The relationship between alcohol consumption and knee osteoarthritis in Korean population over 50 years-old

Results from Korea National Health and Nutrition Examination Survey

Seong-Kyu Kim, MD, PhD, Jisuk Bae, MD, PhD, Jung-Yoon Choe, MD, PhD

Abstract
There is still debate regarding the pathogenic relationship between alcohol intake and osteoarthritis (OA). This study investigated the association between alcohol consumption and knee OA in a Korean population.

Among 8058 subjects who participated in the Korea National Health and Nutrition Examination Survey (KNHANES) 2012, a total of 2917 subjects over the age of 50 and taken plain radiography was included in this analysis. Knee OA was classified based on the Kellgren–Lawrence (K–L) grading scale. Multivariate logistic regression analyses were used to evaluate the odds ratios (ORs) and 95% confidence intervals (CIs) of variables for knee OA (K–L grade ≥ 2).

There were 1022 subjects with knee OA (29.2%). Subjects with knee OA tended to have lower daily alcohol intake (g/day) than did those without knee OA (10.4 [6.2–14.6] vs. 15.8 [12.9–18.8], P = .04). Similarly, those with knee OA demonstrated less makgeolli intake than did those without knee OA (P = .002). Subjects who consumed >0.6 g/day of beer also demonstrated less knee OA than did those who consumed <0.6 g/day of beer (OR 0.68, 95% CI 0.46–0.99). However, knee OA was not associated with the categories of alcohol consumption amount (g/day), including total daily alcohol intake (g/day), soju daily intake (g/day), and makgeolli daily intake (g/day) (P > .05 of all).

Alcohol consumption was negatively associated with prevalence of knee OA in a Korean population. This preliminary observation will need to be confirmed in future studies.

Keywords: alcohol, Kellgren-Lawrence grade, knee, osteoarthritis, radiography

1. Introduction
Osteoarthritis (OA) is the most common joint disease leading to structural and functional impairment caused by articular cartilage loss, subchondral bone remodeling, synovial inflammation, and osteophyte formation.[1,2] OA leads to physical disability and pain and worsens quality of life. Although many studies have tried to identify the risk factors for OA development and progression in the last several decades, the results were unclear. A recent study defined variable modifiable and non-modifiable factors of OA to include age, sex, obesity, trauma, prior sports injury, inflammation, and genetic predisposition.[3,4] Diverse dietary and nutritional components, such as vitamins and fatty acids, may also contribute to OA pathogenesis.[5]

Alcohol consumption has paradoxically beneficial effects on several inflammatory rheumatic diseases including rheumatoid arthritis (RA), axial spondyloarthritis (axSpA), and systemic lupus erythematosus.[6–9] In contrast, the detrimental effects of alcohol on the musculoskeletal system (bone, muscle, and cartilage) can increase risk of osteoporosis and myopathies.[10,11] There is potent evidence that alcohol intake is an environmental risk factor for increasing or decreasing the risk and severity of hand, knee, or hip OA.[12–16] Some clinical studies did not find a relationship between alcohol intake and OA.[17–19] Based on inconsistent prior results, the objective of this study is to
determine the association between alcohol consumption by quantitative assessment and radiographic knee OA.

2. Subjects and methods

2.1. Study population

The Korea National Health and Nutrition Examination Survey (KNHANES) is a national surveillance system conducted by the Korean Centers for Disease Control and Prevention since 1998 to assess the health and nutritional status of the Korean population. We used data from KNHANES 2012, which not only includes health interview and nutrition surveys, but also health examination information. In the KNHANES 2012, data of 8058 participants were initially collected (Fig. 1). Participants under 50 years of age or who did not take plain radiography of knee joint were excluded. There were data to assess the Kellgren–Lawrence (K-L) grade (range, 0–4) to define the prevalence of knee OA in 3187 study participants among adults ≥50 years. Among them, subjects without data about information on alcoholic beverages were again excluded. The records of 2917 participants were included in the final analysis. This study used a K-L grade ≥2 as the radiographic criterion of knee OA. The Institutional Review Board (IRB) at Daegu Catholic University Medical Center approved this study (IRB no. CR-19-093-L).

2.2. Data collection

The health interview data were used to obtain information on sex, age (≥50–59, 60–69, 70–79, and ≥80 years), education (primary, secondary, and tertiary), marital status (married, widowed, divorced, and others [never married, separated, etc.]), cigarette smoking (non-smoker, former smoker, and current smoker), and regular exercise (walking ≥5 days/week for ≥30 min/day; yes/no). Information on total energy intake (kcal/day) was obtained from the nutrition survey data. The health examination data, which were collected according to standardized protocols, were used to gather information on anthropometric measures of body mass index (BMI; kg/m²), waist circumference (cm), systolic blood pressure (SBP; mmHg), and diastolic blood pressure (DBP; mmHg). Fasting serum glucose (mg/dL), total cholesterol (mg/dL), and triglyceride (mg/dL) levels were measured using enzymatic methods within the Hitachi Automatic Analyzer 7600 (Hitachi, Japan).

2.3. Radiographic assessment

Data from plain radiography of the knee joint were obtained in collaboration with academic societies to provide technical advice and medical personnel. Plain radiography of both knees using anteroposterior view with weight-bearing position was performed to evaluate knee radiographic grading. We used the K–L grading scale to assess the radiographic severity of both knee joints.[20]

2.4. Alcoholic beverage assessment

Alcohol consumption was categorized into the following three groups: non-drinker, former drinker, and current drinker. Excessive alcohol use was assessed using the Korean Version of Alcohol Use Disorder Identification Test (AUDIT-K; range, 0–34).[21] An AUDIT ≥8 was defined as hazardous or harmful alcohol use. Information regarding consumption of alcoholic beverages (i.e., soju, beer, and makgeolli) was obtained during a face-to-face interview using a semi-quantitative food frequency questionnaire (FFQ; composed of 112 food items). The FFQ identified the average frequency (9 categories ranging from “never or rare” to “3 times/day”) and portion size (a 360 mL bottle of soju, a 200 mL glass of beer, and a 210 mL bowl of makgeolli) of each alcoholic beverage over the past year. The average daily intake of each alcoholic beverage (g/day) was calculated by multiplying the consumption of each alcoholic beverage by its ethanol content (19% in soju, 4.5% in beer, and 6% in makgeolli). The average daily alcohol intake (g/day) was calculated by combining the average daily intake of soju, beer, and makgeolli.

2.5. Statistical analysis

All descriptive statistics are presented as the unweighted count and weighted percentage for categorical variables and the unweighted mean and 95% confidence interval (CI) for continuous variables. Differences in categorical and continuous variables (according to knee OA status) were assessed using chi-square tests and Student’s t tests, respectively. Multivariate logistic regression models were used to estimate the odds ratios (ORs) of knee OA (and corresponding 95% CIs) according to categorical alcohol consumption. The covariates in Model 1 were sex and age (50–59, 60–69, 70–79, and ≥80 years). Model 2 additionally adjusted for education (primary, secondary, and tertiary); marital status (married, widowed, divorced, and others [never married, separated, etc.]); cigarette smoking (non-smoker, former smoker, and current smoker); regular exercise (walking ≥5 days/week for ≥30 min/day; yes/no); BMI (kg/m²; continuous); and SBP (mmHg; continuous), fasting serum glucose (mg/dL; continuous), and triglyceride levels (mg/dL; continuous). Lastly, Model 3 additionally adjusted for total energy intake (kcal/day; continuous). Statistical significance was denoted at P-value <.05. All statistical analyses were performed using IBM SPSS Statistics 19.0 (IBM Corp, Armonk, NY).

3. Results

3.1. General characteristics of study population

A total of 2917 subjects was analyzed, including 1191 men (45.8%) and 1726 women (54.2%), as shown in Table 1. There

![Flow chart of study population. KNHANES = Korea National Health and Nutrition Examination Survey, OA = osteoarthritis.](image-url)
were 1022 (29.2%) subjects with knee OA and 1895 (70.8%) without knee OA. There were significant differences between the groups with regard to sex, age, education, marital status, cigarette smoking, BMI, waist circumference, SBP, DBP, and daily energy intake. In contrast, the prevalence of regular exercise, fasting serum glucose, total cholesterol, and triglyceride level were not different between the two groups.

### 3.2. Comparison of alcohol consumption according to knee OA

Frequency of alcohol consumption was significantly different between subjects with and without knee OA (P < .0001) (Table 2). There were significantly fewer subjects with hazardous or harmful alcohol use (≥8 of AUDIT-K) in the knee OA group than there were in the non-knee OA group (P < .0001). Daily alcohol intake in subjects with knee OA was less than that of those without knee OA (P = .04). Subjects with knee OA do not drink alcohol or drink less daily than do those without OA (P < .0001). Participants with knee OA also consume much less makgeolli than do those without knee OA (P = .002). In contrast, there were no differences between the two groups with regard to soju and beer consumption (P = .05 and P = .94, respectively).

### 3.3. Determination for alcohol intake-related factors for knee OA

Multivariate logistic regression analysis showed that alcohol consumption status, AUDIT-K, daily alcohol intake, and soju and makgeolli consumption were not associated with knee OA (Table 3). In contrast, after statistical adjustment, those with knee OA were less likely to consume excessive beer than were those without OA (OR 0.68, 95% CI 0.46–0.99).

### 4. Discussion

Although many prior studies have investigated the relationship between alcohol intake and OA, the association had not been previously defined. The reasons for these inconclusive results might be due to variable study designs, study populations, and affected joints (Table 4). This cross-sectional study assessed the relationship between alcohol consumption and knee OA using data from the national health and nutritional survey, which represents the Korean population. The main observation in this study is that alcohol consumption was much less prevalent in subjects with knee OA than it was in those without knee OA. In addition, consumption of some alcoholic beverages, including beer and makgeolli, was negatively associated with knee OA.
Knee OA is the most common articular disease in the general population, followed by hand OA. The prevalence of knee OA gradually increases with age.\(^1\)\(^,\)\(^2\) It well recognized that there are modifiable and non-modifiable risk factors of knee OA. To reduce the risk of knee OA, we must pay attention to risk factors that can be modified in its progression and development. How alcohol consumption affects knee OA has been a question for several decades. The ROAD study evaluated incidence of radiographic knee OA and knee pain over 3 years of follow-up in Japan.\(^19\) Alcohol intake was found to be a risk factor for incidence of OA with K-L grade ≥3 in univariate logistic regression (OR 0.66, 95% CI 0.49–0.89); however, its significance was lost after statistical adjustment. In addition, alcohol consumption was not an independent risk factor for progressive knee OA and knee pain. Another case-control study of a Caucasian population demonstrated that increasing beer consumption was associated with increasing risk of knee and hip OA. However, less wine drinking increased the risk of knee OA.\(^15\)\(^1\) In contrast, a Korean population-based study demonstrated that moderate or heavy alcohol drinking was less frequent in subjects

### Table 2

| Variables                  | Total subjects (n= 2917) | Subjects without knee OA (n= 1895) | Subjects with knee OA (n= 1022) | \(P^*\) |
|----------------------------|--------------------------|-----------------------------------|-------------------------------|------|
| Alcohol consumption        |                          |                                   |                               |      |
| Non-drinker                | 625 (18.8)               | 330 (15.1)                        | 295 (28.1)                    | <.0001|
| Former drinker             | 1005 (35.0)              | 643 (33.6)                        | 362 (38.3)                    |      |
| Current drinker            | 1124 (46.2)              | 833 (51.3)                        | 291 (33.6)                    |      |
| AUDIT-K                    | 5.96 (5.49–6.43)         | 6.55 (5.97–7.13)                  | 4.21 (3.66–4.77)              | <.0001|
| 0–7                       | 1598 (69.7)              | 1056 (65.8)                       | 542 (81.4)                    | <.0001|
| ≥8                        | 526 (30.3)               | 418 (34.2)                        | 108 (18.6)                    | <.0001|
| Daily alcohol intake (g/d) |                          |                                   |                               |      |
| Non-drinker                | 14.8 (12.3–17.4)         | 15.8 (12.6–18.8)                  | 10.4 (6.2–14.6)               | .04  |
| <10.0                      | 625 (26.5)               | 330 (19.7)                        | 295 (49.9)                    | <.0001|
| 10.0–34.9                  | 613 (49.1)               | 645 (52.3)                        | 168 (36.4)                    |      |
| ≥35.0                      | 154 (11.6)               | 134 (13.6)                        | 20 (5.1)                      |      |
| Soju (g/d)                 | 10.5 (8.4–12.6)          | 11.2 (8.8–13.7)                   | 7.1 (4.0–10.2)                | .05  |
| Beer (g/d)                 | 2.2 (1.7–2.8)            | 2.2 (1.7–2.8)                     | 2.3 (0.9–3.7)                 | .94  |
| Makgeolli (g/d)            | 2.1 (1.5–2.6)            | 2.3 (1.6–3.0)                     | 1.0 (0.6–1.5)                 | .002 |

AUDIT-K = the Korea Version of Alcohol Use Disorder Identification Test.

Data were expressed as n (weighted %) for categorical variables and mean (95% confidence interval) for continuous variables.

\(^*\) Calculated by chi-square tests for categorical variables and Student’s t-tests for continuous variables.

### Table 3

| Variables                  | Model 1             | Model 2             | Model 3             |
|----------------------------|---------------------|---------------------|---------------------|
| Alcohol consumption        | 1.00 (reference)    | 1.00 (reference)    | 1.00 (reference)    |
| Non-drinker                | 1.03 (0.79–1.35)    | 1.03 (0.76–1.39)    | 1.02 (0.76–1.39)    |
| Former drinker             | 0.95 (0.70–1.27)    | 0.89 (0.65–1.22)    | 0.88 (0.64–1.21)    |
| Current smoker             |                     |                     |                     |
| AUDIT-K                    | 0.79 (0.58–1.07)    | 0.77 (0.56–1.07)    | 0.76 (0.55–1.06)    |
| Daily alcohol intake (g/d) | 1.00 (reference)    | 1.00 (reference)    | 1.00 (reference)    |
| Non-drinker                | 1.28 (0.89–1.84)    | 1.35 (0.93–1.96)    | 1.33 (0.92–1.93)    |
| <10.0                      | 1.11 (0.59–2.10)    | 1.07 (0.55–2.07)    | 1.06 (0.55–2.05)    |
| 10.0–34.9                  | 0.65 (0.34–1.26)    | 0.70 (0.35–1.40)    | 0.67 (0.33–1.37)    |
| ≥35.0                      |                     |                     |                     |
| Soju (g/d)                 | 0.93 (0.58–1.48)    | 0.96 (0.60–1.53)    | 0.93 (0.58–1.48)    |
| Beer (g/d)                 | 1.00 (reference)    | 1.00 (reference)    | 1.00 (reference)    |
| Q1–Q3 (<2.9)               | 0.72 (0.49–1.06)    | 0.69 (0.47–1.01)    | 0.68 (0.46–0.99)    |
| Q4 (≥2.9)                  | 1.00 (reference)    | 1.00 (reference)    | 1.00 (reference)    |
| Q1–Q3 (<0.6)               | 0.84 (0.53–1.34)    | 0.84 (0.53–1.33)    | 0.82 (0.52–1.30)    |

CI = confidence interval, OR = odds ratio.

Logistic regression models were used to calculate ORs and 95% CIs: Model 1, adjusted for sex and age; Model 2, adjusted for sex, age, education, marital status, cigarette smoking, regular exercise, body mass index, systolic blood pressure, fasting serum glucose, and triglyceride; and Model 3, additionally adjusted for total energy intake.
with knee and hip OA than it was in those without OA. After adjusting for confounding factors, heavy alcohol drinking was not associated with OA in either sex. However, moderate drinking was negatively associated with OA in men (OR, 0.69, 95% CI 0.49–0.97) but not in women (OR 0.95, 95% CI 0.77–1.17). The present study showed a lower prevalence of OA in alcohol drinkers than in non-drinkers. These findings are consistent with those of a prior Korean study. However, our study also included a detailed analysis of different types of alcohol and quantities consumed. We found that subjects with knee OA consumed significantly less makgeolli than did those without OA. In addition, beer intake was inversely related to knee OA. These inconsistent results regarding the relationship between alcohol and knee OA must be clarified through future prospective studies.

Enhanced breakdown of articular cartilage is a crucial feature in the pathogenesis of knee OA. Various factors are known to induce cartilage degradation in OA, including aging, obesity, and inflammation. There has also been inconsistent molecular biological evidence regarding the effects of ethanol on chondrocytes or cartilage. It is well established that the TGF-β signaling pathway is involved in progression and development of OA through tight regulation of bone and cartilage formation and remodeling. Offspring of pregnant rats treated with ethanol showed poor differentiation of bone marrow-derived stroma cells into chondrocytes. This effect resulted from alcohol’s inhibition of the TGF-β signaling pathway. Another study using a culture of articular chondrocytes showed that alcohol consumption caused cartilage breakdown in vitro. In addition, Kc et al provided experimental evidence that an OA-like C57BL/6 mouse model fed an alcohol diet (containing 4.5% ethanol) experienced severe changes in articular cartilage of the knee or shoulder joint. In another study, prenatal ethanol exposure was shown to inhibit the insulin-like growth factor-1 signaling pathway and damage articular cartilage, which resulted in increased risk of OA development. These findings suggest that ethanol has a negative effect on chondrocyte differentiation, disturbing cartilage homeostasis. These experimental OA-related data support the clinical findings that alcohol intake can exacerbate classic radiographic changes in OA.

In contrast, ethanol treatment induced expression of cartilage-specific genes, including type II collagen and cartilage proteoglycan (aggrecan), in in vitro experiments using several kinds of mesenchymal cells. Clinical studies have shown that alcohol consumption does not increase the risk of OA development, which may explain the beneficial effects of alcohol on cartilage metabolism. Muthuri et al showed a protective effect of wine intake on the risk of knee OA. These observations suggest that alcohol has a stimulatory effect on chondrogenesis. Nevertheless, the definite pathogenic mechanism by which alcohol influences OA development remains unclear. Therefore, there is need for further evidence regarding the mechanism of alcohol involvement in differentiation and formation of chondrocytes and cartilage homeostasis.

In their experimental study using a collagen type II-immunized arthritis DBA/1 mouse model, Jonsson et al recently demonstrated a preventive effect of ethanol on development of arthritis through suppression of peritoneal leukocyte migration and inflammatory transcription factor NF-κB activation. The relationship between ethanol and inflammatory arthritis is consistent with the finding that alcohol consumption decreases the risk of RA in a prospective population-based cohort in Sweden. In patients with a xSpA, another form of inflammatory arthritis, alcohol consumption has been shown to be beneficial to disease activity and physical function. Considering these findings, the benefits of alcohol in a xSpA and RA are relatively consistent. It is well known that the pathologies of OA, a xSpA, and RA differ significantly. However, the inconsistent effect of alcohol in OA may be related to the divergent pathological mechanisms of other inflammatory arthritis.

There is evidence that explains our observation that makgeolli intake and beer intake are inversely related to knee OA. Beer, which is mainly composed of ethanol and polyphenols, has been found to have divergent effects on several human diseases, such as...
cardiovascular disease or crystal-induced arthritis. Polyphenols have antioxidant potential and the ability to block monocyte adhesion. This property may explain the protective effect of beer on inflammatory diseases. There has also been some experimental evidence that acute alcohol exposure inhibited the inflammatory response. Makgeolli, a traditional Korean alcoholic beverage produced from fermented rice, contains a variety of compositions such as nutrients, lactic acid, lactobacilli bacteria, and alcohol. Several studies have demonstrated the anti-inflammatory and immunomodulatory effects of makgeolli through its inhibition of oxidative molecules (including hexanaldehyde) and enhanced anti-complementary activity. The anti-inflammatory effects of beer and makgeolli may be associated with their significant amounts of total polyphenols and ethanol.

This study had several limitations. First, it used cross-sectional population-based data that cannot fully explain the direct causal relationship between alcohol consumption and knee OA. In addition, the KNHANES data did not evaluate radiographic change of articular joints every year, and the population who participated in the survey participants was variable from year to year. Therefore, follow-up data are limited. Second limitation is that this study did not provide the total alcohol intake of each subject, because there were no data regarding duration of alcohol consumption. Instead, we calculated the daily amount of each alcohol intake using the FFQ. In addition, physical activity index related to cardiovascular disease was used to evaluate regular exercise. It may be slightly inappropriate as this physical activity index related to knee OA. In the future, research using exercise indexes suitable for knee OA is considered necessary. Despite these limitations, use of a large population-based data set can be considered the study’s strength.

In conclusion, this cross-sectional study revealed that frequency of alcohol consumption in knee OA was less than that in those without knee OA. In particular, beer intake was found to have a protective effect in knee OA. This study provides clinical evidence to understand the effects of alcohol on the pathogenesis of knee OA. The mechanism of the negative relationship between knee OA and alcoholic beverage intake must be further clarified.

Author contributions
Conceptualization: Seong-Kyu Kim, Jisuk Bae, Jung-Yoon Choe.
Data curation: Seong-Kyu Kim, Jisuk Bae, Jung-Yoon Choe.
Formal analysis: Seong-Kyu Kim, Jisuk Bae.
Investigation: Seong-Kyu Kim, Jisuk Bae, Jung-Yoon Choe.
Methodology: Seong-Kyu Kim, Jung-Yoon Choe.
Software: Jisuk Bae.
Supervision: Seong-Kyu Kim.
Writing – original draft: Seong-Kyu Kim.
Writing – review & editing: Seong-Kyu Kim.

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