



## ORIGINAL ARTICLE

# The effects of hidden female smokers on the association between smoking and chronic obstructive pulmonary disease in Korean adults



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## KEYWORDS

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## Abstract

**Objective:** Smoking is an important causative factor of chronic obstructive pulmonary disease (COPD), and females are considered more susceptible to the effects of smoking than males. However, in previous Korean studies, the effects of sex differences on the association between smoking and COPD have been controversial. In this study, the effects of sex differences on the association between smoking and COPD and the effects of female hidden smokers on that association in Korean adults were investigated.

**Methods:** Data were acquired from the Korea National Health and Nutrition Examination Surveys (KNHANES).

**Results:** The multivariate logistic regression analysis showed that self-reported smoking status for ex-smoker and current smoker correlated with COPD (odds ratio, OR: 1.67 and OR: 2.41, respectively). Self-reported smoking status for ex-smoker and current smoker correlated with COPD in men (OR: 1.61, OR: 2.43, respectively). Female self-reported current smoking status correlated with COPD (OR: 2.52), but female ex-smoker status was not significantly correlated with COPD. The ratios of cotinine-verified to self-reported smoking rates were 1.95 for women and 1.07 for men.

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*Conclusion:* The results of this study were that sex differences might affect the association between COPD and smoking and that female hidden smoking might affect the association between smoking and COPD in Korean adults.

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## Introduction

Chronic obstructive pulmonary disease (COPD) is a leading cause of morbidity and mortality<sup>1</sup> and the economic burden of COPD is increasing.<sup>2</sup>

Smoking is the most important causative factor of COPD. However, while more than 4000 chemical substances contained in a cigarette have adverse effects on various pulmonary diseases, the pathophysiological mechanisms underlying the association between smoking and COPD have not been fully elucidated.<sup>3</sup>

The effects of gender on COPD are well known, and women are widely considered more susceptible to the effects of smoking than men.<sup>4,5</sup> The suggested reasons for the increased susceptibility of women to the effects of smoking include a smaller airway size compared with men<sup>6</sup> and female sex hormone-mediated metabolism differences.<sup>7</sup>

In a Norwegian study, more women were current smokers. The authors hypothesized that females were more susceptible to the lung damaging effects of cigarette smoking.<sup>4</sup> In other studies based on larger reductions in forced expiratory volume in 1 second (FEV1) and after adjustment for smoking intensity, female smokers were shown to develop COPD more often than male smokers.<sup>8,9</sup>

However, the effects of sex on the association between current smoker status and COPD in Korean adults are controversial. In a community-based cohort Korean study, current smoker status was significantly associated with COPD in men (risk ratio, RR: 2.28, 95% confidence interval, CI: 1.86–2.80) and in women (RR: 4.04, 95% CI: 2.84–5.75).<sup>10</sup> However, in another population sample-based study in which a non-smoking group of Korean adults was used for comparison, the odds ratio (OR, 95% CI) for COPD in the current smoker group was 3.49 (2.44–5.00) in men and 3.45 (2.20–5.40) in women.<sup>11</sup>

In addition, one previous study showed the ratios of cotinine-verified to self-reported smoking rates were 2.36 for females and 1.12 for males in Korea,<sup>12</sup> and another study showed the effects of female hidden smoking on the association between smoking and hypertension in Korean adults.<sup>13</sup>

Therefore, in this study, we investigated the effects of sex differences on the association between smoking and COPD and the effects of female hidden smoking on the association between smoking and COPD in Korean adults.

## Methods

### Study population

This study was based on data obtained from the 2008 to 2016 Korea National Health and Nutrition Examination Surveys (KNHANES), a cross-sectional survey designed to examine the health and nutritional status of the non-institutionalized Korean population and conducted by the Division of Chronic Disease Surveillance at the Korea Centers for Disease Control and Prevention (KCDC).

The study included 76,909 KNHANES participants; 62,552 participants were excluded due to the following criteria: <40 years of age, no smoking history, no COPD information, no urine cotinine test results, no weights for the results of pulmonary function test, history of renal failure, or serum creatinine  $\geq 1.5$  mg/dL. The remaining 14,357 participants (6424 males and 7933 females) were included in the final analysis.

### General characteristics, anthropometry, and laboratory tests

KNHANES includes well-established questions to determine the demographic and socioeconomic characteristics of the participants. The questions include sex, age, marital status, employment status, educational level, monthly family income, number of household members, residential area, body mass index (BMI), hypertension, diabetes, myocardial infarction, and stroke. The residential areas of respondents were categorized as urban (an administrative division of a city) or rural (not classified as an administrative division of a city). A city in Korea was defined as an area with >50,000 inhabitants. Monthly family income represents monthly equalized family income and was calculated by dividing the total family income by the square root of the number of household members. In KNHANES, monthly family income is classified into quartiles to determine the monthly household income level (1: low, 2: middle low, 3: middle high, and 4: high). Educational levels were defined as less than middle school, middle school, high school, or college or more. BMI was calculated as weight (kg) divided by height squared ( $m^2$ ) and was categorized into three groups: underweight ( $<18.5$  kg/ $m^2$ ), normal (18.5–23 kg/ $m^2$ ), and overweight ( $\geq 23$  kg/ $m^2$ ).<sup>14</sup>

**Table 1** Definition of survey cotinine-verified smoking status.

	Cotinine-verified smoking status	
	Non-smoker ( $\leq 50$ ng/mL)	Current smoker ( $> 50$ ng/mL)
<i>Self-reported smoking status</i>		
Non-smoker	Non-smoker ( $n = 8,289$ )	Current smoker ( $n = 317$ )
Ex-smoker	Ex-smoker ( $n = 2,919$ )	Current smoker ( $n = 207$ )
Current smoker	Current smoker ( $n = 65$ )	Current smoker ( $n = 2,560$ )

Cigarette smoking status was divided into three categories: smoker, ex-smoker, and never smoker. Respondents who reported having smoked  $\geq 100$  cigarettes in their lifetime or responded "yes" to the question, "Do you smoke cigarettes now?" were regarded as current smokers. Participants answering "no" to the same question were classified as ex-smokers. Respondents who consumed  $< 100$  cigarettes in their lifetime were regarded as never smokers.

Urinary cotinine was measured using tandem mass spectrometry (tandem mass API 4000; Applied Biosystems, Carlsbad, CA, USA) and gas chromatography/mass spectrometry (Perkin Elmer Clarus 600T; PerkinElmer, Turku, Finland). Respondents with urinary cotinine levels  $\geq 50$  ng/mL were considered cotinine-verified smokers, and those with cotinine levels  $< 50$  ng/mL were cotinine-verified non-smokers.<sup>15</sup>

COPD was defined as FEV1/forced vital capacity (FEV1/FVC, % FEV1)  $< 0.7$  on pulmonary function test in subjects  $> 40$  years of age. Hypertension was defined as elevated blood pressure (BP; systolic BP, SBP  $\geq 140$  mmHg and/or diastolic BP, DBP  $\geq 90$  mmHg) or taking anti-hypertensive medication. Diabetes was defined as fasting blood glucose (FBG) of 126 mg/dL or a diabetes diagnosis from a physician and taking diabetes medication or starting insulin therapy.

To better understand the link between COPD and smoking, a new variable was used to define smoking status (survey cotinine-verified smoking status, SCS; Table 1). In using this variable, we assumed smoking meant all kinds of smoking types, including light smoking, intermittent smoking, passive smoking, hidden smoking, and active heavy smoking (Table 1).

## Statistical analysis

All statistical analyses were conducted using SPSS complex sample procedures because KNHANES data were collected through a representative, stratified, and clustered sampling method. Multivariate logistic regression analysis was performed to identify the relationships between risk factors and the prevalence of COPD. Multivariate logistic regression analysis was also used to evaluate the relationship between self-reported and cotinine-verified smoking status and the presence of COPD. Statistical analyses were conducted using the Statistical Package for the Social Sciences (SPSS) version 21.0 (SPSS Inc. Chicago, IL, USA). For all analyses,  $p$ -values were two-tailed; a  $p$ -value  $< 0.05$  was considered statistically significant.

## Results

### Clinical characteristics

A total of 14,357 subjects from the KNHANES were included in this study. Mean age was  $57.11 \pm 10.71$  years. The majority of participants were married (85.06%), employed (64.86%), and had an educational level of high school or less (74.16%). Most subjects lived in urban areas (80.21%; Table 2). The prevalence of self-reported smoking was 21.82% and the prevalence of cotinine-verified smoking in the overall population was 25.14% (Table 2).

### Relationship between COPD and smoking

Based on univariate analysis, compared to subjects without COPD, subjects with COPD tended to be male ( $p < 0.01$ ), older ( $p < 0.01$ ), single (separated or divorced;  $p < 0.01$ ), unemployed ( $p < 0.01$ ), less educated ( $p < 0.01$ ), and obese ( $p < 0.01$ ). Those with COPD had a lower monthly family income ( $p < 0.01$ ), had fewer household members ( $p < 0.01$ ), lived in a rural setting ( $p < 0.01$ ), were over or underweight ( $p < 0.01$ ), and had higher prevalence of hypertension ( $p < 0.01$ ) and diabetes ( $p < 0.01$ ) compared to subjects without COPD.

Multivariate logistic regression analysis showed that for self-reported smoking status, ex-smoker and current smoker status correlated with COPD (OR: 1.67, 95% CI: 1.34–2.07 and OR: 2.41, 95% CI: 1.92–3.01, respectively). In addition, current smoking status correlated with COPD based on cotinine-verified smoking status (OR: 1.68, 95% CI: 1.44–1.95); ex-smoker status and current smoker status correlated with COPD in SCS (OR: 1.60, 95% CI: 1.29–1.99 and OR: 2.23, 95% CI: 1.81–2.75, respectively; Table 3).

To determine the effects of sex on smoking and COPD, sex differences were analyzed separately. For male participants, self-reported ex-smoker and current smoker status correlated with COPD (OR: 1.61, 95% CI: 1.25–2.07 and OR: 2.43, 95% CI: 1.86–3.18, respectively). Based on cotinine-verified smoking status, current smoker status correlated with COPD (OR: 1.65, 95% CI: 1.40–1.96), and, based on SCS, ex-smoker and current smoker status correlated with COPD (OR: 1.58, 95% CI: 1.22–2.05 and OR: 2.29, 95% CI: 1.76–2.99, respectively). Self-reported and SCS-based current smoker status in women also correlated with COPD (OR: 2.52, CI: 1.66–3.83 and OR: 2.13, 95% CI: 1.51–3.02, respectively). However, self-reported and SCS-based ex-smoker status were not significantly correlated with COPD.

**Table 2** Demographic characteristics of study subjects.

Characteristics	Sample size	Estimate % (95% CI)
<b>Sex (n = 14,357)</b>		
Male	6,424	49.60 (48.79–50.41)
Female	7,933	50.40 (49.59–51.21)
<b>Age (years; n = 14,357)</b>		
40–49	4,187	35.75 (34.60–36.91)
50–59	4,432	31.25 (30.24–32.28)
60–69	3,644	19.79 (18.98–20.61)
≥70	2,094	13.22 (12.45–14.02)
<b>Marital status (n = 14,276)</b>		
Married	11,943	85.06 (84.23–85.86)
Single (separated or divorced)	2,104	12.78 (12.07–13.52)
Never married	229	2.16 (1.85–2.51)
<b>Employment status (n = 14,088)</b>		
Employed	8,805	64.86 (63.74–65.96)
Unemployed	5,283	35.14 (34.04–36.26)
<b>Educational level (n = 14,084)</b>		
<High school	6,345	41.04 (39.65–42.45)
High school	4,393	33.12 (32.06–34.19)
>High school	3,346	25.84 (24.48–27.25)
<b>Monthly family income (n = 14,234)</b>		
<25th	2,882	18.53 (17.52–19.58)
25–50th	3,645	24.97 (23.90–26.06)
50–75th	3,625	26.91 (25.82–28.02)
≥75th	4,082	29.60 (28.13–31.11)
<b>Number of household members (n = 14,352)</b>		
1	1,314	6.58 (6.08–7.12)
2	4,864	28.87 (27.86–29.91)
3	3,349	24.48 (23.51–25.47)
4	3,261	26.94 (25.84–28.08)
≥5	1,564	13.12 (12.26–14.03)
<b>Residential area (n = 14,357)</b>		
Urban	10,973	80.21 (77.84–82.39)
Rural	3,384	19.79 (17.61–22.16)
<b>Smoking status</b>		
<i>Self-reported (n = 14,357)</i>		
Non-smoker	8,606	55.84 (54.93–56.75)
Ex-smoker	3,126	22.33 (21.57–23.12)
Current smoker	2,625	21.82 (20.97–22.70)
<i>Cotinine-verified (n = 14,357)</i>		
Non-smoker	11,273	74.86 (73.95–75.76)
Current smoker	3,084	25.14 (24.24–26.05)
<i>Survey cotinine-verified (n = 14,357)</i>		
Non-smoker	8,289	53.52 (52.60–54.44)
Ex-smoker	2,919	20.80 (20.04–21.58)
Current smoker	3,149	25.68 (24.78–26.61)
<b>BMI (n = 14,344)</b>		
<18.5	133	0.89 (0.72–1.09)
18.5–23	5,016	34.58 (33.61–35.58)
≥23	9,195	64.53 (63.53–65.51)
<b>Hypertension (n = 14,167)</b>	5,509	37.80 (36.77–38.85)
<b>Diabetes (n = 13,592)</b>	1,851	13.19 (12.51–13.90)
<b>COPD (n = 14,357)</b>	2,006	13.08 (12.42–13.77)

**Table 3** Adjusted OR and 95% CI for the prevalence of COPD.

Characteristics	Self-reported	Cotinine-verified	Survey cotinine-verified
<b>Sex</b>			
Male	3.29 (2.63–4.12)	4.68 (3.97–5.53)	3.50 (2.83–4.32)
Female	Reference	Reference	Reference
<b>Age (years)</b>			
40–49	Reference	Reference	Reference
50–59	2.42 (1.91–3.07)	2.42 (1.91–3.07)	2.43 (1.92–3.08)
60–69	6.19 (4.76–8.04)	6.22 (4.79–8.09)	6.19 (4.76–8.05)
≥70	11.84 (8.94–15.70)	11.84 (8.94–15.69)	11.82 (8.91–15.68)
<b>Marital status</b>			
Married	Reference	Reference	Reference
Single (separated or divorced)	1.14 (0.90–1.44)	1.17 (0.93–1.47)	1.14 (0.91–1.45)
Never married	0.96 (0.53–1.74)	0.96 (0.53–1.73)	0.98 (0.54–1.77)
<b>Employment status</b>			
Employed	Reference	Reference	Reference
Unemployed	1.09 (0.94–1.27)	1.11 (0.95–1.29)	1.09 (0.94–1.27)
<b>Educational level</b>			
<High school	1.54 (1.25–1.90)	1.56 (1.27–1.92)	1.54 (1.25–1.90)
High school	1.19 (0.97–1.47)	1.22 (0.99–1.50)	1.20 (0.97–1.47)
>High school	Reference	Reference	Reference
<b>Monthly family income</b>			
<25th	1.12 (0.90–1.40)	1.10 (0.88–1.37)	1.11 (0.89–1.39)
25–50th	1.02 (0.82–1.27)	1.02 (0.82–1.26)	1.02 (0.82–1.26)
50–75th	1.07 (0.88–1.31)	1.06 (0.87–1.30)	1.06 (0.87–1.30)
≥75th	Reference	Reference	Reference
<b>Number of household members</b>			
1	1.01 (0.73–1.39)	1.03 (0.75–1.42)	1.02 (0.74–1.40)
2	1.06 (0.84–1.35)	1.08 (0.85–1.37)	1.06 (0.84–1.35)
3	1.11 (0.86–1.44)	1.12 (0.86–1.44)	1.10 (0.85–1.43)
4	0.98 (0.75–1.29)	0.99 (0.75–1.29)	0.98 (0.75–1.28)
≥5	Reference	Reference	Reference
<b>Residential area</b>			
Urban	Reference	Reference	Reference
Rural	1.02 (0.87–1.20)	1.01 (0.86–1.19)	1.02 (0.87–1.19)
<b>Smoking status</b>			
<i>Self-reported</i>			
Non-smoker	Reference	–	–
Ex-smoker	1.67 (1.34–2.07)	–	–
Current smoker	2.41 (1.92–3.01)	–	–
<i>Cotinine-verified</i>			
Non-smoker	–	Reference	–
Current smoker	–	1.68 (1.44–1.95)	–
<i>Survey cotinine-verified</i>			
Non-smoker	–	–	Reference
Ex-smoker	–	–	1.60 (1.29–1.99)
Current smoker	–	–	2.23 (1.81–2.75)
<b>BMI</b>			
<18.5	1.24 (0.77–1.98)	1.28 (0.81–2.03)	1.25 (0.79–1.99)
18.5–23	Reference	Reference	Reference
≥23	0.72 (0.62–0.83)	0.72 (0.63–0.84)	0.72 (0.62–0.83)
<b>Hypertension</b>			
No	Reference	Reference	Reference
Yes	0.94 (0.83–1.08)	0.94 (0.82–1.07)	0.94 (0.82–1.08)
<b>Diabetes</b>			
No	Reference	Reference	Reference
Yes	1.04 (0.87–1.23)	1.05 (0.88–1.25)	1.04 (0.88–1.24)

**Table 4** Adjusted OR and the associated 95% CI for the prevalence of COPD in males.

Characteristics	Self-reported	Cotinine-verified	Survey cotinine-verified
<b>Age (years)</b>			
40–49	Reference	Reference	Reference
50–59	2.61 (1.98–3.44)	2.60 (1.98–3.42)	2.62 (1.99–3.45)
60–69	7.06 (5.18–9.61)	7.04 (5.19–9.54)	7.02 (5.16–9.54)
≥70	14.52 (10.27–20.53)	14.21 (10.11–19.98)	14.40 (10.19–20.33)
<b>Marital status</b>			
Married	Reference	Reference	Reference
Single (separated or divorced)	1.11 (0.74–1.66)	1.14 (0.76–1.70)	1.12 (0.75–1.68)
Never married	1.24 (0.64–2.40)	1.24 (0.64–2.38)	1.27 (0.66–2.44)
<b>Employment status</b>			
Employed	Reference	Reference	Reference
Unemployed	1.18 (0.96–1.45)	1.21 (0.99–1.48)	1.18 (0.96–1.44)
<b>Educational level</b>			
<High school	1.60 (1.27–2.02)	1.62 (1.29–2.05)	1.59 (1.26–2.01)
High school	1.23 (0.97–1.55)	1.26 (1.01–1.59)	1.23 (0.98–1.55)
>High school	Reference	Reference	Reference
<b>Monthly family income</b>			
<25th	1.24 (0.94–1.63)	1.21 (0.91–1.59)	1.23 (0.93–1.62)
25–50th	1.04 (0.80–1.34)	1.03 (0.79–1.33)	1.03 (0.80–1.34)
50–75th	1.13 (0.89–1.43)	1.12 (0.89–1.42)	1.13 (0.89–1.42)
≥75th	Reference	Reference	Reference
<b>Number of household members</b>			
1	0.66 (0.41–1.06)	0.66 (0.41–1.06)	0.66 (0.41–1.06)
2	0.93 (0.70–1.23)	0.94 (0.70–1.25)	0.93 (0.69–1.23)
3	0.95 (0.70–1.29)	0.96 (0.70–1.30)	0.95 (0.70–1.29)
4	0.97 (0.70–1.34)	0.97 (0.70–1.34)	0.97 (0.70–1.34)
≥5	Reference	Reference	Reference
<b>Residential area</b>			
Urban	Reference	Reference	Reference
Rural	1.03 (0.85–1.24)	1.02 (0.85–1.24)	1.03 (0.85–1.24)
<b>Smoking status</b>			
<i>Self-reported</i>			
Non-smoker	Reference	–	–
Ex-smoker	1.61 (1.25–2.07)	–	–
Current smoker	2.43 (1.86–3.18)	–	–
<i>Cotinine-verified</i>			
Non-smoker	–	Reference	–
Current smoker	–	1.65 (1.40–1.96)	–
<i>Survey cotinine-verified</i>			
Non-smoker	–	–	Reference
Ex-smoker	–	–	1.58 (1.22–2.05)
Current smoker	–	–	2.29 (1.76–2.99)
<b>BMI</b>			
<18.5	1.16 (1.25–2.07)	1.20 (0.67–2.13)	1.17 (0.65–2.08)
18.5–23	Reference	Reference	Reference
≥23	0.83 (0.69–0.99)	0.83 (0.70–0.99)	0.82 (0.69–0.99)
<b>Hypertension</b>			
No	Reference	Reference	Reference
Yes	1.00 (0.85–1.18)	0.99 (0.84–1.17)	0.99 (0.84–1.17)
<b>Diabetes</b>			
No	Reference	Reference	Reference
Yes	1.10 (0.90–1.36)	1.12 (0.91–1.38)	1.11 (0.90–1.36)

**Table 5** Adjusted OR and 95% CI for the prevalence of COPD in females.

Characteristics	Self-reported	Cotinine-verified	Survey cotinine-verified
<b>Age (years)</b>			
40–49	Reference	Reference	Reference
50–59	1.92 (1.23–3.02)	1.91 (1.21–3.02)	1.92 (1.22–3.03)
60–69	4.39 (2.76–6.98)	4.39 (2.72–7.08)	4.44 (2.75–7.15)
≥70	7.71 (4.68–12.70)	7.73 (4.63–12.92)	7.79 (4.67–13.02)
<b>Marital status</b>			
Married	Reference	Reference	Reference
Single (separated or divorced)	1.32 (0.98–1.78)	1.33 (0.99–1.79)	1.32 (0.98–1.78)
Never married	0.28 (0.06–1.33)	1.30 (0.06–1.42)	0.29 (0.06–1.38)
<b>Employment status</b>			
Employed	Reference	Reference	Reference
Unemployed	0.93 (0.74–1.17)	0.93 (0.74–1.17)	0.93 (0.74–1.17)
<b>Education</b>			
<High school	1.45 (0.93–2.26)	1.45 (0.94–2.26)	1.45 (0.93–2.26)
High school	0.97 (0.60–1.56)	0.97 (0.60–1.57)	0.97 (0.60–1.57)
>High school	Reference	Reference	Reference
<b>Monthly family income</b>			
<25th	0.80 (0.54–1.17)	0.79 (0.53–1.16)	0.78 (0.53–1.15)
25–50th	0.86 (0.60–1.25)	0.86 (0.59–1.24)	0.86 (0.59–1.24)
50–75th	0.86 (0.58–1.27)	0.85 (0.57–1.26)	0.85 (0.57–1.26)
≥75th	Reference	Reference	Reference
<b>Number of household members</b>			
1	1.74 (1.01–2.99)	1.78 (1.03–3.08)	1.77 (1.02–3.05)
2	1.39 (0.86–2.26)	1.41 (0.86–2.29)	1.40 (0.86–2.28)
3	1.52 (0.92–2.52)	1.51 (0.91–2.49)	1.51 (0.91–2.50)
4	0.99 (0.59–1.68)	0.99 (0.59–1.68)	0.99 (0.59–1.68)
≥5	Reference	Reference	Reference
<b>Residential area</b>			
Urban	Reference	Reference	Reference
Rural	1.01 (0.78–1.31)	0.98 (0.75–1.27)	0.99 (0.77–1.28)
<b>Smoking status</b>			
<i>Self-reported</i>			
Non-smoker	Reference	–	–
Ex-smoker	1.63 (0.94–2.85)	–	–
Current smoker	2.52 (1.66–3.83)	–	–
<i>Cotinine-verified</i>			
Non-smoker	–	Reference	–
Current smoker	–	2.11 (1.49–2.98)	–
<i>Survey cotinine-verified</i>			
Non-smoker	–	–	Reference
Ex-smoker	–	–	1.49 (0.80–2.79)
Current smoker	–	–	2.13 (1.51–3.02)
<b>BMI</b>			
<18.5	1.26 (0.66–2.39)	1.30 (0.68–2.45)	1.29 (0.68–2.45)
18.5–23	Reference	Reference	Reference
≥23	0.54 (1.66–3.83)	0.55 (0.43–0.70)	0.55 (0.43–0.70)
<b>Hypertension</b>			
No	Reference	Reference	Reference
Yes	0.86 (0.68–1.09)	0.86 (0.68–1.09)	0.86 (0.68–1.09)
<b>Diabetes</b>			
No	Reference	Reference	Reference
Yes	0.89 (0.63–1.27)	0.89 (0.63–1.26)	0.89 (0.63–1.26)

Based on cotinine-verified smoking status, current smoker was associated with COPD (OR: 2.11, 95% CI: 1.49–2.98; Tables 4 and 5).

## Discussion

The main findings of this study were that ex-smoker and current smoker status were significantly associated with COPD in the overall population. In addition, sex effects were observed as well as an effect of female hidden smokers on the relationship between smoking and COPD in Korean adults.

The effects of sex on COPD are well established, and females are widely considered more susceptible to the effects of smoking than males.<sup>4,5</sup> There are several hypotheses that explain sex-related variation in COPD prevalence. First, women may experience greater exposure to cigarette smoke due to possessing smaller airways than men.<sup>6</sup> Second, female sex hormones may contribute to oxidative stress and, eventually, greater airway injury. During smoking, numerous smoking chemicals are metabolized in two phases. Phase I is mediated largely by cytochrome P450 (CYP) enzymes; these are responsible for detoxifying cigarette smoke into intermediate metabolites. Subsequently, these metabolites are conjugated by phase II enzymes and excreted. Because several intermediate metabolites are toxic, estradiol upregulates CYP enzymes without necessarily altering the expression of phase II enzymes. This causes the female lungs to be more susceptible to oxidant damage in response to cigarette smoke.<sup>7,16</sup>

Compared with other previous foreign studies, the results in previous Korean studies regarding the effects of sex on the association between current smoking status and COPD were controversial.<sup>4,8–11</sup> In a community-based cohort Korean study, current smoking was significantly associated with COPD in males (RR: 2.28, 95% CI 1.86–2.80) and in females (RR: 4.04, 95% CI 2.84–5.75).<sup>10</sup> However, in another population sample-based study, results showed that, compared with a non-smoking group of Korean adults, the OR (95% CI) for COPD in the current smoker group was 3.49 (2.44–5.00) in men and 3.45 (2.20–5.40) in women.<sup>11</sup>

Consistent with a previous study using similar data (2008–2016 KNHANES in this study and 2007–2015 KNHANES in the previous Korean study), we did not find sex differences in the association between COPD and current smoking.<sup>11</sup> In our study, male self-reported and cotinine-verified current smoking status were correlated with COPD (OR: 2.43, 95% CI: 1.86–3.18 and OR: 1.65, 95% CI: 1.40–1.96, respectively) and female self-reported and cotinine-verified current smoking status also correlated with COPD (OR: 2.52, 95% CI: 1.66–3.83 and OR: 2.11, 95% CI: 1.49–2.98, respectively).

Interestingly, in the association between COPD and ex-smoking, this study and previous studies showed ex-smoking was associated with COPD in men and not in women.<sup>10,11</sup>

We assumed the different effects of sex differences between COPD and current smoking in two previous studies might be due to selection bias associated with the sampling of different groups.<sup>10,11</sup> One study used a region-based sample, while the other used a nationally representative sample.<sup>10,11</sup> In addition, a previous Korean study reported large geographic variation in the prevalence of COPD in

Korea and emphasized the importance of nationally representative sampling.<sup>17,18</sup>

In a previous study, a significant number of female hidden smokers in Korea was reported compared with other countries.<sup>12</sup> Similar results were observed in this study. One hypothesis suggests that self-reported smoking in Korean females underestimates the true prevalence as a result of Confucianism. The adoption of Confucianism can result in a patriarchal culture in which female smoking is stigmatized.<sup>19</sup>

In a previous Korean study, the ratios of cotinine-verified to self-reported smoking rates were 2.36 for women and 1.12 for men,<sup>12</sup> indicating that women are more likely than men to be hidden smokers. Conversely, in a study from other countries, sex differences in underreporting the rate of past or present smoking was not observed.<sup>20,21</sup>

In this study, the ratios of cotinine-verified to self-reported smoking rates were 1.95 (632/325) for women and 1.07 (2452/2300) for men. These rates were similar to the findings in a previous Korean study.<sup>12</sup> Sex differences in underreporting the rate of past or present smoking were observed in this study: a greater number of hidden smokers were women. The discrepancy in the underreporting rates between the sexes could lead to statistical issues. In addition, a larger effect of hidden smokers was found in the association between COPD and smoking in females. In male participants, the adjusted OR for self-reported current smoking associated with COPD was 2.43 (95% CI: 1.86–3.18) and 2.29 (95% CI: 1.76–2.99) based on SCS. In women, the adjusted OR for self-reported current smoking status associated with COPD was 2.52 (95% CI: 1.66–3.83) and 2.13 (95% CI: 1.51–3.02) based on SCS.

The results from this study showed the risk of COPD associated with current smoking was lower in Korean adults than in those of other nationalities.<sup>22,23</sup> One hypothesis is that this result was due to different lung functions and genetic polymorphisms among nationalities.<sup>22</sup> In this study, an association between ex-smoker and COPD was observed; however, the association was not significant in women. These results might be due to lower amount of smoking by women than men, which was similar to results reported in a previous Korean study.<sup>11,22</sup>

Light and social smokers are often not detected because many of these individuals are self-reported non-smokers.<sup>24,25</sup> Recently, a report was published showing that light smoking was associated with COPD and amount of smoking was associated with progressively higher risk of COPD than never smoking.<sup>22</sup>

To better understand the association between COPD and smoking, a new variable, SCS, was used in this study to evaluate the effects of hidden smoking and other types of smoking. This new variable showed similar results compared with self-reported smoking status. Therefore, passive and light smoking may affect COPD development similar to active smoking.

Parental smoking was a major risk factor for second-hand smoke exposure in children; and maternal, not paternal, smoking was known as a risk factor for decreased lung function and COPD in children.<sup>26–28</sup> However, because there are many hidden female smokers in Korea, maternal hidden smokers should be considered when determining the impact of maternal smoking on lung function in Korean children.



This study had several limitations. First, because this study was based on a survey, selection and recall biases may have existed. Second, because this study was cross-sectional in design, the causal relationship between smoking and COPD could not be confirmed. Finally, potential confounding factors, including amount and duration of smoking, diet patterns, and genetic variations affecting nicotine metabolism were not evaluated. Further prospective studies are needed to clarify the effects of hidden female smokers on COPD by country.

However, the notable strength of our study is the use of national and widely sampled data to assess sex-specific relationships between smoking status and COPD. The other strength is the evaluation of the effects of sex and hidden smokers on the relationship between smoking and COPD.

## Conclusions

This large population-based cross-sectional study showed that sex differences might affect the association between COPD and smoking status. Depending on country, hidden female smokers should be considered in the study on the relationship between smoking and COPD.

## Authors' contributions

Ju Suk Lee conceived and supervised all aspects of this study. Hye Sung Ock contributed to the concept of study and wrote the final version of this manuscript. Sang Won Hwang analyzed data and contributed to design of our study. Hae Jeong Lee, Cheol Hong Kim, and Sung Hoon Kim collected data. Tae Hong Kim and Jun Hwa Lee collected data and carried out statistical analysis.

## Conflict of interests

The authors have no commercial relationships or potential conflicts of interest to declare.

## References

1. Buist AS, Vollmer WM, McBurnie MA. Worldwide burden of COPD in high- and low-income countries. Part I. The burden of obstructive lung disease (BOLD) initiative. *Int J Tuberc Lung Dis.* 2008;12:703–8.
2. Guarascio AJ, Ray SM, Finch CK, Self TH. The clinical and economic burden of chronic obstructive pulmonary disease in the USA. *Clinicoecon Outcomes Res.* 2013;5:235–45.
3. Thomson NC, Chaudhuri R, Livingston E. Asthma and cigarette smoking. *Eur Respir J.* 2004;24:822–33.
4. Sorheim IC, Johannessen A, Gulsvik A, Bakke PS, Silverman EK, DeMeo DL. Gender differences in COPD: are women more susceptible to smoking effects than men? *Thorax.* 2010;65:480–5.
5. Aryal S, Diaz-Guzman E, Mannino DM. COPD and gender differences: an update. *Transl Res.* 2013;162:208–18.
6. Martin TR, Castile RG, Fredberg JJ, Wohl ME, Mead J. Airway size is related to sex but not lung size in normal adults. *J Appl Physiol* (1985). 1987;63:2042–7.
7. Tam A, Morrish D, Wadsworth S, Dorscheid D, Man SF, Sin DD. The role of female hormones on lung function in chronic lung diseases. *BMC Womens Health.* 2011;11:24.
8. Prescott E, Bjerg AM, Andersen PK, Lange P, Vestbo J. Gender difference in smoking effects on lung function and risk of hospitalization for COPD: results from a Danish longitudinal population study. *Eur Respir J.* 1997;10:822–7.
9. Chen Y, Horne SL, Dosman JA. Increased susceptibility to lung dysfunction in female smokers. *Am Rev Respir Dis.* 1991;143:1224–30.
10. Leem AY, Park B, Kim YS, Jung JY, Won S. Incidence and risk of chronic obstructive pulmonary disease in a Korean community-based cohort. *Int J Chron Obstruct Pulmon Dis.* 2018;13:509–17.
11. Kim Y, Cho W-K. Effects of smoking on disease risk among South Korean adults. In: *Tobacco induced diseases*; 2018. p. 16.
12. Jung-Choi KH, Khang YH, Cho HJ. Hidden female smokers in Asia: a comparison of self-reported with cotinine-verified smoking prevalence rates in representative national data from an Asian population. *Tob Control.* 2012;21:536–42.
13. Kim SH, Lee JS. The association of smoking and hypertension according to cotinine-verified smoking status in 25,150 Korean adults. *Clin Exp Hypertens.* 2019;41:401–8.
14. Inoue S, Zimmet P, Caterson I, Chunming C, Ikeda Y, Khalid A, et al. The Asia-Pacific perspective: redefining obesity and its treatment. Australia: Health Communication Australia; 2000. [https://apps.who.int/iris/bitstream/handle/10665/206936/0957708211\\_eng.pdf](https://apps.who.int/iris/bitstream/handle/10665/206936/0957708211_eng.pdf)
15. Haufroid V, Lison D. Urinary cotinine as a tobacco-smoke exposure index: a minireview. *Int Arch Occup Environ Health.* 1998;71:162–8.
16. Sin DD, Cohen SB, Day A, Coxson H, Pare PD. Understanding the biological differences in susceptibility to chronic obstructive pulmonary disease between men and women. *Proc Am Thorac Soc.* 2007;4:671–4.
17. Kim DS, Kim YS, Jung KS, Chang JH, Lim CM, Lee JH, et al. Prevalence of chronic obstructive pulmonary disease in Korea: a population-based spirometry survey. *Am J Respir Crit Care Med.* 2005;172:842–7.
18. Shin C, In KH, Shim JJ, Yoo SH, Kang KH, Hong M, et al. Prevalence and correlates of airway obstruction in a community-based sample of adults. *Chest.* 2003;123:1924–31.
19. Park M, Chesla C. Revisiting Confucianism as a conceptual framework for Asian family study. *J Fam Nurs.* 2007;13:293–311.
20. Caraballo RS, Giovino GA, Pechacek TF, Mowery PD. Factors associated with discrepancies between self-reports on cigarette smoking and measured serum cotinine levels among persons aged 17 years or older: Third National Health and Nutrition Examination Survey, 1988–1994. *Am J Epidemiol.* 2001;153:807–14.
21. Vartiainen E, Seppala T, Lillsunde P, Puska P. Validation of self reported smoking by serum cotinine measurement in a community-based study. *J Epidemiol Community Health.* 2002;56:167–70.
22. Gilkes A, Hull S, Durbaba S, Schofield P, Ashworth M, Mathur R, et al. Ethnic differences in smoking intensity and COPD risk: an observational study in primary care. *NPJ Prim Care Respir Med.* 2017;27:50.
23. Menezes AM, Perez-Padilla R, Jardim JR, Muino A, Lopez MV, Valdivia G, et al. Chronic obstructive pulmonary disease in five Latin American cities (the PLATINO study): a prevalence study. *Lancet.* 2005;366:1875–81.
24. Schane RE, Glantz SA, Ling PM. Social smoking implications for public health, clinical practice, and intervention research. *Am J Prev Med.* 2009;37:124–31.

25. Husten CG. How should we define light or intermittent smoking? Does it matter? *Nicotine Tob Res.* 2009;11:111–21.
26. Precioso J, Frias S, Silva CN, Rocha V, Cunha-Machado J, Goncalves F, et al. Prevalence of children exposed to secondhand smoke at home and in the car in Azores (Portugal). *Pulmonology.* 2019;25:283–8.
27. Beyer D, Mitfessel H, Gillissen A. Maternal smoking promotes chronic obstructive lung disease in the offspring as adults. *Eur J Med Res.* 2009;14 Suppl. 4:27–31.
28. Perret JL, Walters H, Johns D, Gurrin L, Burgess J, Lowe A, et al. Mother's smoking and complex lung function of offspring in middle age: a cohort study from childhood. *Respirology.* 2016;21:911–9.