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Effects of Genetic Risk and Lifestyle Habits on Gout: A Korean Cohort Study

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ABSTRACT

Background: Gout is a type of inflammatory arthritis caused by monosodium urate crystal deposits, and the prevalence of this condition has been increasing. This study aimed to determine the combined effects of genetic risk factors and lifestyle habits on gout, using data from a Korean cohort study. Identifying high-risk individuals in advance can help prevent gout and its associated disorders.

Methods: We analyzed data from the Korean Genome and Epidemiology Study-Urban Health Examinees cohort (KoGES-HEXA). Genetic information of the participants was collected at baseline, and gout cases were identified based on patient statements. The polygenic risk score (PRS) was calculated using nine independent genome-wide association study datasets, and lifestyle factors and metabolic syndrome status were measured for each participant using the KoGES. Logistic regression models were used to estimate the odds ratios (ORs) for gout in relation to genetic risk, lifestyle habits, and metabolic health status, after adjusting for age and sex.

Results: Among 44,605 participants, 617 were diagnosed with gout. Gout was associated with older age, higher body mass index, and higher prevalence of hypertension, diabetes, and hypertriglyceridemia. High PRS, unfavorable lifestyle habits, and poor metabolic profiles were significantly associated with an increased risk of gout. Compared with that in the low-genetic-risk and healthy lifestyle group or ideal metabolic profile group, the risk of gout was increased in the high-genetic-risk plus unfavorable lifestyle (OR, 3.64; 95% confidence interval [CI], 2.32–6.03) or poor metabolic profile (OR, 7.78; 95% CI, 4.61–13.40) group. Conversely, adherence to favorable lifestyle habits significantly reduced gout risk, especially in high-genetic-risk groups.

Conclusion: Genetic predisposition and unhealthy lifestyle habits significantly increase the risk of gout. Promoting healthy lifestyle habits is crucial to prevent the development of gout, particularly in individuals with high genetic susceptibility.

Keywords: Gout; Polygenic Risk Score; Lifestyle Habits; Metabolic Syndrome; Korean Cohort

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Disclosure
The authors have no potential conflicts of interest to disclose.

Author Contributions
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INTRODUCTION

Gout is a type of inflammatory arthritis in which monosodium urate crystals are deposited in various tissues. The prevalence of gout has been increasing in Korea owing to rapid aging, lifestyle changes, and increased incidence of metabolic syndrome (MetS).[1] In fact, a Korean study revealed that the prevalence of gout increased by approximately five-fold over approximately a decade (from 0.39% in 2002 to 2.01% in 2015).[2] Gout is associated with several disorders, such as hypertension, hyperlipidemia, chronic kidney disease, and cardiovascular disease. Therefore, individuals at high risk of developing gout should be identified in advance to prevent the development of gout and its comorbidities.

Genetic risk prediction is a useful method for identifying individuals at high risk for a certain disease. Because gout is a chronic metabolic disorder, genetic information should include the total number of genetic variants rather than a single variant. The polygenic risk score (PRS) is the sum of the estimated effects of several genetic variants on a specific phenotype or disease. The PRS is calculated by computing the sum of the risk alleles possessed by an individual, weighted by the risk allele effect sizes, as estimated via a genome-wide association study (GWAS) on the phenotype.[3] The PRS is widely used as a marker of genetic risk for major chronic diseases. However, many studies using the PRS have mainly been conducted on Caucasians of European ancestry. A recently published study revealed that 67% of studies using the PRS were exclusively conducted with populations of European ancestry, 19% included East Asian ancestry, and only 3.8% included African, Hispanic, and other populations.[4] To improve the versatility of the PRS, studies targeting more diverse ancestries should be actively conducted. Therefore, we designed this study to develop a gout PRS for Asian populations, using a Korean genome database.

In addition to genetic susceptibility, lifestyle habits, such as alcohol consumption, smoking, diet, and physical activity, play an important role in the development of gout. Although genetic susceptibility cannot be altered, lifestyle habits are important because they are modifiable. Preventive medicine is an effective strategy to reduce the rapidly increasing prevalence of gout. By identifying patients at high risk for gout using the gout PRS and lifestyle factors, individuals can be encouraged to modify their lifestyle, ultimately reducing the risk of developing gout and its complications. Accordingly, we investigated the combined effects of genetic and lifestyle factors on the risk of gout using Korean cohort data and determined whether adherence to favorable lifestyles can reduce the risk of gout.

METHODS

Data

This study included participants from the Korean Genome and Epidemiology Study-Urban Health Examinees cohort (KoGES-HEXA). Genetic information was collected at baseline. Gout cases were identified as those diagnosed either at baseline (2004–2013) or at the first follow-up (2012–2016) based on their statements. Epidemiological data were obtained at the first follow-up of the individuals diagnosed with gout. Epidemiological data, including age, sex, lifestyle habits, and MetS status, were collected at baseline and the first follow-up.

Assessment of lifestyle factors and MetS

Lifestyle was assessed based on five factors: current smoking status (non or past smoker = 1, current smoker = 0), current alcohol consumption (non-drinker = 1, current drinker = 0), obesity defined by body mass index (BMI, BMI < 25 kg/m^2 = 1, BMI ≥ 25 kg/m^2 = 0), regular exercise (number of vigorous activities ≥ 3 days per week = 1, number of vigorous activities < 3 days per week = 0), and eating habits (healthy eating habits = 1, non-healthy eating habits = 0). Each factor was assigned a score that was then summed to create a total lifestyle score for each participant. Collectively, lifestyle behaviors were categorized into three groups: unfavorable (0–1 healthy lifestyle factor), intermediate (2 healthy lifestyle factors), and favorable (≥ 3 healthy lifestyle factors).[5] Detailed components of the lifestyle score and field ID of KoGES are displayed in **Supplementary Table 1**. MetS factors were assessed based on waist circumference (≥ 90 cm for males and ≥ 85 cm for females), hypertriglyceridemia (≥ 150 mg/dL), low high-density lipoprotein levels (male < 40 mg/dL, female < 50 mg/dL), high fasting plasma glucose levels (≥ 110 mg/dL), and high blood pressure (BP) levels (systolic BP ≥ 130 mmHg or diastolic BP ≥ 85 mmHg). Metabolic health status was categorized into three groups: ideal (0 MetS factors), intermediate (1–2 MetS factors), and poor (≥ 3 MetS factors). Detailed components of the MetS score and field ID of the KoGES are shown in **Supplementary Table 2**.

Genotype data quality control (QC) and imputation

Several filtering steps were implemented to ensure data integrity during the pre-imputation QC phase. Initially, duplicate variants and those with genotyping rates < 98% were removed. To assess familial relationships, we filtered out the samples that exhibited second-degree genetic relatedness. Variants that did not meet the Hardy-Weinberg equilibrium (*P* value < 1e-06) and those classified as rare (minor allele frequency [MAF] < 0.01) were excluded from the analysis. Sex chromosomal variants were subjected to QC measures only in females. Samples with a genotyping rate of < 95% were further excluded, and outliers were identified based on heterozygosity and genotyping rates by applying a threshold of greater than five standard deviations for each criterion. Patients with discordant genetic data or self-reported sex were excluded. An in-sample principal component analysis was conducted to exclude population outliers exceeding five standard deviations in either the first or second principal components. Both variants and samples were filtered based on a genotyping rate of 98% and relatedness up to the second degree. All QC processes were conducted using the PLINK[6] and PLINK2[7] software, which are standard tools for genetic data analysis. Following pre-imputation QC, we advanced to the genotype imputation phase. We used Eagle v2.4 for pre-phasing and Minimac4 for the imputation process. The Korean Imputation Service Phase 1 panel, which includes data from 4,799 individuals and is based on the GRCh37/hg19 genome assembly, was employed as the reference panel.[8] For the imputed genotype data, we retained variants exhibiting an imputation quality score (R^2) greater than 0.8. In addition, we selected variants with an MAF of at least 0.01. Only single-nucleotide polymorphisms (SNPs) located in the autosomal regions were included in the analysis.

PRS calculation

To calculate the PRS, we used genetic association data from various GWAS and PRS studies as the base data and specifically targeted gout-related phenotypes. The selected studies included the gout phenotype results ("M13_GOUT" and "GOUT_STRICT") in the FinnGen project (freeze 9; https://r9.finngen.fi/), data from CKDGen,[9] and studies referred to as CER[10] and NCOMMS.[11] In our study, the FinnGen results are referred to as Finngen_M13_GOUT and Finngen_GOUT_STRICT. Additional studies were collected from Polygenic Score (PGS)

Catalogs (https://www.pgscatalog.org/) (PGS IDs: PGS000199,[12] PGS002307,[5] PGS002762,[13] PGS000711,[14] PGS001248,[15] PGS001822,[16] PGS002030,[16] and PGS003329[17]). For studies not involving PGS catalogs, SNPs for PRS calculations were selected using the PRSice clumping and thresholding (C + T) method implemented in PLINK2. Details of the selected SNPs are provided in **Supplementary Table 3**. The PRS for each sample was calculated as the cosine product of the effect sizes of the selected SNPs and genotypes in the sample.

$$\text{PRS} = \sum_{i=1}^{M} \beta_i g_i$$

where M is the number of selected SNPs, β_i is the effect size of SNP i, and g_i is the genotype of SNP i in the sample, recorded as 0, 1, or 2 according to the number of risk-increasing alleles.

Of the 13 datasets, nine (Finngen_M13_GOUT, CKDGen, CER, PGS002762, PGS000711, PGS001248, PGS001822, PGS002030, and PGS003329) showed significant differences in the PRS between gout cases and controls based on the *t* test (*P* value < 0.05).

Statistical analysis

For genetic analysis, we calculated the average effect size of each allele of SNPs identified in the GWAS or those used in the PRS studies.

$$\text{Average effect size of SNP} = \frac{\sum_{j=1}^{N} \beta_j}{N}$$

where N is the number of datasets containing the SNP and β_j is the effect size of the SNP in dataset j. The final PRS for each sample was calculated as the cosine product of the average effect sizes of SNPs and genotypes in the sample. The baseline characteristics of the study population were compared according to the gout status using the *t* test for continuous variables and the χ^2 test for categorical variables. The PRS for gout risk was categorized into three groups (low, middle, and high, representing the lowest, middle, and highest tertiles, respectively) according to genetic risk. Logistic regression models were used to estimate the odds ratios (ORs) and 95% confidence intervals (CIs) of gout in relation to genetic risk, lifestyle habits, and MetS profiles after adjusting for age and sex. To evaluate the interaction among PRS, lifestyle habits, and MetS status, ORs and 95% CI for gout risk were calculated using multiple logistic regression after adjusting for age and sex. All analyses were performed using R version 4.2.0. All *P* values were two-sided, and statistical significance was set at 0.05.

Ethics statement

This study was approved by the Institutional Review Board of Kangwon National Hospital and the requirement for informed consent was waived (IRB No. 2023-06-012-002). This study complied with the Declaration of Helsinki of the World Medical Association.

RESULTS

Baseline characteristics of the study population

The baseline characteristics of the study population are presented in **Table 1**. Among the 44,605 participants, 617 had gout and 43,988 served as controls. A higher proportion of males had gout than females (84.44% vs. 34.29%, *P* < 0.001). Gout was also associated

Table 1. Baseline characteristics of participants

Characteristics	Control (n = 43,988)	Gout (n = 617)	*P* value
Demographic factors			
Male	15,084 (34.3)	521 (84.4)	< 0.001
Age, yr	54 ± 8.02	58 ± 7.74	< 0.001
BMI, kg/m^2	23.69 ± 2.87	25.00 ± 2.90	< 0.001
Lifestyle and comorbidities			
Current smoker	1,143 (2.6)	35 (5.7)	< 0.001
Current drinker	19,349 (44.0)	417 (67.6)	< 0.001
Regular exerciser	9,325 (21.2)	155 (25.1)	0.021
Hypertension	6,417 (14.6)	148 (24.0)	< 0.001
Diabetes mellitus	11,294 (25.7)	256 (41.5)	< 0.001
Hypertriglyceridemia	11,249 (25.6)	286 (46.4)	< 0.001
Genetic risk			< 0.001
Low	14,744 (33.5)	124 (20.1)	
Middle	14,688 (33.4)	180 (29.2)	
High	14,556 (33.1)	313 (50.7)	
Lifestyle index			< 0.001
Favorable	10,905 (24.8)	76 (12.3)	
Intermediate	19,719 (44.8)	261 (42.3)	
Unfavorable	13,364 (30.4)	280 (45.4)	
Metabolic syndrome			< 0.001
Ideal	16,371 (37.2)	139 (22.5)	
Intermediate	23,206 (52.8)	401 (65.0)	
Poor	4,411 (10.0)	77 (12.5)	

Values are presented as number (%) or median ± standard deviation.
BMI = body mass index.

with older age (58.00 vs. 54.00, $P < 0.001$) and higher BMI (25.00 vs. 23.69, $P < 0.001$). The proportions of current smokers, current drinkers, and regular exercisers were higher in the gout group than in the control group. The prevalences of hypertension, diabetes mellitus, and hypertriglyceridemia were higher in the gout group than in the control group. A high genetic risk (50.73% vs. 33.09%, $P < 0.001$), unfavorable lifestyle habits (45.38% vs. 30.38%, $P < 0.001$), and poor MetS profiles (12.48% vs. 10.03, $P < 0.001$) were found in more individuals in the gout group than in the control group.

Gout risk according to genetic risk, lifestyle habits, and MetS

Fig. 1. shows the risk of gout according to genetic risk (**Fig. 1A**), lifestyle habits (**Fig. 1B**), and MetS profiles (**Fig. 1C**). Based on the logistic regression analysis, the OR for gout was 2.68 (95% CI, 2.17–3.32) for participants with a high genetic risk compared to those with a low genetic risk (**Fig. 1A**). The ORs of gout were 1.38 (95% CI, 1.07–1.80) for participants with intermediate lifestyle habits and 1.70 (95% CI, 1.31–2.23) for participants with unfavorable lifestyle habits compared to those with favorable lifestyle habits (**Fig. 1B**). The ORs of gout were 1.70 (95% CI, 1.41–2.08) for participants with an intermediate MetS profile and 2.89 (95% CI, 2.16–3.85) for participants with a poor MetS profile compared to those with the ideal MetS profile.

Effects of the interaction between lifestyle factors and genetic risk on gout

We investigated the combined effects of gout PRS, lifestyle habits, and MetS profile on the development of gout (**Fig. 2**). In the low- and middle-genetic-risk group, the risk of gout was not significant for participants with unfavorable lifestyle habits (OR, 1.28; 95% CI, 0.78–2.20 in the low-genetic-risk group; OR, 1.57; 95% CI, 0.96–2.66 in the middle-genetic-risk group). However, the ORs of gout were 2.80 (95% CI, 1.79–4.65) and 3.64 (95% CI, 2.32–6.03) for individuals with high genetic risk and intermediate and unfavorable lifestyle factors,

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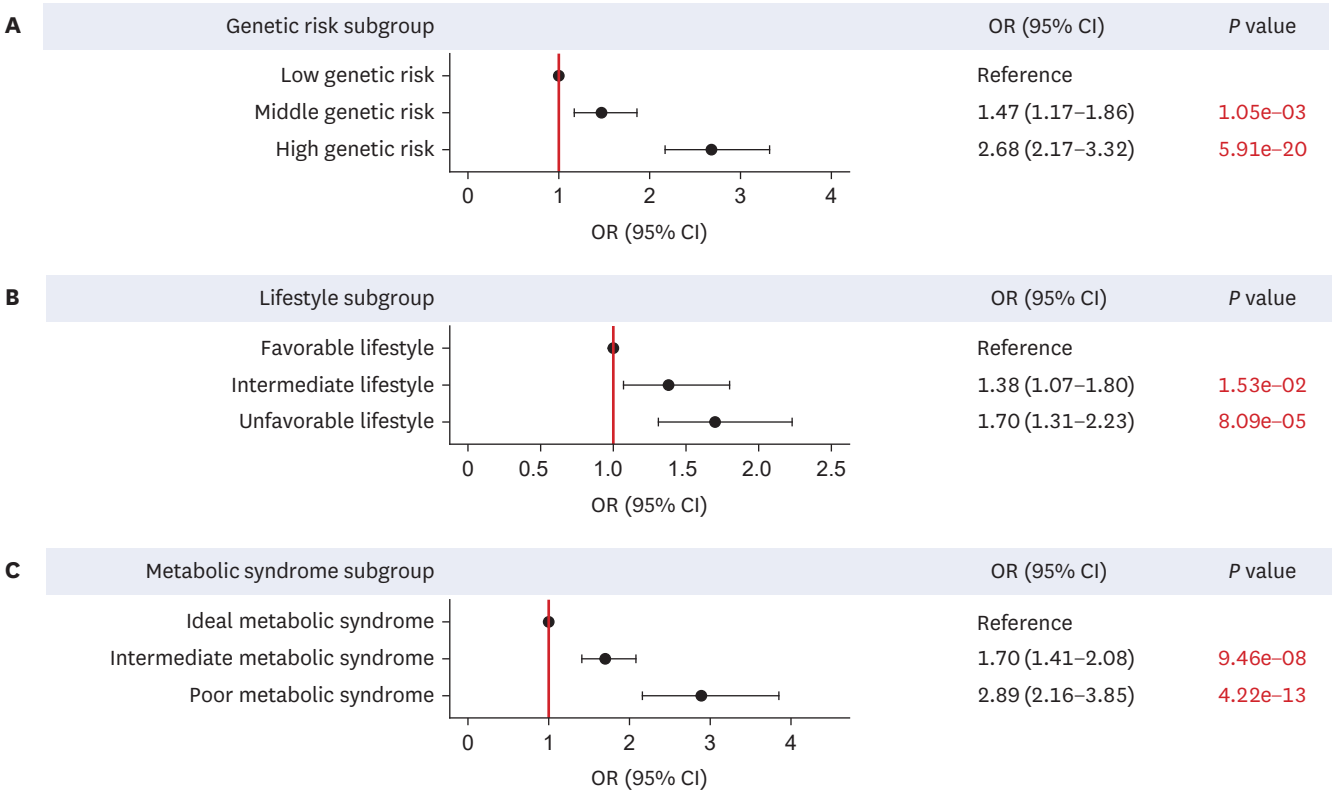

Fig. 1. ORs and 95% CIs for gout according to genetic risk (**A**), lifestyle (**B**), and metabolic status (**C**).
OR = odds ratio, CI = confidence interval.

respectively, compared to those with low genetic risk and favorable lifestyle habits (**Fig. 2A**). Joint effect analysis of genetic risk and MetS revealed similar patterns (**Fig. 2B**). A poor MetS profile did not significantly increase the risk of gout in the low-genetic-risk group (OR, 2.20; 95% CI, 0.96–4.61) but significantly increased the risk of gout in the middle- and high-genetic-risk groups (OR, 7.33; 95% CI, 4.30–12.60 in the middle-genetic-risk group; OR, 7.78; 95% CI, 4.61–13.40 in the high-genetic-risk group) compared to that in the groups with low genetic risk and ideal MetS profile.

Impact of modifiable lifestyle factors on the risk of gout

Fig. 3. shows the changes in gout risk after modifying lifestyle behaviors and metabolic health status. In the high-genetic-risk group, the OR for gout was 0.55 (95% CI, 0.38–0.78) in participants with favorable lifestyle habits, with unfavorable lifestyle as the reference (**Fig. 3A**). Adherence to lifestyle habits may reduce the risk of gout by 45%. A risk-reduction effect was also observed in the middle- and low-genetic-risk groups by modifying lifestyle habits. These trends were also observed in metabolic health profiles. Using the poor MetS profile as a reference, the OR for gout was 0.48 (95% CI, 0.32–0.74) for individuals with an ideal MetS profile in the high-genetic-risk group (**Fig. 3B**). By shifting MetS from a poor to an ideal status, the risk of gout was reduced by 52% in the high-genetic-risk group, and this effect was observed in the middle- and low-genetic-risk groups.

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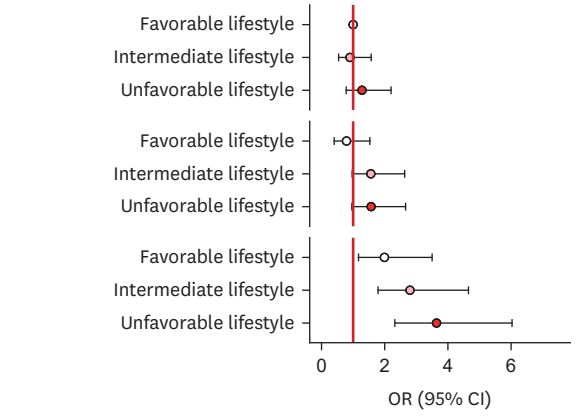
A

Genetic risk for gout	Lifestyle subgroup	No. of event/ Total No.	Absolute risk (%)	OR (95% CI)	*P* value
Low genetic risk	Favorable lifestyle	20/3,641	0.55	Reference	
	Intermediate lifestyle	47/6,643	0.71	0.90 (0.54–1.57)	7.05e–01
	Unfavorable lifestyle	57/4,584	1.24	1.28 (0.78–2.20)	3.48e–01
Middle genetic risk	Favorable lifestyle	16/3,637	0.44	0.79 (0.40–1.53)	4.81e–01
	Intermediate lifestyle	77/6,694	1.15	1.56 (0.97–2.63)	8.05e–02
	Unfavorable lifestyle	69/4,537	1.52	1.57 (0.96–2.66)	8.27e–02
High genetic risk	Favorable lifestyle	40/3,703	1.08	1.99 (1.17–3.50)	1.27e–02
	Intermediate lifestyle	137/6,643	2.06	2.80 (1.79–4.65)	2.12e–05
	Unfavorable lifestyle	154/4,523	3.4	3.64 (2.32–6.03)	1.02e–07



B

Genetic risk for gout	Metabolic syndrome subgroup	No. of event/ Total No.	Absolute risk (%)	OR (95% CI)	*P* value
Low genetic risk	Ideal metabolic syndrome	24/5,640	0.43	Reference	
	Intermediate metabolic syndrome	91/7,797	1.17	2.31 (1.50–3.72)	2.86e–04
	Poor metabolic syndrome	9/1,431	0.63	2.20 (0.96–4.61)	4.60e–02
Middle genetic risk	Ideal metabolic syndrome	35/5,486	0.64	1.51 (0.90–2.57)	1.24e–01
	Intermediate metabolic syndrome	112/7,930	1.41	2.89 (1.89–4.61)	2.89e–06
	Poor metabolic syndrome	33/1,452	2.27	7.33 (4.30–12.60)	3.29e–13
High genetic risk	Ideal metabolic syndrome	80/5,384	1.49	3.77 (2.42–6.09)	1.62e–08
	Intermediate metabolic syndrome	198/7,880	2.51	5.23 (3.49–8.23)	3.07e–14
	Poor metabolic syndrome	35/1,605	2.18	7.78 (4.61–13.40)	3.27e–14

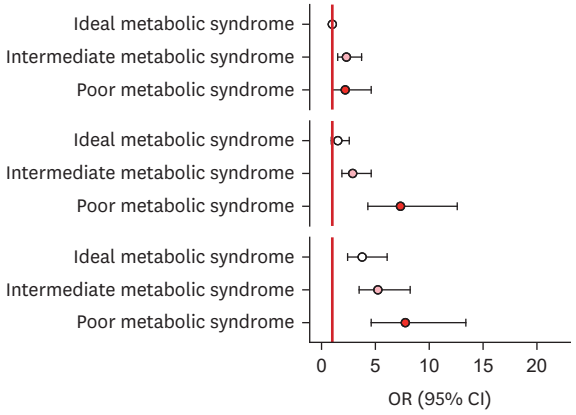


Fig. 2. ORs and 95% CIs for gout based on the interaction between genetic risk and lifestyle habits (**A**) and between genetic risk and metabolic status (**B**).
OR = odds ratio, CI = confidence interval.

DISCUSSION

In this study, we investigated the combined effects of genetic risk, lifestyle, and metabolic health on the risk of gout. The risk of gout was the highest in participants with a high genetic risk, unfavorable lifestyle, or poor MetS status. Several studies have assessed the interaction between the genetic risk of gout and lifestyle habits in the development of gout. A study using the UK Biobank data revealed that the risk of gout increased in participants with middle and high PRS plus unfavorable lifestyle habits than in those with low PRS and a favorable lifestyle.[5] Another study with European and Polynesian cohort data revealed that the gout PRS, calculated using 19 genetic variants, was associated with earlier age at onset and tophaceous gout in men.[17] Traditionally, diet habits are closely associated with the incidence of gout. Sugar-sweetened beverage consumption and *SLC2A9* genotype have been reported to increase the risk of gout in New Zealand and Europe.[18] Based on another study using UK Biobank data, ultra-processed food is related to a higher risk of gout, particularly in participants with high genetic susceptibility.[19]

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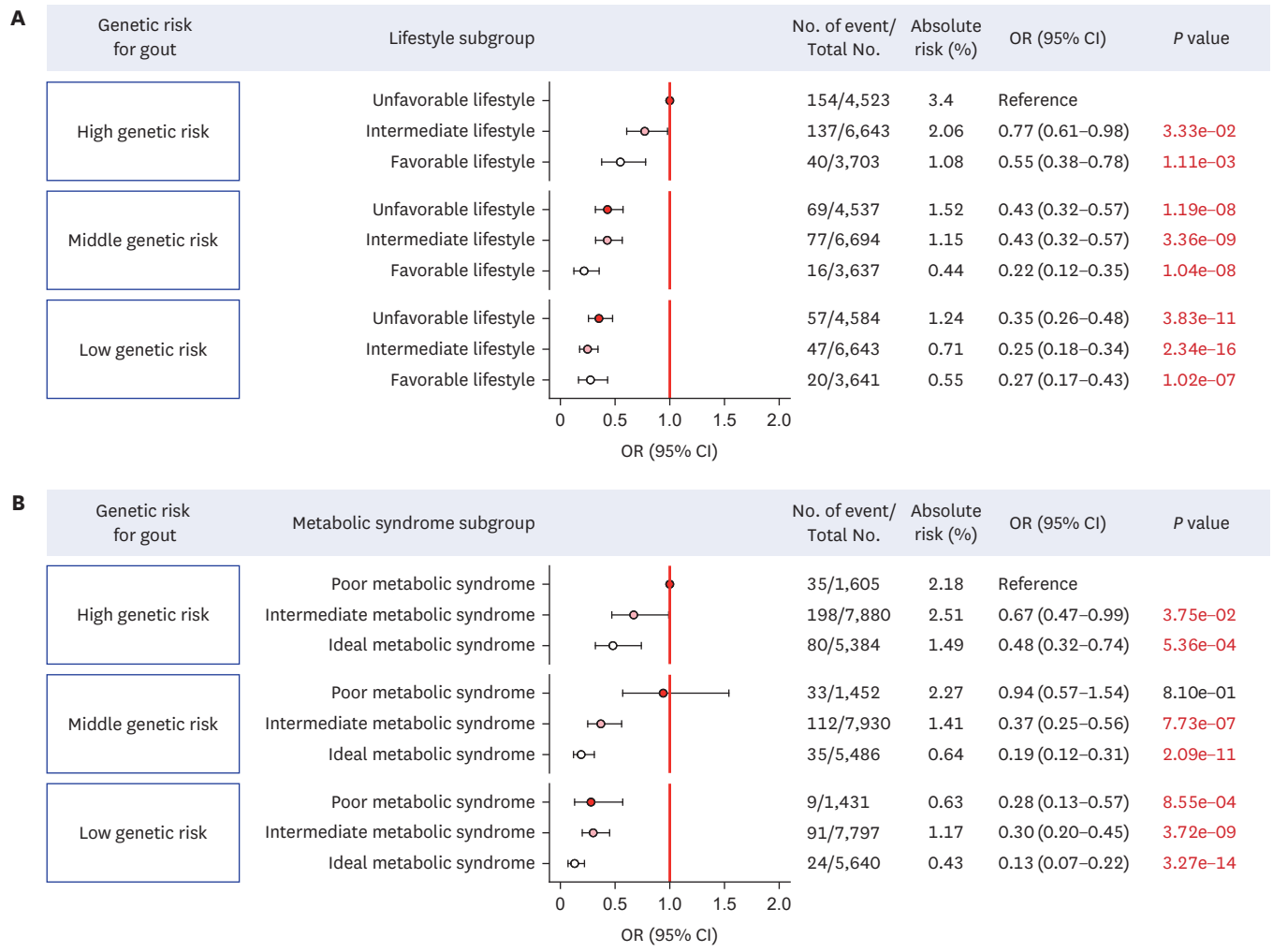

Fig. 3. Forest plot for gout risk reduced by lifestyle habits (**A**) and metabolic health status (**B**) in the genetic risk group.
OR = odds ratio, CI = confidence interval.

Previous studies on the PRS have mainly included Caucasians of European ancestry. Therefore, more studies comprising other ethnic groups should be conducted to improve the predictability and generalizability of the PRS. Recently, PRS studies have been actively conducted not only in Europe but also in Asia. According to a Chinese study, a meat dietary pattern and *ABCG2* phenotype were associated with hyperuricemia in a Chinese cohort.[20] A Taiwanese study reported that genetic score, including the urate transporter gene, and alcohol use could predict gout and tophi occurrence.[21] Korean data were also obtained from the same database KoGES used in this study. Jeon and Yoo[22] reported that genetic factors interact with lifestyle habits in incident gout; however, their analysis differed from that performed in this study in several respects. They calculated the PRS from 15 SNPs in the healthy examinee database; however, in the present study, the PRS was derived from nine independent GWAS databases. In addition, Jeon and Yoo[22] used only a few lifestyle factors (exercise, drinking, and smoking) for their analysis, whereas we used a structured lifestyle scoring system and MetS score. We also showed that the risk of gout could be lowered by adjusting lifestyle habits.

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In the present study, we opted to use the average effect size of each effect allele of the selected SNPs rather than classic meta-analysis methods, such as inverse variance weighting, which comprise studies with a large population. Notably, most studies have predominantly involved European populations. Moreover, comparatively fewer studies, such as those involving the CER cohort, which included Asian populations, were significantly smaller in scale than those comprising European populations.[10] Consequently, based on the sample size of the study, a meta-analysis was deemed inappropriate for calculating PRS in the Korean population. Furthermore, obtaining raw GWAS summary statistics for all PRS studies suitable for meta-analysis using tools, such as METAL, was not feasible.[23] This limitation introduced the potential for bias owing to the selective availability of data from certain studies. Moreover, meta-analyses often require assumptions regarding the use of fixed- or random-effects models, which can complicate the interpretation of results. By employing a more straightforward approach, we discerned universal clinical trends in the joint effects of genetic factors, lifestyle, and MetS on the risk of developing gout, thereby obtaining valuable insights without the complexities associated with the traditional meta-analysis methods.

Unhealthy lifestyle habits appeared to have a poorer effect on gout development in participants with high genetic risk than in those with low genetic risk. Uncontrolled lifestyle habits or poor metabolic profiles did not significantly affect the risk of gout in the low-genetic-risk group; however, an unhealthy lifestyle significantly increased the risk of gout in the middle- or high-genetic-risk groups. Conversely, the effects of reducing gout risk by adhering to a favorable lifestyle or ideal MetS seemed to be greater in the high-genetic-risk group. Lin et al.[24] investigated the interaction between genetic predisposition and adherence to Dietary Approaches to Stop Hypertension diet, a representative healthy diet, on incident female gout using four prospective cohorts. They revealed that the multivariate relative risk for incident gout among women with healthy diet score was 0.67 (95% CI, 0.60–0.76) in the higher PRS group and 0.91 (95% CI, 0.78–1.05) in the lower PRS group compared to that in women with an unhealthy diet score. Zhang et al.[25] evaluated the effect of the interaction between genetics and lifestyle on the development of hyperuricemia using a Chinese cohort comprising 2,796 participants; the median follow-up period was 4.2 years. In the high-genetic-risk group, healthy lifestyle could reduce the incident hyperuricemia by 40%. These findings suggest that adherence to a healthy lifestyle has a greater effect on individuals with high genetic risk than on those with low genetic risk. Additionally, the effects of modifiable factors on incident gout seem to differ according to ethnicity. By evaluating the effect of modifiable factors on incident gout in a multiethnic cohort, Thompson et al.[26] found that alcohol had a greater effect on the occurrence of gout in Japanese individuals than in Caucasians, whereas a healthy diet had the largest effect on the decrease in gout risk in Caucasians than in individuals of other ethnicities.

The present study highlights the significant interaction between genetic predisposition and lifestyle habits in the development of gout. Although genetic factors are unmodifiable, lifestyle habits and metabolic health profiles can be modified. Our findings emphasize the importance of preventive strategies that focus on lifestyle modifications, particularly for individuals at high genetic risk. If individuals with a high genetic risk are identified and their lifestyle habits are modified, we can reduce not only the incidence of gout but also subsequent comorbidities. We believe that this study is valuable as we investigated the interaction between genetic risk and lifestyle habits using Korean genome data and revealed that the risk of gout can be reduced by modifying unhealthy lifestyle habits. However, this study has several limitations. First, we did not analyze new-onset gout alone; therefore, we

could not reveal time-dependent causality. Second, gout was diagnosed based on patient statements, which may have resulted in misclassification bias. Third, we could not provide direct evidence that modifying lifestyle habits lowers the risk of gout. Such evidence can be obtained by observing a well-designed cohort over a long period of time.

In conclusion, genetic predisposition and unhealthy lifestyle habits were associated with an increased risk of gout. Adherence to a healthy lifestyle is important for preventing gout, especially in individuals with high genetic risk.

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SUPPLEMENTARY MATERIALS

Supplementary Table 1

Detailed components on lifestyle score in KoGES

Supplementary Table 2

Detailed components on metabolic health status in KoGES

Supplementary Table 3

Top and bottom 15 variants and their corresponding effect sizes utilized in PRS calculation analyzed for their joint effect with lifestyle factor or MetS status

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