaneous adipose tissue; TAT, total adipose tissue; VAT, visceral adipose tissue. These results were adjusted for site of recruitment, age,² height, smoking status (never, past or current), pack years and moderate activity (yes or no). The beta coefficients and 95% CIs in air pollution were scaled to the interquartile range for each pollutant (9.2 μg m⁻³ for PM₁₀ and 13.9 ppb for NO₂).

concentrations were 49.0 μg m⁻³ and 31.5 ppb, respectively, and their IQRs were 9.2 μg m⁻³ and 13.9 ppb, respectively. There was a significant positive correlation between PM₁₀ and NO₂ values ($r=0.430$, $P<0.001$) (Supplementary Material; Supplementary Table S1). The concentrations of PM₁₀ and NO₂ in each subgroup of VAT, SAT and TAT were also demonstrated in Supplementary Table S2. There was no significant difference in air pollutant concentrations among the subgroups (all $P>0.05$) (Supplementary Material; Supplementary Table S2). In addition, we have investigated the associations of moderate activity and smoking status with lung function. As a result, smoking status and pack years were associated with decreased FEV₁, although no significant association between smoking status and FVC was observed. However, moderate activity was not significantly associated with FEV₁ and FVC (data not shown).

Table 2 shows the results of the analysis of the associations between air pollution or adiposity-related traits and lung function including FEV₁ and FVC. NO₂ concentration was significantly associated with FEV₁ ($P=0.0131$); there was a 2.5% decrease in FEV₁ (95% CI=-4.6, -0.5%) with IQR (13.9 ppb) increase in NO₂ concentration. Similarly, FVC was significantly associated with NO₂ concentration ($P=0.0102$); there was a 2.9% decrease in FVC (95% CI=-5.1, -0.7%) for IQR (13.9 ppb) increase in NO₂ concentration. However, PM₁₀ was not significantly associated with a reduction in FEV₁ or FVC (both $P>0.05$). Analysis of the associations between adiposity-related traits and lung function showed that BMI was not significantly associated with FEV₁ or FVC (both $P>0.05$). However, overall obesity, defined as a BMI ≥ 25 kg m⁻², was significantly associated with FVC ($P=0.0230$). All abdominal adiposity traits such as VAT, SAT and TAT were significantly associated with both FEV₁ and FVC (all $P<0.0001$). Compared with BMI, the adiposity variables quantified using CT, including VAT area, were more strongly related to FEV₁ and FVC.

To examine the effects of air pollution on lung function according to the degree of adiposity, we performed subgroup analysis by classifying the adiposity traits VAT, SAT and TAT into three levels (Figure 1). The effects of air pollutants on FEV₁ and FVC were much greater in the high-fat group with a VAT > 200 cm². Similar to VAT, the negative association between air pollution and lung function was stronger in the high-fat group with an SAT area > 200 cm² than in the group with an SAT area ≤ 200 cm². For TAT area, the negative associations between air pollution, and FEV₁ and FVC were strongest in the high-fat group with a TAT area > 300 cm². The negative association between TAT and FEV₁ was smaller in the moderate fat group than in the low- and high-fat groups, whereas the relationship

between TAT and FVC was smaller in the low-fat group than in the other two groups.

Table 3 shows the results of the regression analysis in the low- and high-adiposity groups with cut-off points of 200, 200 and 300 cm² for VAT, SAT and TAT areas, respectively. Similar to the results for obesity classified by BMI (Supplementary Material; Supplementary Table S3), the effects of air pollution on lung function were much stronger in the high- than in the low-adiposity group. In the low-adiposity group, none of the air pollutants showed significant effects on FEV₁, whereas in the high-adiposity group, PM₁₀ and NO₂ concentrations were significantly associated with decreased FEV₁ (both $P<0.05$). In the high-VAT group (VAT area > 200 cm²), FEV₁ decreased 8.1% ($\beta=-0.0812$; 95% CI=-0.1590, -0.0035) and 9.8% ($\beta=-0.0979$; 95% CI=-0.1611, -0.0346) for each IQR increase in PM₁₀ and NO₂, respectively. The high-SAT group (SAT area > 200 cm²) showed a pattern similar to the high-VAT group. In the high-TAT group (TAT area > 300 cm²), FEV₁ decreased 4.3% ($\beta=-0.0426$; 95% CI=-0.0810, -0.0042) and 5.5% ($\beta=-0.0545$; 95% CI=-0.0864, -0.0226) for each IQR increase in PM₁₀ and NO₂ concentration, respectively.

In the high-adiposity group, air pollution was also associated with decreased FVC. In the high-VAT group, FVC decreased 10.6% ($\beta=-0.1056$; 95% CI=-0.1770, -0.0343) for each IQR increase in NO₂ concentration. PM₁₀ ($P=0.0262$) and NO₂ ($P=0.0198$) concentrations were also significantly associated with a decrease in FVC in the high-SAT group; FVC decreased 8.7 ($\beta=-0.0868$; 95% CI= -0.1629, -0.0108) and 7.5% ($\beta=-0.0752$; 95% CI=-0.1379, -0.0125) for each IQR increase in PM₁₀ and NO₂ concentration. Overall, the effects of NO₂ were greater than those of PM₁₀ when analyzed according to VAT area, whereas the effects of PM₁₀ were greater than those of NO₂ when analyzed according to SAT area. In the high-TAT group (TAT area > 300 cm²), FVC decreased 6.1% ($\beta=-0.0607$; 95% CI=-0.0967, -0.0248) for IQR increase in NO₂ concentration.

DISCUSSION

This study investigated the associations between exposure to ambient air pollution, as shown by the PM₁₀ and NO₂ levels, and lung function in Korean men, and whether these associations are modified by adiposity level. We observed a significant negative relationship between annual average concentration of NO₂ and lung function ($P<0.05$), showing 2.5% ($\beta=-0.0254$; 95% CI= -0.0455, -0.0053) FEV₁ and 2.9% ($\beta=-0.0292$; 95% CI= -0.0514, -0.0070) FVC decrease per IQR (13.9 ppb) increase in the NO₂

Figure 1. The effect estimates of each air pollutant on (a) FEV₁ and (b) FVC according to VAT categories, (c) FEV₁ and (d) FVC according to SAT categories, and (e) FEV₁ and (f) FVC according to TAT categories.

concentration. Interestingly, in the subgroup analyses, the associations of PM₁₀ and NO₂ concentrations were much stronger in the high- than in the low-adiposity group. In the high-VAT group, each IQR increase in PM₁₀ and NO₂ concentration was associated with a decrease in FEV₁ (β (95% CI) for PM₁₀ = -0.0812 (-0.1590, -0.0035) and β (95% CI) for NO₂ = -0.0979 (-0.1611, -0.0346)), compared with the low-VAT group. In the high-VAT group, FVC was also negatively associated with NO₂ concentration; there was a 10.6% (β = -0.1056; 95% CI = -0.1770, -0.0343) decrease in FVC for increase in IQR. This pattern was similar in the subgroups classified according to subcutaneous and total abdominal fat.

Considering the negative impacts of air pollution on health, the increase in air pollution in South Korea has become an inevitable social issue. A recent report documented that Korea is expected to

experience the greatest increase in premature deaths and economic damage caused by air pollution among the Organization for Economic Cooperation and Development (OECD) countries, if Korea's air pollution continues its current trend by 2060.¹⁷ The median values of PM₁₀ ($\mu\text{g m}^{-3}$) and NO₂ (ppb) concentrations estimated in our study were 49 and 31.5, respectively. In particular, the level of PM₁₀ concentration is considerably higher than the measured PM₁₀ concentration near the busy road in Germany.¹⁹ However, when compared to the average concentrations of 31 major provincial cities in China (average concentration for PM₁₀ in 2014 = 109.8 $\mu\text{g m}^{-3}$), the level of PM₁₀ concentration in our study was much lower.²⁰

Epidemiological studies have reported significant associations between exposure to air pollutants and a decreased lung function

Table 3. Results of stratified analyses by abdominal adiposity traits for the association between lung function and exposure to ambient air pollution

Adiposity	Trait	Exposure	Low-adiposity group		High-adiposity group	
			β (95% CI)	P-value	β (95% CI)	P-value
VAT (VAT cut-off point for low- and high-adiposity groups = 200 cm ²)						
FEV ₁ (L)	PM ₁₀ (μg m ⁻³)	NO ₂ (ppb)	-0.0013 (-0.0264, 0.0237)	0.9172	-0.0812 (-0.1590, -0.0035)	0.0417
		NO ₂ (ppb)	-0.0164 (-0.0375, 0.0047)	0.1267	-0.0979 (-0.1611, -0.0346)	0.0028
FVC (L)	PM ₁₀ (μg m ⁻³)	NO ₂ (ppb)	0.0110 (-0.0165, 0.0386)	0.4339	-0.0490 (-0.1372, 0.0391)	0.2774
		NO ₂ (ppb)	-0.0199 (-0.0431, 0.0033)	0.0941	-0.1056 (-0.1770, -0.0343)	0.0042
SAT (SAT cut-off point for low- and high-adiposity groups = 200 cm ²)						
FEV ₁ (L)	PM ₁₀ (μg m ⁻³)	NO ₂ (ppb)	0.0024 (-0.0231, 0.0278)	0.8557	-0.0948 (-0.1627, -0.0268)	0.0069
		NO ₂ (ppb)	-0.0164 (-0.0379, 0.0051)	0.1334	-0.0828 (-0.1390, -0.0267)	0.0041
FVC (L)	PM ₁₀ (μg m ⁻³)	NO ₂ (ppb)	0.0164 (-0.0114, 0.0441)	0.2494	-0.0868 (-0.1629, -0.0108)	0.0262
		NO ₂ (ppb)	-0.0210 (-0.0446, 0.0027)	0.0819	-0.0752 (-0.1379, -0.0125)	0.0198
TAT (TAT cut-off point for low- and high-adiposity groups = 300 cm ²)						
FEV ₁ (L)	PM ₁₀ (μg m ⁻³)	NO ₂ (ppb)	0.0027 (-0.0272, 0.0327)	0.8583	-0.0426 (-0.0810, -0.0042)	0.0305
		NO ₂ (ppb)	-0.0073 (-0.0328, 0.0181)	0.5727	-0.0545 (-0.0864, -0.0226)	0.0009
FVC (L)	PM ₁₀ (μg m ⁻³)	NO ₂ (ppb)	0.0188 (-0.0137, 0.0512)	0.2588	-0.0337 (-0.0771, 0.0098)	0.1291
		NO ₂ (ppb)	-0.0086 (-0.0361, 0.0189)	0.5417	-0.0607 (-0.0967, -0.0248)	0.0010

Abbreviations: CI, confidence interval; FEV₁, forced expiratory volume in 1 s; FVC, forced vital capacity; NO₂, nitrogen dioxide; PM₁₀, particulate matter with aerodynamic diameter ≤10 μm; SAT, subcutaneous adipose tissue; TAT, total adipose tissue; VAT, visceral adipose tissue. These results were adjusted for site of recruitment, age², height, smoking status (never, past or current), pack years and moderate activity (yes or no). The beta coefficients and 95% CI were scaled to the interquartile range for each pollutant (9.2 μg m⁻³ for PM₁₀ and 13.9 ppb for NO₂).

in adults.^{18,19,21} In 1997, significant relationships between the annual mean levels of air pollutants such as PM₁₀, NO₂ and SO₂, and lung function were observed in adults aged 18–60 years residing in Switzerland.²¹ In 2005, Schikowski *et al.*¹⁹ found that chronic exposure to PM₁₀ and NO₂ was related with increased risk of chronic obstructive pulmonary disease in 55-year-old women in Germany. Forbes *et al.*¹⁸ reported a significant association between chronic exposure to air pollution and FEV₁ in a large English population, and reported a 3% decline in FEV₁ per 10 μg m⁻³ increase in PM₁₀ concentration. However, these effects of air pollution on lung function in adults were found in specific European populations.

More recent evidence has suggested an additive effect of air pollution and obesity on lung function decline.^{6,13,14} In 2013, Schikowski *et al.*¹⁴ investigated whether the effect of improved air quality on lung function is modified by obesity status. They reported significant interactions between a change in PM₁₀ concentration and BMI; after a decrease in PM₁₀ concentration, the annual rates of decline in lung function were smaller in the groups with low or normal BMI compared with those defined as obese according to BMI. Dong *et al.*¹³ found that the risks for asthma and respiratory symptoms including cough were greater in obese children than in normal weight children. In particular, the interaction effects with obesity on cough and phlegm were significant for NO₂ and PM₁₀ concentrations. One European adult study based on the multicenter cohorts in the European Study of Cohorts for Air Pollution Effects (ESCAPE) identified a larger effect of exposure to air pollution including PM₁₀ and NO₂ on lung function in the obese group.⁶

To date, the mechanisms underlying the synergistic effects of obesity on the link between ambient air pollution and lung function remain unclear, but several possible physiological mechanisms linked to adipocyte have been suggested. One plausible mechanism is the inflammatory pathway. Exposure to ambient air pollution promotes airway inflammation, which can lead to a decline in lung function and/or lung injury.²² Similarly, a significant correlation between obesity and systemic inflammation has been reported.²³ Adipokines such as leptin and adiponectin, which mediate the inflammatory response, are produced mainly in adipose tissue. Inflammatory cytokines including tumor necrosis

factor-α and interleukin-6 are also released by adipocytes. These molecules are directly linked to the inflammatory process. In addition, macrophage migration inhibitory factor, a proinflammatory protein, is known to be a crucial factor in inflammation of chronic adipose tissue.²⁴ Immune cells including macrophages can also infiltrate adipose tissue. The macrophages within adipose tissue not only contribute to the production of inflammatory cytokines, but also lead to increased local inflammation.²⁵ Both air pollution and high adiposity are closely related to increased inflammation, and the synergistic effect of air pollution and adiposity in the high-fat group may be explained by the combined effects of adipose tissue and ambient air pollution on airway and/or systemic inflammation. Another possible explanation is that air pollution and high adiposity can both increase oxidative stress.^{12,26,27} Many components of ambient air pollutants cause lung damage through oxidative stress, either by acting directly on reactive oxygen species production or by the indirect induction of local inflammation.²⁸ Accumulated adipose tissue also promotes the production of proinflammatory adipokines, which trigger the production of reactive oxygen species.²⁶ Oxidative stress is significantly associated with the decline in lung function.^{29–31} These plausible hypotheses are supported by present findings in adipose tissue as well as the CDH13 gene-by-PM₁₀ interaction effect identified previously.^{10,11}

Most studies have primarily focused on short-term or acute effects in a restricted region or a specific population, particularly children. The present study showed significant associations between abdominal adipose tissue, as well as the negative effects of air pollution on FEV₁ and FVC using nationwide data in Korean adults. To our knowledge, we have shown for the first time that high adiposity strengthens an inverse relationship between air pollution and lung function in Asian men. However, our study does have some limitations. First, the study design was cross sectional, which means that no causal inferences can be made about the observed effects of adiposity on the relationship between air pollution and lung function. Second, we did not measure the exposure time to ambient air pollutants in individuals.

CONCLUSION

Our study identified a synergistic effect of adiposity on the relationship between prolonged exposure to air pollution and FEV₁ and FVC decreases in Asian men. Our findings provide the first evidence that accumulated abdominal fat intensifies the adverse effects of air pollutants on lung function.

CONFLICT OF INTEREST

The authors declare no conflict of interest.

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