Association between changes in facial flushing and hypertension across drinking behavior patterns in South Korean adults

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Abstract

Heavy alcohol drinking has been reported to be associated with hypertension. Moreover, when drinking alcohol, individuals may experience symptoms such as facial flushing. Therefore, this study aimed to examine the association between changes in facial flushing and hypertension across different drinking behavior patterns in South Korean adults.

Data from the Korea Community Health Survey conducted in 2019 were used, and 118,129 (51,047 men and 67,082 women) participants were included. The participants were divided into five groups based on the change in facial flushing (non-drinking, non-flushing to non-flushing, flushing to flushing, non-flushing to flushing, flushing to non-flushing). The risk of hypertension in each facial flushing group was analyzed by multiple logistic regression.

Men in the non-flushing to flushing group had a significantly higher association with hypertension than other groups (men: odds ratio (OR) 1.42, confidence interval (CI) 1.14–1.76). According to the level of alcohol use disorder, the non-flushing to flushing group showed a significantly increased odds of hypertension compared to all levels of drinking (men: mild drinking: OR 1.95, CI 1.40–2.71; moderate drinking: OR 2.02, CI 1.41–2.90; women: moderate drinking: OR 1.71, CI 1.16–2.52; heavy drinking: OR 1.90, CI 1.19–3.04).

This study found a significant association between changes in facial flushing and hypertension among adults in South Korea. In particular, individuals who changed from non-flushing to flushing reactions had an increased association with hypertension than the other groups. Compared to people at the same drinking level, people with non-flushing to flushing reactions were highly associated with hypertension at moderate drinking level.

KEYWORDS
alcohol use disorder, Asian flushing, facial flushing, hypertension

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1 | INTRODUCTION

Hypertension is a commonly occurring and leading preventable risk factor for cardiovascular disease and a subject of great interest to researchers. The Global Burden of Disease study found that hypertension is at risk of placing an increasing economic burden on societies globally. In South Korea, neoplasms caused 158.2 deaths per 100,000 in 2019. In comparison, diseases of the circulatory system caused 117.8 deaths. These included cardiovascular diseases (60.4 deaths) and cerebrovascular diseases (40.2 deaths). It is well recognized that hypertension is associated with traditional risk factors such as age, body mass index (BMI), smoking, and family history. Additionally, drinking behavior, especially excessive or frequent drinking, is also a risk factor for hypertension.

When drinking alcohol, some people experience facial flushing or palpitations, shortness of breath, headache, and vomiting due to the accumulation of acetaldehyde. In particular, East Asian ethnic groups, such as Korean, Chinese, and Japanese populations, have a higher prevalence of ALDH2 polymorphism than the Western population. Ethanol is metabolized by alcohol dehydrogenase (ADH) to acetaldehyde, which is eliminated by aldehyde dehydrogenase (ALDH). Alcohol dependence is associated with the isozymes ADH2*2 and ADH3*1, which oxidize alcohol rapidly and produce high amounts of acetaldehyde. Moreover, the ALDH2 polymorphism encodes an inactive subunit, resulting in high acetaldehyde levels in the blood after alcohol intake.

A previous study suggested a greater association with hypertension in people who have alcohol-related facial flushing than non-flushers. Moreover, the risk of hypertension in facial flushers is markedly increased with excessive drinking. More research on specific genotypes associated with alcohol metabolism is necessary because the specific genotypes associated with alcohol metabolism are common in South Korean populations. To the best of our knowledge, no study has examined the association between facial flushing and hypertension changes. Therefore, we examined the association between change in facial flushing and hypertension across different drinking behavior patterns, such as alcohol use disorders, to fill this research gap. We focused both on the presence and absence of facial flushing as well as the occurrence or elimination of facial flushing with time in adults.

2 | METHODS

We used data from the Korea Community Health Survey (KCHS) conducted by the Korea Center for Disease Control and Prevention (KCDC) in 2019. The KCHS is a cross-sectional, nationally representative survey that has been conducted regularly since 2008 to gather regional data for planning, monitoring, and evaluating community health services. The data for providing country-level health indicators is made using a large population-based National Census Registry and a systematic, stratified, and multistage cluster sampling method. The weights allocated to each participant’s data were calculated based on geographic and demographic distributions to generalize the entire population of Korea.

2.1 | Participants

The 2019 survey included 229,099 individuals, and the analysis excluded individuals who were younger than 19 years of age (n = 2200) and pregnant (n = 641). In addition, we excluded individuals who had been undergoing anti-hypertensive drug treatment were excluded (n = 62,286). Some anti-hypertensive drugs cause facial flushing. Finally, after excluding those with missing data (n = 45,843), 118,129 healthy participants were included in this study.

Our study did not require approval from the Institutional Review Board or informed consent because the KCHS is a secondary dataset available in the public domain and does not contain private information.

2.2 | Variables

The dependent variable of this study was the risk of hypertension. Blood pressure was measured thrice with intervals of 1 minute for stabilization, and the final blood pressure was the average of the three measurements. Hypertension was classified as systolic blood pressure ≥140 mmHg or diastolic blood pressure ≥90 mmHg. We classified those who met the hypertension criteria and those who did not meet the hypertension criteria when measuring blood pressure, except for taking anti-hypertensive drugs.

Facial flushing reaction was the primary independent variable of interest. The following question assessed past facial flushing reaction: “In the past year or two, did you experience a quick facial flushing reaction when drinking a small glass of beer?” A current facial flushing reaction was assessed by asking the following question: “Do you currently experience a facial flushing reaction when drinking a small amount of beer?” The data on past and present facial flushing reactions were self-reported.

We divided the study population into five categories: people who have never drunk alcohol (ND, non-drinking); people who never had facial flushing reaction (NN, non-flushing → non-flushing); people who had facial flushing reaction in the past and present (FF, flushing → flushing); people who had facial flushing reaction in the past but not in the present (FN, flushing → non-flushing); and people who did not have facial flushing reaction in the past but did in the present (NF, non-flushing → flushing). Furthermore, we analyzed each group stratified by variables such as alcohol use.

We controlled for covariates such as sociodemographic and socioeconomic factors, health behaviors, and health conditions of the participants. The sociodemographic factors were age (19–29, 30–39, 40–49, 50–59, and ≥60 years) and sex (men and women). The socioeconomic factors were education level (below middle school, high school, and college or higher), region (city and rural areas), marital status (yes and no), occupation (white-collar, pink collar, blue-collar, and unemployed),
and household income (high, middle high, middle-low, and low). Health behavior factors included smoking status (non-smoker, past smoker, and current smoker), BMI (non-obese and obese), diagnosis of diabetes (yes and no), and physical activity assessed to walking practice rate (yes and no). In the female group, menopause status was added (yes and no). Additionally, we used the Alcohol Use Disorder Identification Test Score (AUDIT-C) to assess the pattern of alcohol use. Cut-off scores of AUDIT-C for heavy alcohol drinking were 7 for men and 6 for women, and mild alcohol drinking were 3 for both men and women.22

2.3 Statistical analysis

Independent variables were compared using the chi-squared test to identify the association between changes in facial flushing and hypertension. After adjusting for sociodemographic, economic, and health-related variables, we used a multiple logistic regression analysis to evaluate the association between the change of facial flushing and hypertension. The results were reported using odds ratios (ORs) and confidence intervals (CIs). Moreover, we performed a subgroup analysis stratified by sex and multiple logistic regression analysis was used to examine the associations with change in facial flushing in persons with hypertension according to the level of alcohol use disorder. Differences were considered significant at \( P \)-values of <0.05 as well as at \( P \)-values for trends <0.05. Data were analyzed using SAS 9.4 (SAS Institute Inc; Cary, North Carolina, USA) and a \( P \) value <0.05 was considered to be statistically significant.

3 RESULTS

Table 1 shows the general characteristics of the participants. There were 51,047 men and 67,082 women in this study, and 11,234 (22%) men and 10,406 (15.5%) women had a risk of hypertension. Participants were grouped into five categories based on the change in facial flushing reaction. Of the men, 57,988 (11.4%) reported they have never drunk alcohol, 29,044 (56.9%) reported non-flushing to alcohol, 11,592 (22.7%) reported flushing in the past but not in the present, 37,111 (7.3%) reported facial flushing reaction in the past but not in the present, and 902 (1.8%) reported facial flushing reaction in the present but not in the past. Of the women, 18,060 (26.9%) reported they have never drunk alcohol, 32,616 (48.6%) reported non-flushing to alcohol, 11,476 (17.1%) reported flushing in the past and present, 39,585 (5.9%) reported facial flushing reaction in the past but not in the present, and 972 (1.4%) reported facial flushing reaction in the present but not in the past.

Table 2 reports the findings of logistic regression analysis for the association between change in facial flushing and hypertension stratified by sex. Men in the NF group had a higher OR of hypertension than other groups (men: OR 1.42, CI 1.14–1.76); among women, there was no statistically significant relationship between change in facial flushing and hypertension. Additionally, participants who drank moderately (men: OR 1.20, CI 1.11–1.30, women: OR 1.16, CI 1.07–1.27) and heavily (men: OR 1.83, CI 1.69–1.98, women: OR 1.93, CI 1.76–2.13) were strongly associated with an increased risk for hypertension.

Figure 1 shows the results of stratified analyses of the association of the changes in facial flushing on hypertension according to alcohol consumption. Overall, taking the non-drinking group as the reference category, the OR of the NF was high in mild and moderate drinking levels among men. (mild drinking: OR 1.95, CI 1.40–2.71; moderate drinking: OR 2.02 CI, 1.41–2.90). Also, the OR of the NF was high in moderate and heavy drinking levels among women. (moderate drinking: OR 1.71, CI 1.16–2.52; heavy drinking: OR 1.90 CI, 1.19–3.04)

Finally, Table 3 reports the subgroup analysis stratified by independent variables. Men diagnosed with diabetes had an increased association with hypertension in the NF group (OR 2.24, CI 1.22–4.11). Additionally, men who did not exercise had an increased risk of hypertension in the NF group (OR 1.68, CI 1.26–2.25).

4 DISCUSSION

We found that change in facial flushing reaction was associated with a higher risk of hypertension. Especially, individuals with facial flushing reaction in the present but not in the past increased the likelihood of hypertension, and we also examined individuals who consumed similar alcohol levels. The association between flushing changes and hypertension was different for each alcohol consumption level. Among those who drink mild or moderate, men who did not have facial flushing reaction in the past but did in the present were the highest likelihood of hypertension. And women who did not have facial flushing reaction in the past but did in the present were the highest likelihood of hypertension among moderate drinking group.

Some studies link hypertension and alcohol-induced facial flushing.17,23 The likelihood of hypertension was higher in people with facial flushing than in those without facial flushing in previous study. In the result of our study, the difference between the two group was not significant. Since previous studies considered only current facial flushing, different results may have been derived from our study. While polymorphisms partly explained the association in alcohol metabolism genes,24 these studies did not find any evidence that facial flushing reaction is associated with the risk of hypertension.25,26 Therefore, further studies are necessary.

In this study, we assessed the association between the presence of facial flushing and alcohol consumption. The reasons for the change in facial flushing can be explained as follows. Facial flushing is a well-known symptom of acetaldehyde accumulation and intolerance to alcohol.9 Some studies showed that the genotype of ADH and ALDH was associated with liver disease.27,28,29 Chronic alcoholics have a higher tolerance to alcohol than others because of the metabolic adaptation of the central nervous system and increased ethanol elimination rate.31 Increased ethanol elimination increases both blood and tissue acetaldehyde levels in chronic alcoholics.32 People with liver injury experience decreasing activities of ADH and proportionally low-K ALDH (ALDH2).33 It is speculated that the decrease in ADH could be due to centrilobular cell necrosis.33,34 Thus, decrease in liver
### TABLE 1  General characteristics of the study population

| Variables                  | Men                  |            | Women                 |            |
|----------------------------|----------------------|------------|-----------------------|------------|
|                            | No.  | %    | No.  | %    | No.  | %    | No.  | %    | P     | No.  | %    | No.  | %    | P     |
| Hypertension               |      |      |      |      |      |      |      |      |       |      |      |      |      |       |
| Faceflushing change        |      |      |      |      |      |      |      |      |       |      |      |      |      |       |
| non-drinking               | 5798 | 11.4 | 1412 | 19.7 | 4696 | 80.3 | <.0001 | 18060 | 26.9 | 3789 | 21.0 | 14271 | 79.0 | <.0001 |
| non-flushing → non-flushing| 29044 | 56.9 | 65303 | 22.5 | 22514 | 77.5 |       | 32616 | 48.6 | 4271 | 13.1 | 28345 | 86.9 |       |
| flushing → flushing        | 11592 | 22.7 | 2314 | 20.8 | 9178 | 79.2 |       | 11476 | 17.1 | 1560 | 13.6 | 9916 | 86.4 |       |
| non-flushing → flushing    | 902 | 1.8 | 255 | 28.3 | 647 | 71.7 |       | 972 | 1.4 | 201 | 20.7 | 771 | 79.3 |       |
| flushing → non-flushing    | 3711 | 7.3 | 893 | 24.7 | 2818 | 75.3 |       | 3958 | 5.9 | 585 | 14.8 | 3373 | 85.2 |       |
| Age (years)                |      |      |      |      |      |      |      |      |       |      |      |      |      |       |
| 19-29                      | 8467 | 16.6 | 816 | 9.6 | 7651 | 90.4 | <.0001 | 8966 | 13.4 | 242 | 2.7 | 8724 | 97.3 | <.0001 |
| 30-39                      | 9619 | 18.8 | 1818 | 18.9 | 7801 | 81.1 |       | 10200 | 15.2 | 714 | 7.0 | 9486 | 93.0 |       |
| 40-49                      | 10865 | 21.3 | 2699 | 24.8 | 8166 | 75.2 |       | 13644 | 20.3 | 1683 | 12.3 | 11961 | 87.7 |       |
| 50-59                      | 9859 | 19.3 | 2560 | 26.0 | 7299 | 74.0 |       | 14468 | 21.6 | 2513 | 17.4 | 11955 | 82.6 |       |
| ≥60                        | 12237 | 24.0 | 3341 | 27.3 | 8896 | 72.7 |       | 19804 | 29.5 | 5254 | 26.5 | 14550 | 73.5 |       |
| Marital Status             |      |      |      |      |      |      |      |      |       |      |      |      |      |       |
| Living w/ spouse           | 33383 | 65.4 | 7703 | 23.1 | 25680 | 76.9 | <.0001 | 44096 | 65.7 | 6883 | 15.6 | 37213 | 84.4 | .3433 |
| Living w/o spouse          | 17664 | 34.6 | 3531 | 20.0 | 1433 | 80.0 |       | 22986 | 34.3 | 3523 | 15.3 | 19463 | 84.7 |       |
| Region                     |      |      |      |      |      |      |      |      |       |      |      |      |      |       |
| City                       | 16621 | 32.6 | 3565 | 21.4 | 13056 | 78.6 | 0.035 | 22173 | 33.1 | 3047 | 13.7 | 19126 | 86.3 | <.0001 |
| Rural                      | 34426 | 67.4 | 7669 | 22.3 | 26757 | 77.7 |       | 44909 | 66.9 | 7359 | 16.4 | 37550 | 83.6 |       |
| Educational level          |      |      |      |      |      |      |      |      |       |      |      |      |      |       |
| Middle school or less      | 7795 | 15.3 | 2147 | 27.5 | 5648 | 72.5 | <.0001 | 18886 | 28.2 | 5098 | 27.0 | 13788 | 73.0 | <.0001 |
| High school                | 15344 | 30.1 | 3830 | 25.0 | 11514 | 75.0 |       | 20188 | 30.1 | 3155 | 15.6 | 17033 | 84.4 |       |
| College or over            | 27908 | 54.7 | 5257 | 22.3 | 22651 |       |       | 28008 | 41.8 | 2153 |       | 25855 |       |       |
| Household Income           |      |      |      |      |      |      |      |      |       |      |      |      |      |       |
| Low                        | 8740 | 17.1 | 2225 | 25.5 | 6515 | 74.5 | <.0001 | 15401 | 23.0 | 3760 | 24.4 | 11641 | 75.6 | <.0001 |
| Mid-low                    | 8574 | 16.8 | 2083 | 24.3 | 6491 | 75.7 |       | 11184 | 16.7 | 1918 | 17.1 | 9266 | 82.9 |       |
| Mid-high                   | 15395 | 30.2 | 3407 | 11.98 | 11988 |       |       | 18056 | 26.9 | 2405 |       | 15651 |       |       |
| High                       | 18338 | 35.9 | 3519 | 19.2 | 14819 | 80.8 |       | 22441 | 33.5 | 2323 | 10.4 | 20118 | 89.6 |       |

(Continues)
| Variables                        | Hypertension |          |          |          |          |          |          |          |          |          |          |
|---------------------------------|--------------|----------|----------|----------|----------|----------|----------|----------|----------|----------|----------|
|                                 |              | Men      | Women    | Men      | Women    | Men      | Women    | Men      | Women    | Men      | Women    |
|                                 | TOTAL        | No.     | %        | No.     | %        | No.     | %        | No.     | %        | No.     | %        |
|                                 |              | No.     | %        | No.     | %        | P        |          | No.     | %        | No.     | %        | P        |          |
| Occupational categories<sup>a</sup> |              |          |          |          |          |          |          |          |          |          |          |
| White                           |              | 14534   | 28.5     | 2932    | 20.2     | 11602   | 79.8     | <.0001  | 15564   | 23.2     | 1270    | 8.2      | <.0001  |
| Pink                            |              | 6192    | 12.1     | 1270    | 20.5     | 4922    | 79.5     |          | 12044   | 18.0     | 1775    | 14.7     | 10269   |
| Blue                            |              | 20477   | 40.1     | 4929    | 24.1     | 15548   | 75.9     |          | 12620   | 18.8     | 2730    | 21.6     | 9890    |
| Inoccupation                    |              | 9844    | 19.3     | 2103    | 21.4     | 7741    | 78.6     |          | 26854   | 40.0     | 4631    | 17.2     | 22223   |
| Smoking                         |              |          |          |          |          |          |          |          |          |          |          |          |
| Non smoker                      |              | 15180   | 29.7     | 2666    | 17.6     | 12514   | 82.4     | <.0001  | 63027   | 94.0     | 9673    | 15.3     | 53354   |
| past smoker                     |              | 17362   | 34.0     | 4218    | 24.3     | 13144   | 75.7     |          | 1998    | 3.0      | 331     | 16.6     | 1667    |
| smoker                          |              | 18505   | 36.3     | 4350    | 23.5     | 14155   | 76.5     |          | 2057    | 3.1      | 402     | 19.5     | 1655    |
| BMI                             |              |          |          |          |          |          |          |          |          |          |          |          |
| Non-obesity                     |              | 48115   | 94.3     | 10145   | 21.1     | 37970   | 78.9     | <.0001  | 64865   | 96.7     | 9725    | 15.0     | 55140   |
| Obesity                         |              | 2932    | 5.7      | 1089    | 37.1     | 1843    | 62.9     |          | 2217    | 3.3      | 681     | 30.7     | 1536    |
| Diagnose of diabetes            |              |          |          |          |          |          |          |          |          |          |          |          |
| Yes                             |              | 3152    | 6.2      | 794     | 25.2     | 2358    | 74.8     | <.0001  | 3323    | 5.0      | 749     | 22.5     | 2574    |
| No                              |              | 47895   | 93.8     | 10440   | 21.8     | 37455   | 78.2     |          | 63759   | 95.0     | 9657    | 15.1     | 54102   |
| Physical activity-walk          |              |          |          |          |          |          |          |          |          |          |          |          |
| Yes                             |              | 28240   | 55.3     | 6226    | 22.0     | 22014   | 78.0     | 0.810   | 40054   | 59.7     | 6323    | 15.9     | 33731   |
| No                              |              | 22807   | 44.7     | 5008    | 22.0     | 17799   | 78.0     |          | 27028   | 40.3     | 4083    | 15.1     | 22945   |
| Menopausal status               |              |          |          |          |          |          |          |          |          |          |          |          |
| Yes                             |              | 32882   | 49.0     | 7576    | 23.0     | 25306   | 77.0     | <.0001  |          |          |          |          |          |
| No                              |              | 34200   | 51.0     | 2830    | 8.3      | 31370   | 91.7     |          |          |          |          |          |          |
| Alcohol use disorder            |              |          |          |          |          |          |          |          |          |          |          |          |
| Mild drinking & Non-drinking    |              | 16560   | 32.4     | 3153    | 19.0     | 13407   | 81.0     |          | 44918   | 67.0     | 7512    | 16.7     | 37406   |
| Moderate drinking               |              | 15746   | 30.8     | 3174    | 20.2     | 12572   | 79.8     | <.0001  | 12595   | 18.8     | 1497    | 11.9     | 11098   |
| Heavy drinking                  |              | 18741   | 36.7     | 4907    | 26.2     | 13834   | 73.8     |          | 9569    | 14.3     | 1397    | 14.6     | 8172    |

<sup>a</sup>Three groups (White, Pink, Blue) based on International Standard Classification Occupations codes. Inoccupation group includes housewife.
### TABLE 2  Results of factors associated with hypertension

| Variables                        | Men                          | Women                         |
|----------------------------------|------------------------------|-------------------------------|
|                                  | Hypertension                 |                               |
|                                  | OR   | 95% CI | OR   | 95% CI |
| **Facial flushing change**       |      |       |      |       |
| Non-drinking                     | 1.00 |       | 1.00 |       |
| non-flushing → non-flushing      | 1.11 | (0.99 - 1.25) | 0.93 | (0.86 - 1.01) |
| flushing → flushing              | 1.09 | (0.97 - 1.22) | 1.03 | (0.94 - 1.13) |
| non-flushing → flushing          | 1.42 | (1.14 - 1.76) | 1.11 | (0.90 - 1.37) |
| flushing → non-flushing          | 1.08 | (0.93 - 1.24) | 0.93 | (0.81 - 1.06) |
| **Age (years)**                  |      |       |      |       |
| 19-29                            | 1.00 |       | 1.00 |       |
| 30-39                            | 2.48 | (2.22 - 2.77) | 2.98 | (2.50 - 3.56) |
| 40-49                            | 3.79 | (3.38 - 4.24) | 5.71 | (4.82 - 6.77) |
| 50-59                            | 4.35 | (3.87 - 4.90) | 6.98 | (5.68 - 8.57) |
| ≥60                              | 5.21 | (4.57 - 5.94) | 9.28 | (7.47 - 11.54) |
| **Marital Status**               |      |       |      |       |
| Living with spouse               | 1.00 |       | 1.00 |       |
| Living without spouse            | 1.32 | (1.23 - 1.42) | 1.09 | (1.01 - 1.16) |
| **Region**                       |      |       |      |       |
| City                             | 1.00 |       | 1.00 |       |
| Rural                            | 0.99 | (0.94 - 1.05) | 1.01 | (0.96 - 1.08) |
| **Occupational categories**      |      |       |      |       |
| White                            | 1.00 |       | 1.00 |       |
| Pink                             | 0.95 | (0.86 - 1.04) | 1.06 | (0.95 - 1.17) |
| Blue                             | 1.04 | (0.97 - 1.12) | 1.12 | (1.00 - 1.25) |
| Inoccupation                     | 1.05 | (0.95 - 1.15) | 1.11 | (1.01 - 1.22) |
| **Educational level**            |      |       |      |       |
| Middle school or less            | 1.33 | (1.20 - 1.47) | 1.72 | (1.54 - 1.92) |
| High school                      | 1.22 | (1.14 - 1.30) | 1.31 | (1.20 - 1.42) |
| College or over                  | 1.00 |       | 1.00 |       |
| **Household income**             |      |       |      |       |
| Low                              | 1.12 | (1.02 - 1.22) | 1.25 | (1.14 - 1.37) |
| Mid-low                          | 1.17 | (1.08 - 1.28) | 1.20 | (1.10 - 1.32) |
| Mid-high                         | 1.11 | (1.04 - 1.19) | 1.13 | (1.05 - 1.23) |
| High                             | 1.00 |       | 1.00 |       |
| **Smoking**                      |      |       |      |       |
| Non smoker                       | 1.00 |       | 1.00 |       |
| Past smoker                      | 1.06 | (0.98 - 1.14) | 1.36 | (1.16 - 1.61) |
| smoker                           | 1.04 | (0.97 - 1.12) | 1.28 | (1.10 - 1.48) |
| **BMI**                          |      |       |      |       |
| Non-obesity                      | 1.00 |       | 1.00 |       |
| Obesity                          | 3.25 | (2.94 - 3.59) | 3.57 | (3.08 - 4.14) |
| **Diagnose of diabetes**         |      |       |      |       |
| Yes                              | 1.00 |       | 1.00 |       |
| No                               | 1.17 | (1.05 - 1.31) | 1.06 | (0.94 - 1.20) |
### TABLE 2 (Continued)

| Variables                      | Hypertension |          |          |
|-------------------------------|--------------|----------|----------|
|                               | Men          | 95% CI   | Women    | 95% CI   |
| Physical activity-walk        |              |          |          |
| Yes                           | 1.00         | 1.00     | 1.00     |          |
| No                            | 0.91         | (0.87 - 0.97)| 0.96     | (0.90 - 1.01)|
| Menopausal status             |              |          |          |
| Yes                           | 1.17         | (1.03 - 1.34)|        |          |
| No                            | 1.00         |          |          |
| Alcohol use disorder          |              |          |          |
| mild drinking & non-drinking  | 1.00         |          | 1.00     |          |
| moderate drinking             | 1.20         | (1.11 - 1.30)| 1.16     | (1.07 - 1.27)|
| heavy drinking                | 1.83         | (1.69 - 1.98)| 1.93     | (1.76 - 2.13)|

*(White, Pink, Blue) based on International Standard Classification Occupations codes. Inoccupation group includes housewife.

### FIGURE 1

Stratified analysis of the changes in facial flushing with respect to hypertension by alcohol consumption

Function may be associated with a decrease in the activity of the enzyme that metabolizes alcohol. This, in turn, leads to the accumulation of alcohol and acetaldehyde in the body and induces symptoms such as facial flushing. Therefore, people who have liver disease with non-facial flushing in the past may develop a facial flushing reaction later.

In our study, people who did not have a facial flushing reaction in the past but did in the present were significantly associated with the risk of hypertension among those who were diagnosed with diabetes or did not exercise. Although the mechanism causing flushing is unknown, it is clear that this is not a good indication or reaction in the body. Research findings have indicated that ALDH2 polymorphism that causes facial flushing is related to cancer risk incidence according to alcohol intake. It is noteworthy that these studies mainly focused on upper oral pharyngeal and laryngeal cancer and esophageal squamous cell carcinoma. Thus, if people have never had facial flushing to
**TABLE 3** The results of subgroup analysis stratified by independent variables

| Variables          | Hypertension | Facial flushing change |
|--------------------|--------------|------------------------|
|                    | OR  | 95% CI  | OR  | 95% CI  | OR  | 95% CI  | OR  | 95% CI  |
| No-drinking        |     |         |     |         |     |         |     |         |
| non-flushing       | 1.00| (0.77 - 1.77) | 1.11| (0.72 - 1.72) | 1.16| (0.49 - 2.75) | 1.11| (0.64 - 1.91) |
| non-flushing → non-flushing |     |         |     |         |     |         |     |         |
| flushing → flushing| 1.00| (0.83 - 1.63) | 0.95| (0.67 - 1.34) | 1.52| (0.84 - 2.76) | 1.05| (0.69 - 1.58) |
| flushing → flushing| 1.00| (0.98 - 1.71) | 1.22| (0.93 - 1.62) | 1.61| (1.00 - 2.60) | 1.17| (0.85 - 1.61) |
| flushing → non-flushing|     |         |     |         |     |         |     |         |
| ≥60                | 1.00| (0.74 - 1.24) | 1.10| (0.85 - 1.42) | 1.40| (0.86 - 2.28) | 1.00| (0.74 - 1.36) |
|                  |     |         |     |         |     |         |     |         |

**Men**

| Age      | Hypertension | Facial flushing change |
|----------|--------------|------------------------|
| 19-29    | 1.00         | 1.17 (0.77 - 1.77)     | 1.11 (0.72 - 1.72) | 1.16 (0.49 - 2.75) | 1.11 (0.64 - 1.91) |
| 30-39    | 1.00         | 1.16 (0.83 - 1.63)     | 0.95 (0.67 - 1.34) | 1.52 (0.84 - 2.76) | 1.05 (0.69 - 1.58) |
| 40-49    | 1.00         | 1.29 (0.98 - 1.71)     | 1.22 (0.93 - 1.62) | 1.61 (1.00 - 2.60) | 1.17 (0.85 - 1.61) |
| 50-59    | 1.00         | 0.96 (0.74 - 1.24)     | 1.10 (0.85 - 1.42) | 1.40 (0.86 - 2.28) | 1.00 (0.74 - 1.36) |
| ≥60      | 1.00         | 1.04 (0.88 - 1.24)     | 1.14 (0.97 - 1.35) | 1.39 (1.00 - 1.94) | 1.13 (0.90 - 1.43) |

**Diagnose of diabetes**

|          | Hypertension | Facial flushing change |
|----------|--------------|------------------------|
| Yes      | 1.00         | 0.97 (0.67 - 1.40)     | 0.97 (0.66 - 1.43) | 2.24 (1.22 - 4.11) | 0.68 (0.42 - 1.13) |
| No       | 1.00         | 1.13 (1.01 - 1.28)     | 1.11 (0.98 - 1.25) | 1.35 (1.07 - 1.70) | 1.12 (0.96 - 1.29) |

**BMI**

| BMI      | Hypertension | Facial flushing change |
|----------|--------------|------------------------|
| non-obesity | 1.00         | 1.13 (1.01 - 1.27)     | 1.10 (0.98 - 1.24) | 1.40 (1.11 - 1.76) | 1.10 (0.95 - 1.28) |
| Obesity  | 1.00         | 0.91 (0.62 - 1.35)     | 1.00 (0.68 - 1.48) | 1.58 (0.73 - 3.41) | 0.80 (0.48 - 1.34) |

**Physical activity**

|          | Hypertension | Facial flushing change |
|----------|--------------|------------------------|
| Yes      | 1.00         | 1.01 (0.86 - 1.20)     | 0.97 (0.82 - 1.14) | 1.18 (0.85 - 1.63) | 0.91 (0.73 - 1.13) |
| No       | 1.00         | 1.21 (1.03 - 1.42)     | 1.22 (1.04 - 1.42) | 1.68 (1.26 - 2.25) | 1.25 (1.04 - 1.52) |

**Women**

| Age      | Hypertension | Facial flushing change |
|----------|--------------|------------------------|
| 19-29    | 1.00         | 1.25 (0.68 - 2.29)     | 1.28 (0.66 - 2.46) | 0.45 (0.09 - 2.14) | 0.69 (0.29 - 1.63) |
| 30-39    | 1.00         | 1.03 (0.71 - 1.51)     | 0.93 (0.61 - 1.41) | 0.65 (0.28 - 1.48) | 1.23 (0.75 - 2.04) |
| 40-49    | 1.00         | 1.39 (1.10 - 1.76)     | 1.56 (1.21 - 2.01) | 0.97 (0.56 - 1.69) | 1.28 (0.94 - 1.75) |
| 50-59    | 1.00         | 0.96 (0.82 - 1.12)     | 1.14 (0.96 - 1.35) | 1.79 (1.26 - 2.56) | 1.00 (0.78 - 1.28) |
| ≥60      | 1.00         | 0.82 (0.73 - 0.91)     | 0.92 (0.80 - 1.07) | 1.13 (0.79 - 1.62) | 0.89 (0.71 - 1.11) |

**Diagnose of diabetes**

|          | Hypertension | Facial flushing change |
|----------|--------------|------------------------|
| Yes      | 1.00         | 1.07 (0.82 - 1.39)     | 1.11 (0.79 - 1.56) | 0.69 (0.35 - 1.38) | 0.76 (0.44 - 1.33) |
| No       | 1.00         | 0.93 (0.86 - 1.01)     | 1.02 (0.93 - 1.12) | 1.14 (0.92 - 1.42) | 0.93 (0.81 - 1.07) |

**BMI**

| BMI      | Hypertension | Facial flushing change |
|----------|--------------|------------------------|
| Non-obesity | 1.00         | 0.91 (0.84 - 0.99)     | 1.01 (0.92 - 1.12) | 1.12 (0.88 - 1.43) | 0.93 (0.81 - 1.07) |
| Obesity  | 1.00         | 1.47 (1.02 - 2.12)     | 1.43 (0.96 - 2.13) | 1.17 (0.53 - 2.58) | 1.08 (0.56 - 2.08) |

**Physical activity**

|          | Hypertension | Facial flushing change |
|----------|--------------|------------------------|
| Yes      | 1.00         | 0.92 (0.82 - 1.04)     | 1.03 (0.90 - 1.19) | 1.15 (0.82 - 1.61) | 0.87 (0.71 - 1.06) |
| No       | 1.00         | 0.94 (0.85 - 1.04)     | 1.03 (0.91 - 1.16) | 1.07 (0.82 - 1.40) | 0.99 (0.83 - 1.18) |

*Adjusted for other covariates

alcohol before but experience facial flushing now, people need to exercise caution with their alcohol intake. However, as there are no studies in the literature supporting this result, it is difficult to determine an absolute judgment.

This study has some limitations. First, this study was based on data from a cross-sectional survey. Therefore, although the association could be confirmed, the causality could not be evaluated. Second, our data were self-reported; thus, it is subject to recall bias and under-reporting of drinking habits or experience of facial flushing. Therefore, the association of facial flushing with drinking may not be accurate. Moreover, we do not know how long it has been since changes in facial flushing were observed by participants. Third, although the cut-off points used for facial flushing are in accordance with KCHS, it may be difficult to compare our findings in different settings or populations. Fourth, residual confounding factors may exist because taking some medication like steroid that cause facial flushing have not
been identified due to data limitation. These factors should be considered in future studies. Finally, due to lack of similar studies, it is difficult to explain all the findings in this study. Therefore, it is necessary to perform precise measurements of facial flushing in further studies.

Despite these limitations, this study has several strengths. We used the most recent nationally representative database to determine the association between facial flushing and hypertension. Therefore, the results obtained are highly representative of adults in South Korea. Furthermore, in our analysis, we adjusted for several social factors that are known potential confounders for facial flushing pattern or hypertension, including sex, socioeconomic status, and health behaviors, to appropriately estimate the associations across different drinking behavior patterns.

In conclusion, this study found a significant association between change in facial flushing and hypertension among adults in South Korea. In particular, individuals who changed from non-flushing to flushing reactions had an increased association with hypertension than those in the other groups. Compared to people at the same drinking level, people with non-flushing to flushing reactions were highly associated with hypertension at moderate drinking level.

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CONFLICT OF INTEREST
None declared.

AUTHOR CONTRIBUTIONS
Soo Hyun Kang conceived of the presented idea. Yu Shin Park and Soo Hyun Kang developed the theory and performed the computations. Yu Shin Park and Soo Hyun Kang verified the analytical methods. Eun Hyun Kang developed the theory and performed the computations. Soo Hyun Kang conceived of the presented idea. Yu Shin Park and Soo Hyun Kang verified the analytical methods. Eun Hyun Kang developed the theory and performed the computations. Soo Hyun Kang conceived of the presented idea. Yu Shin Park and Soo Hyun Kang verified the analytical methods.

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