Association between Alcohol Drinking Status and Depressive Symptoms in Korean Adults

Jung-Hwa Yang[1], Chang Kyun Choi[2], Hye-Yeon Kim[3,*], Young-Ran Heo[1], and Min-Ho Shin[2]

[1]Department of Food and Nutrition, Chonnam National University, [2]Department of Preventive Medicine, Chonnam National University Medical School, [3]Gwangju-Jeonnam Regional Cardiocerebrovascular Center, Chonnam National University Hospital, Gwangju, Korea

We investigated the association between alcohol drinking status and depressive symptoms in a representative sample of South Korean adults using data from the 2017 Korea Community Health Survey (KCHS), which included 216,771 participants (99,845 men and 116,926 women). Depression was defined as a Patient Health Questionnaire-9 score of ≥10. Multivariate logistic regression using sampling weights was used to assess the relationship between alcohol drinking status and depression after adjusting for potential confounders. Alcohol intake was nonlinearly associated with depression; the risk of depression was the lowest in men who were moderate drinkers and women who were light drinkers. In men, heavy drinkers (odds ratio [OR] 1.41, 95% confidence interval [CI] 1.19-1.67), light drinkers (OR 1.13, 95% CI 0.94-1.36), infrequent drinkers (OR 1.31, 95% CI 1.00-1.73), and lifetime abstainers (OR 1.38, 95% CI 1.09-1.75) were at a higher risk of depression than moderate drinkers. In women, moderate drinkers (OR 1.19, 95% CI 1.02-1.40) and heavy drinkers (OR 1.56, 95% CI 1.33-1.84) were at a higher risk of depression than light drinkers; however, infrequent drinkers and lifetime abstainers were not at a high risk of depression. In both men and women, former drinkers were at a higher risk of depression (OR 1.61, 95% CI 1.34-1.93 and OR 1.25, 95% CI 1.09-1.43, respectively). In conclusion, the association between alcohol drinking status and depression was nonlinear in both sexes. Further investigation of age- and sex-specific factors related to the association between alcohol use and depression is needed.

Key Words: *Alcohol Drinking; Depression; Health Surveys; Patient Health Questionnaire 9*

INTRODUCTION

Alcohol is a toxic and psychoactive substance with dependence-producing properties. Alcohol use is a leading risk factor for preventable mortality and morbidity and is responsible for 6.0% and 1.6% of the global burden of disease among men and women, respectively.[1] In South Korea, 2.6% and 0.5% of all deaths in men and women, respectively, were induced by alcohol in 2018.[2] Alcohol use is associated with a high risk of developing various psychiatric disorders, especially mood disorders. Previous studies have shown that the co-occurrence of alcohol use disorder (AUD) and major depressive disorder (MDD) is higher than that the expected co-occurrence by chance.[3,4] Evidence suggests that the association between AUD and MDD is bidir-

ectional; in other words, AUD may contribute to MDD and vice versa.[4]

Several studies have shown a nonlinear relationship between alcohol intake and depression;[5-8] light-to-moderate alcohol intake has a protective effect against depression, whereas abstinence and heavy alcohol intake are associated with a high risk of depression. However, most previous studies have not clearly distinguished between non-drinkers who were lifelong abstainers and those who were former drinkers. Previous studies on the effect of sex on the association between alcohol consumption and depression have yielded inconsistent findings.[5,7,9]

Previous findings have suggested that alcohol has a more harmful effect on older individuals with functional disorders than on younger individuals.[10] However, few stud-

ies have investigated whether age acts as an effect modifier in the relationship between alcohol use and depression in adults. Two previous studies involving South Korean participants have been conducted; however, the effect of sex and age on the association between alcohol drinking and depression was not sufficiently evaluated.[8,9]

Therefore, we investigated the association between alcohol drinking status and depression and its interaction with age and sex in a representative sample of South Korean adults.

MATERIALS AND METHODS

1. Subjects

We used data from the 2017 Korean Community Health Survey (KCHS).[11] The KCHS is an annual, nationwide health survey of adults aged 19 years and older that has been conducted by the Korean Centers for Disease Control and Prevention since 2008. The KCHS provides population-based estimates of health indicators for the development and assessment of regional health plans and standardized health statistics, making them comparable across regions. The 2017 KCHS survey included 228,381 participants (102,484 men and 125,897 women).

The KCHS data used in this study included 201 questions across 18 fields, including health behavior, physical activity, use of medical services, and social environment. By the Bioethics Act and Article 2 of its enforcement regulations, this study was not reviewed on an institutional review board. In total, 216,771 participants (99,845 men, 116,926 women), without missing values, were included in the final analyses.

2. Alcohol use

Alcohol drinking status was classified according to the National Health Interview Survey categories as: lifetime abstainer, former drinker, current infrequent drinker, current light drinker, current moderate drinker, and current heavy drinker.[9] Lifetime abstainer was defined as a person who had never had an alcoholic drink in their lifetime except for religious observances. Former drinker was defined as no drinks in the past year, but not lifetime abstainers. Current infrequent drinker was defined as 1-11 drinks in the past year. Current light drinker was defined as at least 12 drinks, but no more than 3 drinks per week, in the past year. Current moderate drinker was defined as more than 3 drinks, but no more than 7 drinks, per week in the past year for women and more than 3 drinks, but no more than 14 drinks, per week in the past year for men. Current heavy drinker was defined as more than 7 drinks per week for women and more than 14 drinks per week for men on average in the past year.

3. Depression

The Patient Health Questionnaire-9 (PHQ-9) is a self-administered questionnaire consisting of nine questions that assess depressive symptoms. Each item is scored on a scale of 0-3 with higher scores indicating more severe symptoms. The total PHQ-9 score ranges from 0 to 27, and cutpoints of 5, 10, and 15 represent mild, moderate, and severe levels of depressive symptoms, respectively.[12] In this study, depression is defined as a score ≥ 10. We used the Korean version of the PHQ-9, which has been shown to be valid and reliable.[13,14]

4. Covariates

Body mass index (BMI) was calculated from self-reported height and weight values and categorized as underweight (<18.5 kg/m^2), normal weight (18.5-24.9 kg/m^2), overweight (25-29.9 kg/m^2), or obese (≥ 30 kg/m^2). Physical activity was dichotomized based on whether participants engaged in moderate or vigorous physical activity. Moderate physical activity was defined as moderate-intensity activity (e.g., swimming at a slow pace, table tennis, badminton, and tennis doubles) more than 5 days per week for 30 min or more. Vigorous physical activity was defined as high-intensity physical activity (e.g., swimming at a fast pace, climbing, cycling, squash, and tennis singles) more than 3 days per week for 20 min or more. Smoking status was categorized as never-smoker, ex-smoker, and current smoker. Marital status was coded as single, married, or other (divorce, bereavement or separation). Education level was categorized as less than middle school, middle school, high school, and college or higher. Household income was determined according to self-reported monthly or annual household income, and monthly household income was categorized as less than 1.00, 1.00-1.99, 2.00-2.99, 3.00-3.99, or ≥ 4 million KRW. Residence was classified as urban or rural according to administrative districts. Comorbidities were defined as the presence of conditions under treatment. Self-rated health was scored on a five-point scale and dichotomized as poor (reported as "poor" or "very poor") or good (reported as "very good," "good", or "moderate").[15]

5. Statistical analyses

Baseline characteristics were compared according to alcohol drinking status using a one-way analysis of variance or the chi-square test. Given known sex differences in drinking behavior, all analyses were stratified by sex. Multivariate logistic regression using sampling weights was performed to assess the relationship between alcohol drinking status and depression after adjusting for age, sex, BMI, marital status, education, monthly household income, residence, smoking status, comorbidity (hypertension, diabetes, and arthritis), self-rated health, and physical activity. We assessed the effect modification of age on the association between alcohol drinking status and depression and determined the prevalence of depression according to age after adjusting for confounders. The Wald test was used to test the interaction. All analyses were performed using STATA statistical software version 16.0 (Stata Corp., College Station, TX, USA).

RESULTS

The general characteristics of the study participants are shown according to drinking status in Tables 1 and 2. Of the 99,845 men, 7,825 (7.8%) were lifetime abstainers, 13,452 (13.5%) were former drinkers, 6,130 (6.1%) were infrequent drinkers, 20,034 (20.1%) were light drinkers, 28,493 (28.5%) were moderate drinkers, and 23,911 (23.9%) were heavy drinkers. Overall, more than half of the men were moderate or heavy drinkers. Of the 116,926 women, 29,629 (25.3%) were lifetime abstainers, 17,254 (14.8%) were former drinkers, 19,641 (16.8%) were infrequent drinkers, 31,495 (26.9%) were light drinkers, 10,572 (9.0%) were moderate drinkers, and 8,335 (7.1%) were heavy drinkers. Higher alcohol intakes were associated with younger age in both men and women. Among the 216,771 study par-

ticipants, 2,379 men (2.38%) and 4,628 women (3.96%) met the criteria for depression. Among men, heavy drinkers had a higher BMI, higher education level, higher household income, higher prevalence of current smoker status, and a higher level of physical activity than light drinkers. Among women, heavy drinkers had a higher education level, higher prevalence of current smoker status, and a higher level of physical activity than light drinkers.

The results of the logistic regression analysis of the association between alcohol drinking status and depression according to sex are shown in Table 3. The associations between alcohol drinking status and depression were nonlinear in both men and women, and this association was diffed by sex (p for interaction <0.001). In the model adjusted for socioeconomic status, lifestyle, and comorbidities, the odds ratios (ORs) for depression in light drinkers and life

TABLE 1. General characteristic of study subjects according to alcohol drinking status in men

	Lifetime abstainer	Former drinker	Infrequent drinker	Light drinker	Moderate drinker	Heavy drinker	p
N	7,825 (7.8)	13,452 (13.5)	6,130 (6.1)	20,034 (20.1)	28,493 (28.5)	23,911 (23.9)	
Depression	231 (3.0)	617 (4.6)	142 (2.3)	395 (2.0)	454 (1.6)	540 (2.3)	<0.001
PHQ-9 score	1.6±3.1	2.2±3.6	1.7±2.8	1.6±2.6	1.5±2.5	1.7±2.8	<0.001
Age (years)	59.8±17.8	63.6±15.4	54.1±17.6	49.1±17.4	49.7±16.6	49.5±13.7	<0.001
Body mass index							<0.001
Underweight (<18.5 kg/m^2)	381 (4.9)	691 (5.1)	209 (3.4)	435 (2.2)	547 (1.9)	364 (1.5)	
Normal (18.5-24.9 kg/m^2)	5,260 (67.2)	8,855 (65.8)	3,944 (64.3)	13,043 (65.1)	18,195 (63.9)	14,279 (59.7)	
Overweight (25-29.9 kg/m^2)	1,961 (25.1)	3,503 (26.0)	1,738 (28.4)	5,713 (28.5)	8,689 (30.5)	8,249 (34.5)	
Obese (≥30 kg/m^2)	223 (2.8)	403 (3.0)	239 (3.9)	843 (4.2)	1,062 (3.7)	1,019 (4.3)	
Physical activity	1,917 (24.5)	3,011 (22.4)	1,590 (25.9)	5,558 (27.7)	8,132 (28.5)	6,813 (28.5)	<0.001
Smoking history							<0.001
Never-smoker	3,725 (47.6)	3,105 (23.1)	2,037 (33.2)	7,139 (35.6)	7,125 (25.0)	3,218 (13.5)	
Ex-smoker	2,175 (27.8)	7,577 (56.3)	2,460 (40.1)	7,078 (35.3)	10,598 (37.2)	8,188 (34.2)	
Current smoker	1,925 (24.6)	2,770 (20.6)	1,633 (26.6)	5,817 (29.0)	10,770 (37.8)	12,505 (52.3)	
Marital status							<0.001
Single	1,290 (16.5)	1,245 (9.3)	1,143 (18.6)	5,225 (26.1)	6,212 (21.8)	4,021 (16.8)	
Married	5,737 (73.3)	10,698 (79.5)	4,514 (73.6)	13,608 (67.9)	20,289 (71.2)	17,793 (74.4)	
Divorce/bereavement/separation	798 (10.2)	1,509 (11.2)	473 (7.7)	1,201 (6.0)	1,992 (7.0)	2,097 (8.8)	
Education							<0.001
Less than middle school	1,953 (25.0)	3,913 (29.1)	900 (14.7)	1,988 (9.9)	3,124 (11.0)	2,321 (9.7)	
Middle school	1,269 (16.2)	2,405 (17.9)	716 (11.7)	1,873 (9.3)	2,886 (10.1)	2,594 (10.8)	
High school	2,264 (28.9)	3,920 (29.1)	1,932 (31.5)	5,698 (28.4)	8,677 (30.5)	9,035 (37.8)	
College or more	2,339 (29.9)	3,214 (23.9)	2,582 (42.1)	10,475 (52.3)	13,806 (48.5)	9,961 (41.7)	
Monthly household income (million KRW)							<0.001
Less than 1.00	2,156 (27.6)	4,373 (32.5)	1,028 (16.8)	2,424 (12.1)	3,523 (12.4)	2,319 (9.7)	
1.00-1.99	1,668 (21.3)	2,931 (21.8)	1,110 (18.1)	2,882 (14.4)	3,922 (13.8)	3,206 (13.4)	
2.00-2.99	1,403 (17.9)	2,313 (17.2)	1,153 (18.8)	3,816 (19.0)	5,285 (18.5)	4,760 (19.9)	
3.00-3.99	1,038 (13.3)	1,512 (11.2)	965 (15.7)	3,597 (18.0)	5,090 (17.9)	4,614 (19.3)	
4.00 and more	1,560 (19.9)	2,323 (17.3)	1,874 (30.6)	7,315 (36.5)	10,673 (37.5)	9,012 (37.7)	
Residence (rural)	4,378 (55.9)	7,526 (55.9)	2,561 (41.8)	7,556 (37.7)	11,153 (39.1)	9,908 (41.4)	<0.001
Hypertension	2,343 (29.9)	5,189 (38.6)	1,587 (25.9)	4,481 (22.4)	6,922 (24.3)	6,458 (27.0)	<0.001
Diabetes	1,118 (14.3)	2,849 (21.2)	754 (12.3)	2,061 (10.3)	2,646 (9.3)	2,491 (10.4)	<0.001
Arthritis	732 (9.4)	1,729 (12.9)	497 (8.1)	1,312 (6.5)	1,746 (6.1)	1,355 (5.7)	<0.001
Poor self-rate health	1,910 (24.4)	5,012 (37.3)	1,138 (18.6)	2,546 (12.7)	3,189 (11.2)	2,787 (11.7)	<0.001

PHQ-9: Patient Health Questionnaire-9.

All values were presented as N (%) or mean±standard deviation.

TABLE 2. General characteristic of study subjects according to alcohol drinking status in women

	Lifetime abstainer	Former drinker	Infrequent drinker	Light drinker	Moderate drinker	Heavy drinker	p
N	29,629 (25.3)	17,254 (14.8)	19,641 (16.8)	31,495 (26.9)	10,572 (9.0)	8,335 (7.1)	
Depression	1,295 (4.4)	972 (5.6)	670 (3.4)	862 (2.7)	376 (3.6)	453 (5.4)	<0.001
PHQ-9 score	2.3±3.6	2.8±3.8	2.2±3.1	2.1±2.9	2.4±3.1	2.8±3.6	<0.001
Age (years)	64.5±14.8	57.9±16.3	53.6±15.5	46.6±15.2	42.5±15.7	42.5±13.4	<0.001
Body mass index							<0.001
Underweight (<18.5 kg/m^2)	2,110 (7.1)	1,148 (6.7)	1,193 (6.1)	2,019 (6.4)	788 (7.5)	593 (7.1)	
Normal (18.5-24.9 kg/m^2)	20,502 (69.2)	11,845 (68.7)	13,846 (70.5)	23,103 (73.4)	7,742 (73.2)	6,074 (72.9)	
Overweight (25-29.9 kg/m^2)	6,275 (21.2)	3,742 (21.7)	4,082 (20.8)	5,649 (17.9)	1,769 (16.7)	1,471 (17.6)	
Obese ($\geq$30 kg/m^2)	742 (2.5)	519 (3.0)	520 (2.6)	724 (2.3)	273 (2.6)	197 (2.4)	
Physical activity	5,168 (17.4)	2,782 (16.1)	3,889 (19.8)	6,429 (20.4)	2,203 (20.8)	1,835 (22.0)	<0.001
Smoking history							<0.001
Never-smoker	28,813 (97.2)	16,238 (94.1)	19,108 (97.3)	30,249 (96.0)	9,591 (90.7)	6,830 (81.9)	
Ex-smoker	329 (1.1)	558 (3.2)	261 (1.3)	605 (1.9)	431 (4.1)	452 (5.4)	
Current smoker	487 (1.6)	458 (2.7)	272 (1.4)	641 (2.0)	550 (5.2)	1,053 (12.6)	
Marital status							<0.001
Single	1,386 (4.7)	1,088 (6.3)	2,018 (10.3)	5,814 (18.5)	2,907 (27.5)	1,852 (22.2)	
Married	18,208 (61.5)	11,134 (64.5)	13,697 (69.7)	21,256 (67.5)	6,270 (59.3)	5,259 (63.1)	
Divorce/bereavement/separation	10,035 (33.9)	5,032 (29.2)	3,926 (20.0)	4,425 (14.0)	1,395 (13.2)	1,224 (14.7)	
Education							<0.001
Less than middle school	14,971 (50.5)	6,391 (37.0)	5,112 (26.0)	4,518 (14.3)	1,202 (11.4)	729 (8.7)	
Middle school	4,387 (14.8)	2,199 (12.7)	2,481 (12.6)	3,020 (9.6)	810 (7.7)	680 (8.2)	
High school	5,830 (19.7)	4,129 (23.9)	5,324 (27.1)	9,637 (30.6)	3,217 (30.4)	3,459 (41.5)	
College or more	4,441 (15.0)	4,535 (26.3)	6,724 (34.2)	14,320 (45.5)	5,343 (50.5)	3,467 (41.6)	
Monthly household income (million KRW)							<0.001
less than 1.00	10,912 (36.8)	4,955 (28.7)	3,612 (18.4)	3,323 (10.6)	1,048 (9.9)	667 (8.0)	
1.00-1.99	6,062 (20.5)	2,998 (17.4)	3,068 (15.6)	4,192 (13.3)	1,342 (12.7)	1,111 (13.3)	
2.00-2.99	4,422 (14.9)	2,920 (16.9)	3,266 (16.6)	5,448 (17.3)	1,758 (16.6)	1,575 (18.9)	
3.00-3.99	3,092 (10.4)	2,480 (14.4)	3,139 (16.0)	5,680 (18.0)	1,952 (18.5)	1,659 (19.9)	
4.00 and more	5,141 (17.4)	3,901 (22.6)	6,556 (33.4)	12,852 (40.8)	4,472 (42.3)	3,323 (39.9)	
Residence (rural)	16,571 (55.9)	7,741 (44.9)	7,653 (39.0)	10,895 (34.6)	3,426 (32.4)	2,769 (33.2)	<0.001
Hypertension	12,229 (41.3)	5,736 (33.2)	4,935 (25.1)	5,061 (16.1)	1,374 (13.0)	1,074 (12.9)	<0.001
Diabetes	4,736 (16.0)	2,502 (14.5)	1,846 (9.4)	1,705 (5.4)	429 (4.1)	270 (3.2)	<0.001
Arthritis	9,865 (33.3)	4,731 (27.4)	4,283 (21.8)	4,198 (13.3)	1,103 (10.4)	747 (9.0)	<0.001
Poor self-rate health	11,051 (37.3)	5,983 (34.7)	3,980 (20.3)	3,867 (12.3)	1,151 (10.9)	900 (10.8)	<0.001

PHQ-9: Patient Health Questionnaire-9.

All values were presented as N (%) or mean±standard deviation.

abstainers were reduced, whereas the OR for heavy drinkers remained significant. There was a U-shaped association between alcohol intake and depressive symptoms, with the lowest risk in moderate drinkers in men. Compared to moderate drinkers, in men, heavy drinkers (odds ratio [OR] 1.41, 95% confidence interval [CI] 1.19-1.67), light drinkers (OR 1.13, 95% CI 0.94-1.36), infrequent drinkers (OR 1.31, 95% CI 1.00-1.73), and lifetime abstainers (OR 1.38, 95% CI 1.09-1.75) had an increased risk of having depression. Former drinker also had an increased risk of depression (OR 1.61, 95% CI 1.34-1.93). There was a J-shaped association between alcohol intake and depression, with the lowest risk in light drinkers in women. Compared to light drinkers, moderate drinkers (OR 1.19, 95% CI 1.02-1.40) and heavy drinkers (OR 1.56, 95% CI 1.33-1.84) had an increased risk of having depression, but infrequent drinkers and lifetime abstainers were not at high risk. Former drinker also had an increased risk of depression (OR 1.25, 95% CI 1.09-1.43).

Fig. 1 shows the estimated age-stratified prevalence of depression according to sex. In both men and women, the association between alcohol drinking status and depression was more marked in older participants than in younger ones. The modifying effect of age on the association between alcohol drinking status and depression was statistically significant in women (p for interaction<0.001), but not in men (p for interaction=0.156).

DISCUSSION

Our large population-based study using data from a nationwide survey revealed a nonlinear association between alcohol consumption and depression, with the lowest risk in men who were moderate drinkers and women who were

TABLE 3. Logistic regression analysis of association between alcohol drinking status and depressive symptoms

	Model 1	Model 2	Model 3	Model 4
Men				
Lifetime abstainer	1.80 (1.45-2.25)	1.42 (1.13-1.78)	1.56 (1.24-1.96)	1.38 (1.09-1.75)
Former drinker	2.70 (2.27-3.20)	2.09 (1.75-2.50)	2.19 (1.83-2.62)	1.61 (1.34-1.93)
Infrequent drinker	1.49 (1.15-1.93)	1.39 (1.07-1.80)	1.46 (1.12-1.90)	1.31 (1.00-1.73)
Light drinker	1.20 (1.01-1.44)	1.16 (0.97-1.39)	1.22 (1.02-1.46)	1.13 (0.94-1.36)
Moderate drinker	1 (reference)	1 (reference)	1 (reference)	1 (reference)
Heavy drinker	1.53 (1.30-1.80)	1.58 (1.34-1.86)	1.45 (1.23-1.71)	1.41 (1.19-1.67)
Women				
Lifetime abstainer	1.38 (1.23-1.56)	1.16 (1.03-1.32)	1.19 (1.05-1.35)	1.05 (0.92-1.19)
Former drinker	1.74 (1.54-1.98)	1.54 (1.35-1.76)	1.50 (1.32-1.72)	1.25 (1.09-1.43)
Infrequent drinker	1.13 (0.99-1.29)	1.13 (0.99-1.30)	1.15 (1.00-1.32)	1.10 (0.96-1.27)
Light drinker	1 (reference)	1 (reference)	1 (reference)	1 (reference)
Moderate drinker	1.44 (1.23-1.68)	1.27 (1.09-1.48)	1.17 (1.00-1.37)	1.19 (1.02-1.40)
Heavier drinker	2.14 (1.85-2.48)	1.94 (1.67-2.25)	1.54 (1.31-1.80)	1.56 (1.33-1.84)

Values are presented as 'odds ratio (95% confidence interval)'.
Model 1 was adjusted for age.
Model 2 was further adjusted for marital status, education, household income, and residential area.
Model 3 was further adjusted for body mass index, physical activity, and smoking status.
Model 4 was further adjusted for hypertension, diabetes, arthritis, and self-rated health.
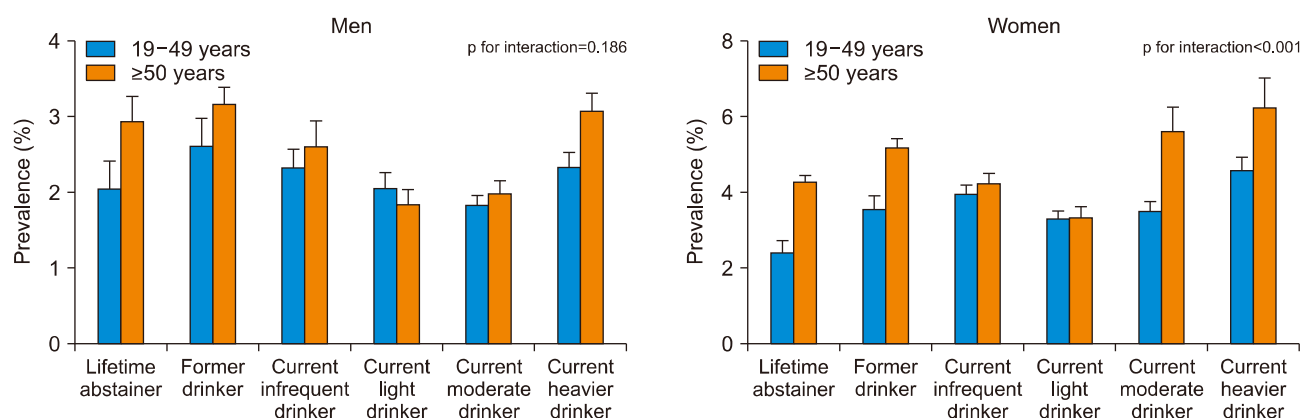

FIG. 1. Age-stratified analysis for estimated prevalence of depressive symptoms according to sex. All models were adjusted for age, marital status, education, household income, residential area, body mass index, smoking status, hypertension, diabetes, arthritis, and self-rated health.

light drinkers. Moreover, this association was the most marked in older women.

The relationship between alcohol consumption and depression was U-shaped in men and J-shaped in women, indicating that light or moderate drinkers were less likely to be depressed than non-drinkers and heavy drinkers. Our findings are similar to those of the Nationwide Survey on Dementia in Korea (NaSDeK). The NaSDeK study found a U-shaped association between the amount of daily alcohol consumption and depression, with the lowest risk of depression in men who were mild drinkers.[8] However, other studies involving South Korean adults with a moderate risk of alcohol dependence found that men had the lowest prevalence of depression and that women who were non-drinkers had the lowest prevalence of depression.[7,9] In these studies, drinking behaviors were classified according to alcohol dependence. Further, our results are consistent with those of studies involving other ethnic groups. In a recent meta-analysis, the association between alcohol consumption and the risk of depression was J-shaped. However, there were no differences between men and women.[5] In the Health, Alcohol and Psychosocial Factors in Eastern Europe study (HAPIEE), which compared three urban Eastern European populations,[6] a nonlinear association between drinking behavior and depression was reported in Russian and Polish populations; however, in the Czech Republic population, only abstainers had a high prevalence of depression. Neither the HAPIEE nor the NaSDeK study reported an effect modification of sex on alcohol consumption.[6,8] The discrepancies between our findings and those of previous studies may be explained by differences in the measurement of alcohol intake and depressive

symptoms or perceived cultural and social norms for drinking behavior. We used the PHQ-9 questionnaire to assess the severity of depressive symptoms, whereas other studies used either the Center for Epidemiological Studies Depression Scale (CES-D)[6,7,9] or the Short form Geriatric Depression Scale.[8]

The association between heavy alcohol consumption and depression may be explained by the shared or common risk factors. The prevalence of comorbid AUD and MDD is between 30% and 50% in AUD cases.[4,16] The bidirectional relationship between AUD and MDD is well known.[17] However, AUD seems to cause MDD rather than AUD and MDD having a reciprocal causal relationship. In longitudinal studies using structural equation models, the causal role of AUD in MDD is stronger than that of MDD in AUD or the reciprocal causal relationship.[4,18] There are several possible explanations for the causal link between alcohol and depression. First, alcohol misuse can causes legal troubles or difficulties in employment, making it difficult to maintain a social life.[19] Further, these social difficulties can lead to depression. Second, metabolic changes caused by alcohol can induce depression. Ethanol reduces the production of MTHFR,[20] and low folate levels caused by decreased MTHFR can induce depression.[21]

In our study, men who were lifetime abstainers, former drinkers, or infrequent alcohol drinkers were at a higher risk of depression. This finding may be owing to unmeasured confounders or reverse causality. Unmeasured differences between lifetime abstainers or infrequent drinkers and light or moderate drinkers, including diet and other lifestyle factors, may confound the association between alcohol consumption and depression. The distinction between former drinkers and lifetime abstainers in participants categorized as non-drinkers is important for the controlling bias in epidemiological studies on alcohol consumption.[22] Moreover, lifetime abstainers, former drinkers, and infrequent drinkers may have different health determinants that are different from those of current drinkers. Compared to light drinkers, former drinkers and lifetime abstainers have lower utilization rates of preventive services such as vaccinations and cancer screenings.[23] However, misclassification of drinking status (such as underreporting of alcohol consumption or inconsistency of reported lifetime abstainers or light drinkers)[24,25] or changes in drinking status due to health outcomes (such as sick-quitters)[26] are common issues in epidemiological studies on alcohol. Therefore, future prospective studies or Mendelian randomization studies that control unmeasured confounders or reverse causation are needed.

We found that older participants were more susceptible to the effect of alcohol on depression than younger participants. The findings of several health surveys indicate that alcohol consumption decreases after middle age.[27] However, the prevalence of AUD, such as alcohol abuse and dependency, tends to be independent of alcohol consumption patterns according to age.[10] Since AUD is a causal factor for MDD, the relationship between alcohol consumption and depression is more marked in older individuals owing to the age-related increase in susceptibility to alcohol.

In our study, the relationship between alcohol consumption and depression differed according to sex, and this difference was larger in former and heavy drinkers. Unlike in women, in men, former drinkers were associated with a high risk of depression. This is because the characteristics of former drinkers are different according to sex differences in postabstinence responses such as alcohol craving. Previous studies reported that the effect of alcohol rewards decreased after abstinence,[28,29] and these signs of neurological recovery were greater in men than in women.[30] However, since the periods of abstinence in previous studies for postabstinence response were short, further evaluation is needed on the effects of abstinence on health outcomes according to sexes. Our finding that women were more susceptible to the effects of alcohol on depression than men may be because the effect of alcohol on neurotransmitter receptor signaling and endocrine responses differs between the sexes. The depressant effects of alcohol are mediated by the modulation of hypothalamus–pituitary–adrenal (HPA) axis activity and gamma-aminobutyric acid receptor activity.[31] In a Mendelian randomization study, high cortisol levels were associated with a high depression score.[32] Animal studies have shown that alcohol consumption increases cortisol secretion and that responses to alcohol intoxication are sex specific.[33] These sex-specific differences are presumed to be because of estrogen. Estrogen activates the HPA axis by inducing the release of corticotropin-releasing hormone,[34] and because of this effect of estrogen, women who were light drinkers seem to have a significantly high risk of depression, unlike men. However, in women, since estrogen levels are affected by the menstrual cycle and oral contraception,[34] further studies including these variables are needed.

The strength of our study is the large sample size and the categorization of alcohol drinking status, which reflects various drinking behaviors. However, our study was limited to the effect of alcohol consumption on the severity of depression. Depressive symptoms occur in several mood disorders, including dysthymia, bipolar disorder, and MDD. Unlike CES-D, an instrument for investigating depression scale in the general population, PHQ-9 is a screening instrument for MDD. Therefore, it is necessary to assess the relationship between alcohol consumption and the various mood disorder subtypes based on the diagnosis. In addition, because the KCHS is a cross-sectional survey, it had limitations in evaluating the casual relationship between alcohol consumption and depression. In order to evaluate the bidirectional relationship between alcohol consumption and depression, further evaluation including genetic variants is required. In previous genetic studies, the effects of genetic variants on AUD or MDD varied, including raising only the risk of comorbid depression and AUD,[35] or raising both the risk of MDD and AUD.[36]

In conclusion, we found that the relationship between alcohol consumption and depression differed according to sex

and age. Additional studies are needed to clarify the biological and social factors that influence these differences.

CONFLICT OF INTEREST STATEMENT

None declared.

REFERENCES

1. GBD 2016 Alcohol Collaborators. Alcohol use and burden for 195 countries and territories, 1990-2016: a systematic analysis for the Global Burden of Disease Study 2016. Lancet 2018;392:1015-35.
2. Shin HY, Kim J, Lee S, Park MS, Park S, Huh S. Cause-of-death statistics in 2018 in the Republic of Korea. J Korean Med Assoc 2020;63:286-97.
3. Blanco C, Alegría AA, Liu SM, Secades-Villa R, Sugaya L, Davies C, et al. Differences among major depressive disorder with and without co-occurring substance use disorders and substance-induced depressive disorder: results from the National Epidemiologic Survey on Alcohol and Related Conditions. J Clin Psychiatry 2012;73:865-73.
4. Flensborg-Madsen T, Mortensen EL, Knop J, Becker U, Sher L, Grønbaek M. Comorbidity and temporal ordering of alcohol use disorders and other psychiatric disorders: results from a Danish register-based study. Compr Psychiatry 2009;50:307-14.
5. Li J, Wang H, Li M, Shen Q, Li X, Zhang Y, et al. Effect of alcohol use disorders and alcohol intake on the risk of subsequent depressive symptoms: a systematic review and meta-analysis of cohort studies. Addiction 2020;115:1224-43.
6. Bell S, Britton A, Kubinova R, Malyutina S, Pajak A, Nikitin Y, et al. Drinking pattern, abstention and problem drinking as risk factors for depressive symptoms: evidence from three urban Eastern European populations. PLoS One 2014;9:e104384.
7. Noh JW, Juon HS, Lee S, Kwon YD. Atypical epidemiologic finding in association between depression and alcohol use or smoking in Korean male: Korean Longitudinal Study of Aging. Psychiatry Investig 2014;11:272-80.
8. Park JH, Kim KW, Kim MH, Kim MD, Kim BJ, Kim SK, et al. A nationwide survey on the prevalence and risk factors of late life depression in South Korea. J Affect Disord 2012;138:34-40.
9. Ryu SY, Crespi CM, Maxwell AE. Drinking patterns among Korean adults: results of the 2009 Korean community health survey. J Prev Med Public Health 2013;46:183-91.
10. O'Connell H, Chin AV, Cunningham C, Lawlor B. Alcohol use disorders in elderly people--redefining an age old problem in old age. BMJ 2003;327:664-7.
11. Kang YW, Ko YS, Kim YJ, Sung KM, Kim HJ, Choi HY, et al. Korea Community Health Survey data profiles. Osong Public Health Res Perspect 2015;6:211-7.
12. Kroenke K, Spitzer RL, Williams JB. The PHQ-9: validity of a brief depression severity measure. J Gen Intern Med 2001;16:606-13.
13. Park SJ, Choi HR, Choi JH, Kim KW, Hong JP. Reliability and validity of the Korean version of the Patient Health Questionnaire-9 (PHQ-9). Anxiety and Mood 2010;6:119-24.
14. Han C, Jo SA, Kwak JH, Pae CU, Steffens D, Jo I, et al. Validation of the Patient Health Questionnaire-9 Korean version in the elderly population: the Ansan Geriatric study. Compr Psychiatry 2008;49:218-23.
15. Jylhä M. What is self-rated health and why does it predict mortality? Towards a unified conceptual model. Soc Sci Med 2009;69:307-16.
16. Brière FN, Rohde P, Seeley JR, Klein D, Lewinsohn PM. Comorbidity between major depression and alcohol use disorder from adolescence to adulthood. Compr Psychiatry 2014;55:526-33.
17. Boden JM, Fergusson DM. Alcohol and depression. Addiction 2011;106:906-14.
18. Fergusson DM, Boden JM, Horwood LJ. Tests of causal links between alcohol abuse or dependence and major depression. Arch Gen Psychiatry 2009;66:260-6.
19. Foster JH, Powell JE, Marshall EJ, Peters TJ. Quality of life in alcohol-dependent subjects--a review. Qual Life Res 1999;8:255-61.
20. McEachin RC, Keller BJ, Saunders EF, McInnis MG. Modeling gene-by-environment interaction in comorbid depression with alcohol use disorders via an integrated bioinformatics approach. BioData Min 2008;1:2.
21. Bender A, Hagan KE, Kingston N. The association of folate and depression: a meta-analysis. J Psychiatr Res 2017;95:9-18.
22. Knott CS, Coombs N, Stamatakis E, Biddulph JP. All cause mortality and the case for age specific alcohol consumption guidelines: pooled analyses of up to 10 population based cohorts. BMJ 2015;350:h384.
23. Green CA, Polen MR. The health and health behaviors of people who do not drink alcohol. Am J Prev Med 2001;21:298-305.
24. Rehm J, Irving H, Ye Y, Kerr WC, Bond J, Greenfield TK. Are lifetime abstainers the best control group in alcohol epidemiology? On the stability and validity of reported lifetime abstention. Am J Epidemiol 2008;168:866-71.
25. Stockwell T, Donath S, Cooper-Stanbury M, Chikritzhs T, Catalano P, Mateo C. Under-reporting of alcohol consumption in household surveys: a comparison of quantity-frequency, graduated-frequency and recent recall. Addiction 2004;99:1024-33.
26. Rehm J, Poznyak V. On monitoring unrecorded alcohol consumption. Alcohol Drug Addict 2015;28:79-89.
27. Chaiyasong S, Huckle T, Mackintosh AM, Meier P, Parry CDH, Callinan S, et al. Drinking patterns vary by gender, age and country-level income: cross-country analysis of the International Alcohol Control Study. Drug Alcohol Rev 2018;37 Suppl 2:S53-62.
28. van Eijk J, Demirakca T, Frischknecht U, Hermann D, Mann K, Ende G. Rapid partial regeneration of brain volume during the first 14 days of abstinence from alcohol. Alcohol Clin Exp Res 2013;37:67-74.
29. Bartsch AJ, Homola G, Biller A, Smith SM, Weijers HG, Wiesbeck GA, et al. Manifestations of early brain recovery associated with abstinence from alcoholism. Brain 2007;130(Pt 1):36-47.
30. Plawecki MH, White K, Kosobud AEK, Grahame N, Zimmermann US, Crabb D, et al. Sex differences in motivation to self-administer alcohol after 2 weeks of abstinence in young-adult heavy drinkers. Alcohol Clin Exp Res 2018;42:1897-908.
31. Sanna E, Talani G, Busonero F, Pisu MG, Purdy RH, Serra M, et al. Brain steroidogenesis mediates ethanol modulation of GABAA receptor activity in rat hippocampus. J Neurosci 2004;24:6521-30.
32. Zhou X, Qiao N. Association of cortisol levels with neuropsychi-

atric functions: a Mendelian randomization analysis. Front Endocrinol (Lausanne) 2019;10:564.

33. Sharrett-Field L, Butler TR, Reynolds AR, Berry JN, Prendergast MA. Sex differences in neuroadaptation to alcohol and withdrawal neurotoxicity. Pflugers Arch 2013;465:643-54.

34. Kirschbaum C, Kudielka BM, Gaab J, Schommer NC, Hellhammer DH. Impact of gender, menstrual cycle phase, and oral contraceptives on the activity of the hypothalamus-pituitary-adrenal axis. Psychosom Med 1999;61:154-62.

35. Sjöholm LK, Kovanen L, Saarikoski ST, Schalling M, Lavebratt C, Partonen T. CLOCK is suggested to associate with comorbid alcohol use and depressive disorders. J Circadian Rhythms 2010; 8:1.

36. Andersen AM, Pietrzak RH, Kranzler HR, Ma L, Zhou H, Liu X, et al. Polygenic scores for major depressive disorder and risk of alcohol dependence. JAMA Psychiatry 2017;74:1153-60.