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Association between long-term exposure to ambient air pollution and an increased risk of steatotic liver disease

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Steatotic liver disease (SLD), the most common chronic liver disease, imposes significant health and economic burdens. This study examined the association between long-term exposure to ambient air pollutants and SLD risk and severity in a population with relatively lower pollution levels. We analyzed 20,553 participants who underwent health screening from 2015–2019. Five-year exposures to $PM_{2.5}$, PM_{10}, NO_2, SO_2, and CO were estimated using nationwide monitoring data and modeled concentrations. SLD was diagnosed using ultrasonography and graded as mild, moderate, or severe. Multivariate and ordinal logistic regression analyses were used to evaluate the associations among air pollutant exposure, SLD risk, and severity. An interquartile range increase in 5-year pollutant exposure was associated with increased SLD risk: $PM_{2.5}$ (OR: 1.04, 95% CI: 1.01–1.07), PM_{10} (OR: 1.06, 95% CI: 1.01–1.11), NO_2 (OR: 1.10, 95% CI: 1.04–1.16), and CO (OR: 1.07, 95% CI: 1.02–1.12). Additionally, $PM_{2.5}$, NO_2, and CO exposure was associated with greater SLD severity. Subgroup analyses revealed heightened susceptibility in individuals with a higher body mass index and waist circumference. These findings suggest that even modest increases in air pollutant concentrations are associated with a higher SLD risk and severity, particularly in metabolically vulnerable individuals.

Keywords Steatotic liver disease, Air pollution, Exposure, Metabolic risk factor

Metabolic dysfunction-associated steatotic liver disease (MASLD), formerly known as non-alcoholic fatty liver disease (NAFLD), is the most common chronic liver disease worldwide and imposes significant health and economic burdens. A recent meta-analysis estimated the global prevalence of MASLD at 32.4%,[1] with deaths and disability-adjusted life years nearly doubling between 1990 and 2019[2]. The new classification of steatotic liver disease (SLD) emphasizes metabolic dysfunction, encompassing MASLD, alcohol-related liver disease (ALD), and metabolic dysfunction-associated liver disease with increased alcohol intake (MetALD)[3]. The revised nomenclature classifies individuals with cardiometabolic risk factors as having SLD regardless of alcohol consumption, emphasizing the central role of metabolic dysfunction in the progression of liver disease and the interplay between alcohol intake and metabolic risk in worsening liver fibrosis, underscoring the importance of managing metabolic dysfunction for its prevention and treatment.

Air pollution, particularly fine particulate matter ($PM_{2.5}$), has been widely studied because of its adverse health effects on respiratory and cardiovascular diseases[4]. Recent studies have explored its impact on metabolic disorders, including SLD. Although growing evidence suggests a link between air pollution and liver disease, most studies were conducted in regions with high levels of air pollution and had varied criteria for classifying liver diseases, which potentially affects the accuracy of the findings[5,6].

Given these gaps, it is crucial to examine the relationship between air pollution and SLD using consistent and updated disease classification criteria, particularly in regions with low baseline air pollutant levels. This study aimed to assess the association between long-term exposure to various air pollutants and the risk of developing SLD using newly defined diagnostic criteria, focusing on a population with relatively low air pollution exposure.

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Methods

Study population

The individuals involved in this study were adults aged ≥ 19 years who underwent a health screening program at the Seoul National University Hospital Health Promotion Center between 2015 and 2019. The health-screening program comprised anthropometric data collection, blood tests, major cancer screenings including abdominal ultrasound, and surveys designed to obtain health-related information. Of the 22,579 participants, we excluded individuals with missing data on the variables. Participants without other SLD were defined as the final study subjects (Fig. 1). The Institutional Review Board (IRB) of the Seoul National University Hospital (Seoul, Republic of Korea) approved this study (IRB no. H-2202–073-1299). Informed consent from participants was waived by the IRB of the Seoul National University Hospital. All the experiments were performed in accordance with the 1964 Declaration of Helsinki and its amendments.

Air pollution exposure

Hourly concentrations of particulate matter 2.5 ($PM_{2.5}$), particulate matter 10 (PM_{10}), sulfur dioxide (SO_2), nitrogen dioxide (NO_2), and carbon monoxide (CO) were collected from nationwide monitoring stations and were publicly accessible through the Air Korea database (https://www.airkorea.or.kr/web) operated by the Ministry of Environment of the Republic of Korea.[7] Using hourly data on air pollutants, we calculated the daily average concentrations for each administrative region by matching the hourly concentrations, based on a 9 km resolution, to the 250 administrative codes of cities, counties, and districts in the Republic of Korea. Participants' addresses were converted into administrative codes and integrated with the corresponding air pollution data. Based on this integration, we estimated the 5-year average air pollution exposure levels for all participants, considering the period preceding their health screening dates.

We used the Community Multiscale Air Quality (CMAQ, version 4.7.1) modeling system to estimate air pollutant concentrations for the period prior to the study. To generate the meteorological and emission inputs required for CMAQ, we employed the Weather Research and Forecasting (WRF, version 3.9) and Sparse Matrix Operator Kernel Emissions (SMOKE, version 3.1) models. The modeling process has been extensively described in previous studies.[8,9] Using the CMAQ model, daily air pollutant exposure concentrations were estimated and aggregated for 250 administrative regions across the country.

Steatotic liver disease definition

Steatotic liver disease was diagnosed using ultrasonography and classified as mild, moderate, or severe[10]. Among individuals with hepatic steatosis confirmed by ultrasound, those who met at least one of the following five cardiometabolic criteria were defined as having MASLD or MetALD/ALD: body mass index (BMI) ≥ 23 kg/m^2 or waist circumference (WC) ≥ 90 cm for men or ≥ 85 cm for women (for Korean populations[11]), fasting serum glucose ≥ 100 mg/dL or an HbA1c ≥ 5.7% or medication for diabetes, blood pressure ≥ 130/85 mmHg or antihypertensive treatment, plasma triglycerides ≥ 150 mg/dL or lipid-lowering treatment, and plasma high density lipoprotein (HDL)-cholesterol < 40 mg/dL for men or < 50 mg/dL for women[3]. Individuals

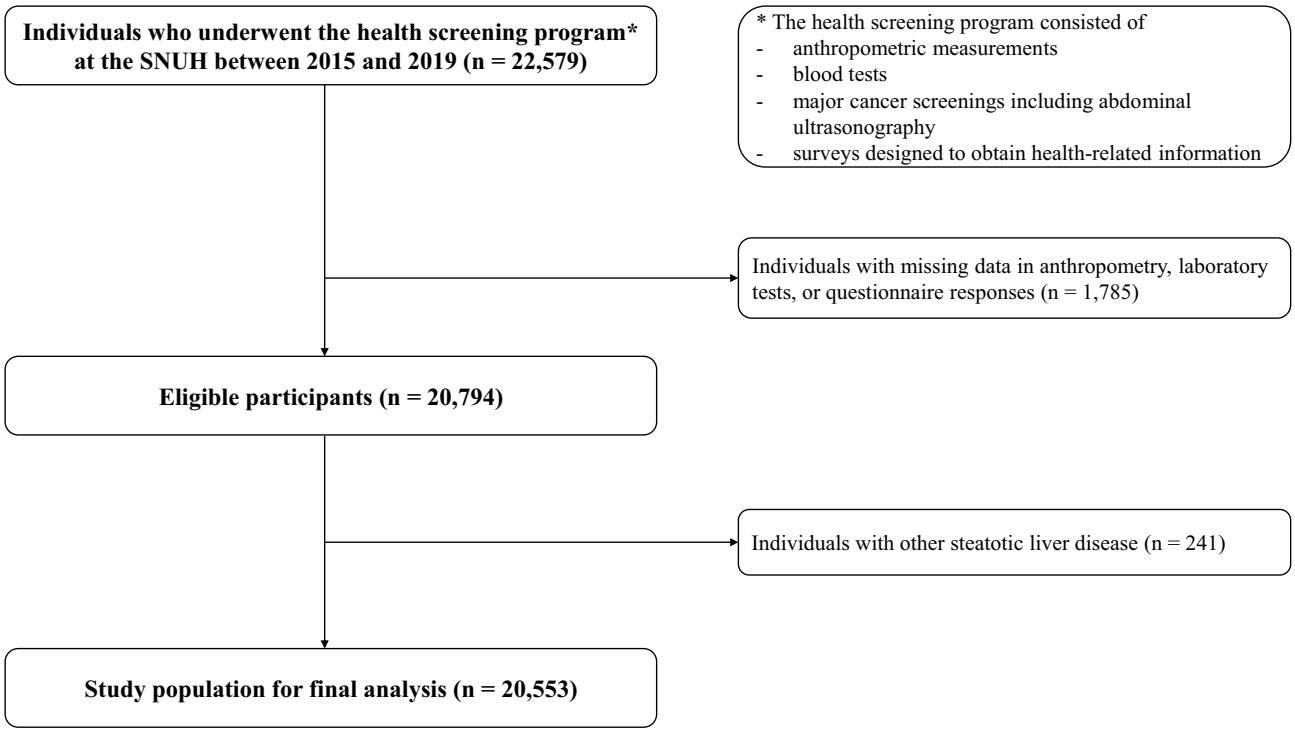

Fig. 1. Flow chart of the study population.

meeting the above criteria were classified based on their weekly alcohol consumption into MASLD (for women consuming < 140 g of alcohol per week and men consuming < 210 g of alcohol per week), MetALD (for women consuming 140–350 g of alcohol per week and men consuming 210–420 g of alcohol per week), and ALD (for those with higher alcohol consumption) groups[3]. Steatotic liver disease cases that did not meet the cardiometabolic criteria were classified as having other SLD.

Covariable definitions

Participants responded to questionnaires regarding their medical history and health behaviors such as smoking, alcohol consumption, and physical activity. By smoking status, participants were categorized as never smoker, former smoker, and current smoker. By alcohol consumption status, participants were categorized as light, moderate, or heavy drinkers based on the weekly alcohol intake criteria used for subclassifying SLD, as mentioned above. Adequate physical activity was defined as engaging in moderate-intensity physical activity for at least 150 min per week, vigorous-intensity physical activity for at least 75 min per week, or an equivalent combination thereof[12].

Comorbidities such as hypertension, diabetes, and dyslipidemia were defined by survey responses indicating the use of medication for the underlying conditions or if the respective diagnostic criteria were met (systolic blood pressure ≥ 140 mmHg or diastolic blood pressure ≥ 90 mmHg for hypertension, fasting blood glucose ≥ 126 mg/dL or HbA1c ≥ 6.5% for diabetes, and low-density lipoprotein (LDL) cholesterol ≥ 130 mg/dL for dyslipidemia) in the results of the health screening program.

Statistical analysis

The baseline characteristics of the participants were compared according to the presence of SLD using Student t-test for continuous variables and the chi-square test for categorical variables. Data are presented as mean (standard deviation) or number (%). Pearson correlation analysis was conducted to examine the association between the outcomes of interest and levels of exposure to each air pollutant. Multivariate logistic regression analyses were performed to obtain odds ratios (ORs) and 95% confidence intervals (CIs) of SLD associated with an interquartile range (IQR) increase in exposure to air pollutants, using the 5-year average exposure concentrations to assess the effects of long-term exposure to air pollutants. The risk of SLD was analyzed after adjusting for possible confounding factors, with sex, smoking status, alcohol consumption, physical activity, and underlying conditions such as hypertension, diabetes, and dyslipidemia treated as categorical variables and age, WC, and BMI treated as continuous variables. Model 1 was adjusted for age and sex, and model 2 was additionally adjusted for BMI, WC, and lifestyle factors (smoking status, alcohol consumption, and physical activity). Model 3 was further adjusted for a history of hypertension, diabetes, and dyslipidemia. Based on Model 3, interactions between the covariates and air pollutants that showed significant results were assessed to evaluate whether the covariates modified the effect. For continuous variables, the predicted probability of SLD was plotted across the 5th–95th percentile range of air pollutant concentrations, using the 5th–95th percentile range of the covariate divided into equal intervals. For categorical variables, stratified analyses were conducted to evaluate the interaction effects. To evaluate whether increasing average concentrations of air pollutants were associated with SLD severity (categorized as mild, moderate, or severe), ordinal logistic regression analysis was performed using a partial proportional odds model. This approach allowed for the relaxation of the proportional odds assumption, where necessary, ensuring a more flexible evaluation of the relationship between air pollutant exposure and disease severity[13]. Statistical analyses were performed using STATA software (MP, version 17.0; StataCorp, College Station, TX, USA), and statistical significance was defined as a two-sided $p < 0.05$.

Results

Baseline characteristics of the study population

Table 1 summarizes the baseline characteristics of the study population, highlighting significant differences between the SLD (n = 8,438) and non-SLD (n = 12,115) groups. The SLD group was older, had a higher proportion of men, and exhibited significantly higher BMI, abdominal obesity, blood pressure, and adverse metabolic parameters such as elevated fasting glucose, hemoglobin A1c, triglyceride, LDL cholesterol, AST, ALT, and GGT levels, along with lower HDL cholesterol levels ($p < 0.01$ for all). Lifestyle factors also differed, with the SLD group showing higher proportions of current smokers and moderate-to-heavy alcohol consumers, lower physical activity levels, and a greater prevalence of hypertension, diabetes, and dyslipidemia ($p < 0.01$ all). Regarding air pollutants, the SLD group was exposed to significantly lower concentrations of all the pollutants ($p < 0.01$).

Average concentrations and distribution of air pollutants

Table 2 summarizes the average concentrations, distribution, and correlations of air pollutants to which the participants had been exposed over the past five years from the date of screening. The mean concentrations of $PM_{2.5}$ and PM_{10} were 24.22 μg/m^3 (SD 2.33), and 44.32 μg/m^3 (SD 5.10), respectively. The IQR for $PM_{2.5}$ and PM_{10} were 2.06 μg/m^3 and 6.99 μg/m^3, respectively. For gaseous pollutants, the average concentrations were 25.93 ppb (SD 8.95) for NO_2; 4.14 ppb (SD 0.92), SO_2; and, 493.77 ppb (SD 75.12), CO. Notably, all correlation coefficients were statistically significant ($p < 0.001$), indicating a significant interrelationship between different air pollutants, and suggested that exposure to one pollutant is likely associated with exposure to others. Additionally, to examine the regional distribution of the average exposure concentrations of air pollutants, a map depicting the distribution of annual air pollutant exposure concentrations in 2017 by administrative unit based on the quintiles of the overall distribution is shown in Supp. Figure 1, which also illustrates the nationwide geographic distribution of the participants' residences.

	No SLD	SLD†	
	(n = 12,115)	(n = 8,438)	P-value
Age (years)	53.9 (13.8)	55.7 (11.8)	< 0.01
Sex (n, %)			< 0.01
Male	5,202 (42.9)	5,132 (60.8)	
Female	6,913 (57.1)	3,306 (39.2)	
BMI (kg/m2)	22.3 (2.8)	25.7 (3.2)	< 0.01
Waist circumference (cm)	80.2 (8.8)	90.6 (8.5)	< 0.01
Abdominal obesity (n, %)	2,433 (20.1)	5,261 (62.4)	< 0.01
Blood pressure (mmHg)			
Systolic	119.6 (17.4)	127.9 (15.9)	< 0.01
Diastolic	70.8 (11.3)	75.6 (10.8)	< 0.01
Fasting glucose (mg/dL)	93.2 (18.7)	105.0 (26.0)	< 0.01
Hemoglobin A1c (%)	5.7 (0.6)	6.0 (0.8)	< 0.01
Total cholesterol (mg/dL)	195.5 (37.3)	200.6 (41.7)	< 0.01
Triglyceride (mg/dL)	92.5 (49.9)	144.6 (96.1)	< 0.01
HDL-cholesterol (mg/DL)	62.6 (16.6)	51.8 (13.6)	< 0.01
LDL-cholesterol (mg/DL)	117.4 (34.1)	124.4 (38.5)	< 0.01
AST (IU/L)	23.7 (14.0)	28.0 (16.5)	< 0.01
ALT (IU/L)	22.0 (17.5)	34.2 (26.4)	< 0.01
GGT (IU/L)	27.7 (44.9)	44.5 (54.9)	< 0.01
Smoking status (n, %)			< 0.01
Never	7,911 (65.3)	4,404 (52.2)	
Previous	2,551 (21.1)	2,350 (27.8)	
Current	1,653 (13.6)	1,684 (20.0)	
Alcohol drinking†† (n, %)			< 0.01
Non	6,161 (50.9)	3,990 (47.3)	
Light	5,057 (41.7)	3,525 (41.8)	
Moderate	704 (5.8)	718 (8.5)	
Heavy	193 (1.6)	205 (2.4)	
Physical activity††† (n, %)			< 0.01
No	6,353 (52.4)	4,848 (57.5)	
Inadequate	1,107 (9.2)	717 (8.4)	
Adequate	4,655 (38.4)	2,873 (34.1)	
Comorbidities†††† (n, %)			
Hypertension	3,070 (25.3)	3,722 (44.1)	< 0.01
Diabetes mellitus	965 (8.0)	1,808 (21.4)	< 0.01
Dyslipidemia	5,325 (44.0)	5,075 (60.1)	< 0.01
Concentrations of air pollutants†††††			
Continued			

	No SLD	SLD†	
	(n = 12,115)	(n = 8,438)	P-value
$PM_{2.5}$ (μg/m^3)	24.3 (2.3)	24.2 (2.4)	< 0.01
PM_{10} (μg/m^3)	44.4 (5.1)	44.2 (5.2)	< 0.01
NO_2 (ppb)	26.1 (8.9)	25.7 (9.0)	< 0.01
SO_2 (ppb)	4.2 (0.9)	4.1 (0.9)	< 0.01
CO (ppb)	495.1 (74.2)	491.9 (76.3)	< 0.01

Table 1. Baseline characteristics of the study population. Data are presented as the mean (SD) and number (%). †The definition of steatotic liver disease (SLD) included metabolic dysfunction-associated steatotic liver disease (MASLD), MASLD and increased alcohol intake (metALD), and alcohol-associated liver disease (ALD). ††Light alcohol consumption was defined as consuming < 210 g of alcohol per week for men and < 140 g of alcohol per week for women. Moderate drinking was defined as consuming 210–420 g of alcohol per week for men and 140–350 g of alcohol per week for women. †††Adequate physical activity was defined as at least 150 min per week of moderate-intensity or 75 min per week of vigorous-intensity aerobic physical activity, or an equivalent combination of moderate- and vigorous-intensity aerobic activity. ††††Hypertension was defined as taking antihypertensive medications or having a blood pressure of 140/90 mmHg or higher on the day of examination. Diabetes was defined as taking diabetes medications or having a fasting blood glucose ≥ 126 mg/dl or an HbA1c ≥ 6.5%. Dyslipidemia was defined as the condition where lipid-lowering medication was being taken or LDL-cholesterol was ≥ 130 mg/dl. †††††5-year average concentrations of air pollutants were defined as the concentration of the air pollutant that the participant was exposed to on an average for five years from the date of examination. SLD, steatotic liver disease; BMI, body mass index; HDL, high-density lipoprotein; LDL, low-density lipoprotein; AST, aspartate aminotransferase; ALT, alanine aminotransferase; GGT, gamma-glutamyl transferase; PM, particulate matter; NO_2, nitrogen dioxide; SO_2, sulfur dioxide; CO, carbon monoxide.

				Percentile					Pearson's correlation coefficients				
Air pollutants	Mean	SD	IQR	10th	25th	50th	75th	90th	$PM_{2.5}$	PM_{10}	NO_2	SO_2	CO
$PM_{2.5}$ (μg/m^3)	24.22	2.33	2.06	20.42	23.64	24.69	25.70	26.61	1	0.8567*	0.5998*	0.6773*	0.6933*
PM_{10} (μg/m^3)	44.32	5.10	6.99	37.09	41.47	44.55	48.46	50.51	–	1	0.6998*	0.8025*	0.7230*
NO_2 (ppb)	25.93	8.95	14.69	12.28	18.23	29.25	32.92	35.63	–	–	1	0.7415*	0.8919*
SO_2 (ppb)	4.14	0.92	1.36	2.88	3.54	4.13	4.90	5.21	–	–	–	1	0.7344*
CO (ppb)	493.77	75.12	100.79	383.00	444.91	525.55	545.70	562.86	–	–	–	–	1

Table 2. Average concentrations, distribution, and correlations of air pollutants exposed over the past 5 years from the screening date. * all p-value < .001. PM, particulate matter; NO_2, nitrogen dioxide; SO_2, sulfur dioxide; CO, carbon monoxide.

SLD Odds ratio (95% confidence interval)								
Air pollutant	Unadjusted	p-value	Model 1*	p-value	Model 2†	p-value	Model 3‡	p-value
$PM_{2.5}$	0.97 (0.94, 0.99)	0.006	0.97 (0.94, 0.99)	0.007	1.04 (1.01, 1.07)	0.008	1.04 (1.01, 1.07)	0.009
PM_{10}	0.94 (0.91, 0.98)	0.002	0.96 (0.92, 0.99)	0.020	1.06 (1.01, 1.11)	0.012	1.06 (1.01, 1.11)	0.012
NO_2	0.93 (0.88, 0.97)	0.001	0.95 (0.91, 1.00)	0.050	1.09 (1.04, 1.15)	0.001	1.10 (1.04, 1.16)	0.001
SO_2	0.92 (0.88, 0.96)	< 0.001	0.94 (0.90, 0.98)	0.002	1.04 (0.99, 1.10)	0.080	1.04 (0.99, 1.10)	0.085
CO	0.95 (0.91, 0.98)	0.003	0.96 (0.92, 0.99)	0.027	1.07 (1.02, 1.12)	0.002	1.07 (1.02, 1.12)	0.003

Table 3. The odds ratios of SLD associated with an IQR increase according to 5-year exposure to air pollutants. *Adjusted for age and sex. †Adjusted for variables in model 1 and BMI, WC, smoking, alcohol consumption, and physical activity. ‡Adjusted for variables in model 2 and hypertension, diabetes mellitus, and dyslipidemia. SLD, steatotic liver disease; IQR, interquartile range; PM, particulate matter; BMI, body mass index; WC, waist circumference.

Impact of air pollutant exposure on the risk and severity of SLD

Table 3 shows that the 5-year exposure to $PM_{2.5}$, PM_{10}, NO_2, and CO was significantly associated with an increased SLD risk. The ORs for an IQR increase in exposure were 1.04 (95% CI: 1.01–1.07) for $PM_{2.5}$; 1.06 (95% CI: 1.01–1.11), PM_{10}; 1.10 (95% CI: 1.04–1.16), NO_2; and, 1.07 (95% CI: 1.02–1.12), CO in the fully adjusted model. However, the SO_2 levels showed no significant association with SLD risk.

Ordinal logistic regression analysis revealed that $PM_{2.5}$, NO_2, and CO levels were significantly associated with increased SLD severity (Table 4). The model demonstrated that an IQR increase in the 5-year average exposure to $PM_{2.5}$, NO_2, and CO was significantly associated with higher odds of more severe SLD. Specifically, the ORs for an IQR increase were 1.06 (95% CI: 1.03–1.08) for $PM_{2.5}$; 1.11 (95% CI: 1.06–1.16), NO_2; and, 1.09 (95% CI: 1.05–1.14), CO across all severity levels.

Interaction between covariates and air pollutants exposure on SLD risk

In the multivariate logistic regression analysis, significant interactions were observed between the 5-year air pollutant exposure and both BMI and WC on the risk of SLD. Specifically, the *p* -values for the interactions with BMI were 0.023 for $PM_{2.5}$; 0.003, PM_{10}; 0.004, NO_2; and, 0.001, CO. For WC, the *p* -values for the interactions were 0.018 for $PM_{2.5}$; 0.001, PM_{10}; 0.001, NO_2; and, < 0.001, CO. Figure 2 illustrates the estimated probabilities of SLD occurrence across different levels of air pollutant exposure, stratified by BMI (panel A) and WC (panel B). In subgroups with higher BMI or WC categories, the probability of SLD occurrence increased as air pollutant concentrations increased. Conversely, in subgroups with lower BMI or WC, the increase in SLD probability associated with higher air pollutant exposure was attenuated or even reversed, indicating a decrease in SLD occurrence.

Stratified analyses were performed for categorical covariates; however, significant interactions with air pollutant concentrations were rarely observed. Notably, physical activity showed a significant interaction with the PM_{10} concentration, whereas dyslipidemia exhibited a significant interaction with NO_2 and CO concentrations. Overall, the interactions across subgroups had minimal impact on the risk of SLD, suggesting that the subgroup-specific effects were limited (Supp. Figure 2).

Discussion

This cross-sectional study of 20,553 participants found that long-term exposure to ambient air pollutants, including $PM_{2.5}$, PM_{10}, NO_2, and CO, was significantly associated with a higher risk of SLD. Although evidence of a link between air pollution and hepatic steatosis is emerging, the variability in SLD definitions and baseline air pollution levels across studies contributes to a lack of clarity[5,14,15]. Our study addressed these issues by using precise air pollutant measurements and the gold standard ultrasound technique to assess hepatic steatosis, providing strong evidence of the association between SLD and air pollution.

Among these pollutants, $PM_{2.5}$ is particularly concerning because of its ability to penetrate deep into the respiratory system and enter the bloodstream, triggering oxidative stress and inflammation[16–18]. Additionally, $PM_{2.5}$ generates free radicals, triggers systemic inflammation, and impairs immune function, contributing to insulin resistance, impaired glucose metabolism, and altered lipid metabolism[4,19–21]. These processes ultimately promote fat accumulation and inflammation in the liver, as demonstrated in our study, which establishes a link between $PM_{2.5}$ exposure and SLD risk and disease severity.

Although the mechanism by which NO_2 influences SLD has not been fully elucidated, a study on children with overweight and obesity showed associations between NO_2 exposure and markers of metabolic dysfunction-associated steatohepatitis risk[22]. There is currently no established evidence for the association between exposure to other major air pollutants, such as SO_2 and CO, and SLD. Further research is required to clarify the mechanisms by which air pollutants contribute to the development and progression of SLD.

Long-term exposure to $PM_{2.5}$, NO_2, and CO was significantly associated with increased SLD severity, as assessed using ordinal logistic regression, suggesting that higher levels of these air pollutants not only increase the risk of developing SLD but also exacerbate its progression to more severe forms. Higher grades of fatty liver, as diagnosed using ultrasonography, are associated with an increased risk of metabolic syndrome[23,24]. Considering these findings in conjunction with our results, this suggests that higher concentrations of air pollutants may be independently associated with an increased risk of metabolic syndrome or potentially exacerbate its development by amplifying the underlying metabolic disturbances.

As BMI and WC increase, individuals become more susceptible to the effects of air pollutants on liver lipid metabolism. This is likely because higher body fat levels exacerbate oxidative stress and inflammatory responses in the liver. Prolonged exposure to $PM_{2.5}$ triggers the production of reactive oxygen species, which disrupt lipid metabolism and contribute to liver fat accumulation. In individuals with a higher BMI and WC, these processes

Air pollutant	β	Odds ratio	95% CI	P-value
$PM_{2.5}$	0.055	1.056	1.029 – 1.085	< 0.001
NO_2	0.104	1.109	1.056 – 1.165	< 0.001
CO	0.087	1.091	1.047 – 1.135	< 0.001

Table 4. Ordinal logistic regression results for the association between an IQR increase of air pollutant concentrations and SLD severity. The model was adjusted for age, sex, BMI, WC, smoking, alcohol consumption, physical activity, and comorbidities (hypertension, diabetes, and dyslipidemia). The proportional odds assumption was tested, and a partial proportional odds model was applied when the assumption was violated ($P < 0.05$). In the partial proportional odds model, age, sex, WC, diabetes, dyslipidemia, and alcohol consumption violated the proportional odds assumption and were allowed to have nonproportional effects across severity levels. SLD, steatotic liver disease; IQR, interquartile range; PM, particulate matter; BMI, body mass index; WC, waist circumference.

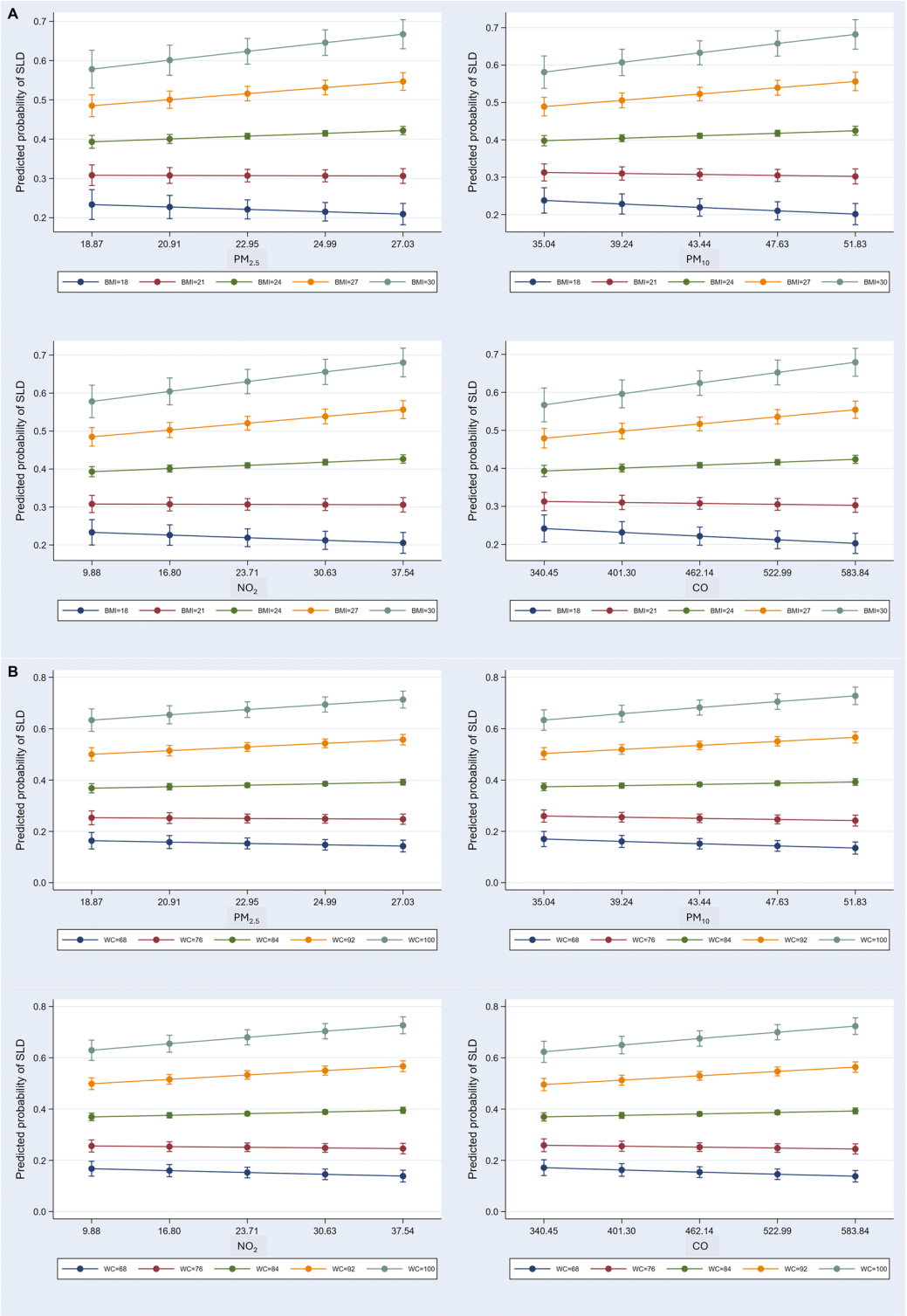

Fig. 2. Effect of air pollutant concentrations on SLD probability stratified by BMI and WC levels, (**A**) BMI (kg/m^2) (**B**) WC (cm), The predicted probability of SLD was plotted across the 5th–95th percentile range of air pollutant concentrations, using the 5th–95th percentile range of the covariate divided into equal intervals. SLD, steatotic liver disease; BMI, body mass index; WC, waist circumference; PM, particulate matter; NO_2, nitrogen dioxide; CO, carbon monoxide.

are more pronounced because of the existing metabolic strain associated with excess body fat. The compounding effect of $PM_{2.5}$ and body fat accumulation likely amplifies hepatic inflammation and lipid dysregulation[20,25,26]. Considering these findings alongside the alarming global surge in obesity rates[27], it becomes evident that mitigating the adverse effects of air pollution on liver health requires not only efforts to reduce air pollution but also comprehensive strategies to lower overall obesity rates. Addressing obesity may help diminish the susceptibility to air pollutant-induced liver fat accumulation and associated metabolic disturbances.

Although the new SLD classification emphasizes the interaction between alcohol consumption and metabolic risk factors in liver fibrosis progression[28], our study did not observe an effect of alcohol consumption on the relationship between air pollution and SLD development. This could be because of the high proportion of participants with alcohol consumption levels consistent with MASLD, making it challenging to assess the role of alcohol in this interaction. Furthermore, the lower air pollution levels in our study compared to those in other regions such as China[5] might explain the lack of significant differences observed in alcohol consumption. Further research is required to better understand the mechanisms underlying these differences.

Our findings are consistent with those of previous studies conducted in China, which also observed a positive association between air pollution and MAFLD[5,6]. However, a distinctive aspect of our study compared to previous research was the lower baseline air pollutant concentrations (76.6 $\mu g/m^3$ vs. 24.2 $\mu g/m^3$ for the average $PM_{2.5}$ concentration). Despite minimal regional variations in $PM_{2.5}$ levels, a notable difference in SLD risk was observed when calculated based on the IQR criteria (32.2 $\mu g/m^3$ vs. 2.1 $\mu g/m^3$ for the IQR). This suggests that even relatively minor variations in $PM_{2.5}$ exposure can have a significant impact on SLD risk, reinforcing the importance of addressing air quality, even in regions with comparatively lower pollution levels.

A major strength of our study lies in the use of the updated SLD classification criteria and precise measurement of long-term air pollutant exposure using the CMAQ model. Thus, our study is noteworthy because it clearly presents the relationship between ambient air pollutants and the risk of SLD. Despite minimal regional variations in air pollution levels (5-year IQR of $PM_{2.5}$ 2.1 $\mu g/m^3$), the strong association between air pollution and SLD risk highlights the need for the reasonable argument for minimizing air pollutant concentrations from a health perspective. Previous studies analyzing the association between hepatic steatosis and air pollutants in Asian regions often faced challenges owing to the generally higher baseline levels of air pollutant concentrations and significant regional variations. Consequently, it is difficult to generalize these studies to a broader global context. In contrast, our study provides a more generalized assessment of the hepatic risk associated with air pollution exposure at a more typical level, offering a global message. Therefore, our research findings provide further support for a global policy consensus, including the WHO, advocating the need to reduce exposure to air pollutants.

This study had several limitations. First, air pollution exposure was estimated based on long-term concentrations at participants' residential addresses, which may not accurately reflect individual exposure, particularly for those with varying daily routines or changes in addresses during the study period. Second, there were regional differences in the average air pollution levels, but we did not consider other socioeconomic factors that may influence residential decisions and consequently affect exposure levels. Finally, given the cross-sectional nature of this study, caution is required while interpreting the causal relationship between air pollution and SLD.

In conclusion, this study demonstrated a significant association between long-term exposure to ambient air pollutants, particularly $PM_{2.5}$, PM_{10}, NO_2, and CO, and the risk of SLD. These findings suggest that even small differences in air pollutant exposure levels can substantially increase the risk of SLD, particularly in individuals with a higher BMI and WC. These results underscore the importance of reducing air pollution levels as a part of the global effort to prevent SLD. Given the relatively lower baseline levels of air pollutants in this study compared with that reported previously in other regions, these findings reinforce the need for stricter air quality standards.

Data availability

The data used in this study are derived from actual health screening records and are accessible only to researchers approved by the Institutional Review Board of Seoul National University Hospital. Owing to privacy and ethical considerations, these datasets cannot be publicly shared. However, they may be made available from the corresponding author (JHP) upon reasonable request and with appropriate institutional approval.

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Author contributions

JMY and JHP provided overall leadership and guidance for the investigation. SHC performed the statistical analysis and data curation. All authors performed the data analysis and interpretation. SHC prepared the original manuscript, and all authors revised the manuscript. All the authors have reviewed and approved the final manuscript. JMY and JHP made the decision to submit the manuscript for publication.

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Declarations

Competing interests

The authors declare no competing interests.

Additional information

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