Nutr Res Pract. 2023 Jan;17(1):62-72
https://doi.org/10.4162/nrp.2023.17.1.62
pISSN 1976-1457·eISSN 2005-6168

Nutrition Research and Practice

Original Article

Check for updates

Minor alleles in the *FTO* SNPs contributed to the increased risk of obesity among Korean adults: meta-analysis from nationwide big data-based studies

OPEN ACCESS

Received: Nov 23, 2022
Revised: Dec 18, 2022
Accepted: Dec 21, 2022
Published online: Jan 6, 2023

§Corresponding Author:
Myoungsook Lee
Department of Food & Nutrition, School of Bio-Health Convergence, Health & Wellness College, Sungshin Women's University, 2 Bomun-ro 34da-gil, Seongbuk-gu, Seoul 02844, Korea.
Tel. +82-2-920-7211
Fax. +82-2-920-2076
Email. mlee@sungshin.ac.kr

*Oh Yoen Kim and Jihyun Park contributed equally to this work.

ORCID iDs
Oh Yoen Kim
https://orcid.org/0000-0001-9262-3309
Jihyun Park
https://orcid.org/0000-0003-1038-2586
Jounghee Lee
https://orcid.org/0000-0001-8240-7602
Cheongmin Sohn
https://orcid.org/0000-0003-0529-7037

Oh Yoen Kim [1,2*], Jihyun Park [2*], Jounghee Lee [3], Cheongmin Sohn [4], Mi Ock Yoon [5], and Myoungsook Lee [6§]

[1]Department of Food Science & Nutrition, Dong-A University, Busan 49315, Korea
[2]Department of Health Science, Graduates School of Dong-A University, Busan 49315, Korea
[3]Department of Food and Nutrition, Kunsan National University, Gunsan 54150, Korea
[4]Department of Food and Nutrition, Wonkwang University, Iksan 54538, Korea
[5]Nutrition Information Center, Korean Nutrition Society, Seoul 04376, Korea
[6]Department of Food & Nutrition, School of Bio-Health Convergence, Health & Wellness College, Sungshin Women's University, Seoul 01133, Korea

ABSTRACT

BACKGROUND/OBJECTIVES: Many studies have revealed an association between fat mass and the obesity-related gene (*FTO*) and obesity. On the other hand, no meta-analysis was conducted with data from only Koreans. Therefore, this study performed a meta-analysis using Korean data to provide evidence for the association between *FTO* single nucleotide polymorphisms (SNPs) and the risk of obesity among Korean adults.
SUBJECT/METHODS: Meta-analysis was finally conducted with data extracted from seven datasets of four studies performed on Korean adults after the screening passed. Five kinds of *FTO* SNPs (rs9939609, rs7193144, rs9940128, rs8050136, and rs9926289) were included, and the relationship between *FTO* SNPs and body mass index (BMI) was investigated using linear regression with an additive model adjusted for covariants, such as age, sex, and area.
RESULTS: The minor alleles of *FTO* SNPs were associated with increased BMI (odds ratio [OR], 1.31; 95% confidence interval [CI], 1.21–1.42). In sub-group analysis, *FTO* rs9939609 T>A was significantly associated with BMI (OR, 1.23; 95% CI, 1.06–1.42). The other *FTO* SNPs together were significantly associated with BMI (OR, 1.37; 95% CI, 1.25–1.49). The publication bias was not observed based on Egger's test.
CONCLUSIONS: This meta-analysis showed that minor alleles in the *FTO* SNPs were significantly associated with an increased BMI among Korean adults. This meta-analysis is the first to demonstrate that minor alleles in the *FTO* SNPs contribute significantly to the increased risk of obesity among Korean adults using data from a Korean population.

Keywords: Obesity; genes; polymorphism, single nucleotide; adult; meta-analysis

Mi Ock Yoon
https://orcid.org/0000-0003-1404-9158
Myoungsook Lee
https://orcid.org/0000-0003-1344-6979

Funding

This work was supported by the Korea Institute of Planning and Evaluation for Technology in Food, Agriculture, and Forestry (IPET) through the High Value-added Food Technology Development Program, funded by the Ministry of Agriculture, Food and Rural Affairs (MAFRA) (321029-05).

Conflict of Interest

The authors declare no potential conflicts of interests.

Author Contributions

Conceptualization: Lee M; Data curation: Kim OY, Park J, Lee J, Sohn C, Yoon MO; Formal analysis: Kim OY, Park J; Investigation: Lee J, Sohn C, Yoon MO, Lee M; Writing - original draft: Kim OY, Park J; Writing - review & editing: Lee M.

INTRODUCTION

The prevalence of obesity has been increasing gradually worldwide over the past few decades [1]. Obesity has also been increasing in Korea for more than ten years, and 38.8% of Koreans were reported to be obese in 2020 [2,3]. Obesity is a public health problem as the main cause of developing non-communicable diseases, such as metabolic syndrome, type 2 diabetes mellitus (T2DM), hypertension, dyslipidemia, and cardiovascular disease (CVD) [1,4,5]. Hence, many endeavors have been made to prevent and manage obesity, e.g., by modifying energy intake, physical activity, eating habits, and lifestyle and suggesting optimal nutrition therapy according to genetic properties [6-9].

In 2007, a genome-wide association study identified a single nucleotide polymorphism (SNP) at the intron 1 of the fat mass and obesity-related gene (*FTO*) located on chromosome 16q12.2 as the first obesity-susceptibility locus [10,11]. *FTO* is associated with the body composition, such as body mass index (BMI), body weight, waist circumference, hip circumference, subcutaneous mass, and energy intake [10-12]. In particular, individuals carrying the minor A allele homozygotes in the *FTO* SNP rs9939609 had a relatively high risk of being overweight and obese compared to those carrying the major T allele homozygotes [10]. Since then, many studies have reported that genetic variants at several SNPs in the *FTO* were linked to an obesity-related trait in diverse ethnicities [13-18]. Meta-analyses were also conducted to elucidate the relationship between *FTO* and obesity [19-21].

A replication study from Korean cohorts also reported that the *FTO* was significantly related to an increased BMI [22]. Currently, the *FTO* is being provided as an obesity-related gene by the direct-to-customer (DTC) gene test, which was approved by the Ministry of Health and Health and Welfare in Korea in June 2016 (notice No. 2016-97) [23]. On the other hand, no meta-analysis has been conducted using data from only Koreans that can provide conclusive evidence for the association between *FTO* and obesity. Therefore, this study performed a meta-analysis using the data from Koreans to provide evidence for the association between *FTO* SNPs and the risk of obesity among Korean adults.

SUBJECTS AND METHODS

Search strategy and inclusion criteria

Comprehensive literature research was conducted in a database (DB) to identify the studies investigating the association between *FTO* SNPs and obesity risk in Koreans (up to September 22, 2022). The database consisted of PubMed, Web of Science, and Korean databases, such as Research Information Sharing Service (RISS) and KoreaMed. The following keywords were used for the search: "*FTO*", "Obesity", "fat mass", "waist", "BMI", "body weight," and "Korean". "Asian" along with "*FTO*" and "obesity" was also searched in PubMed and Web of Science to prevent the omission of the Korean data. A similar search was performed using the Korean language terms in the Korean database (RISS and KoreaMed). The studies included in the meta-analysis should satisfy the following inclusion criteria: 1) The contents can evaluate the association between *FTO* SNPs and obesity-related parameters; 2) Subjects should be Korean adults; and 3) Full-text articles are available in English or Korean. Two researchers, Kim & Park, determined the quality of each article and the consensus reached on the scores calculated by the risk of bias (RoB) through discussion. A third reviewer (Lee M) resolved the disagreement about the ROB. **Fig. 1** presents the flow diagram for the search strategy of the

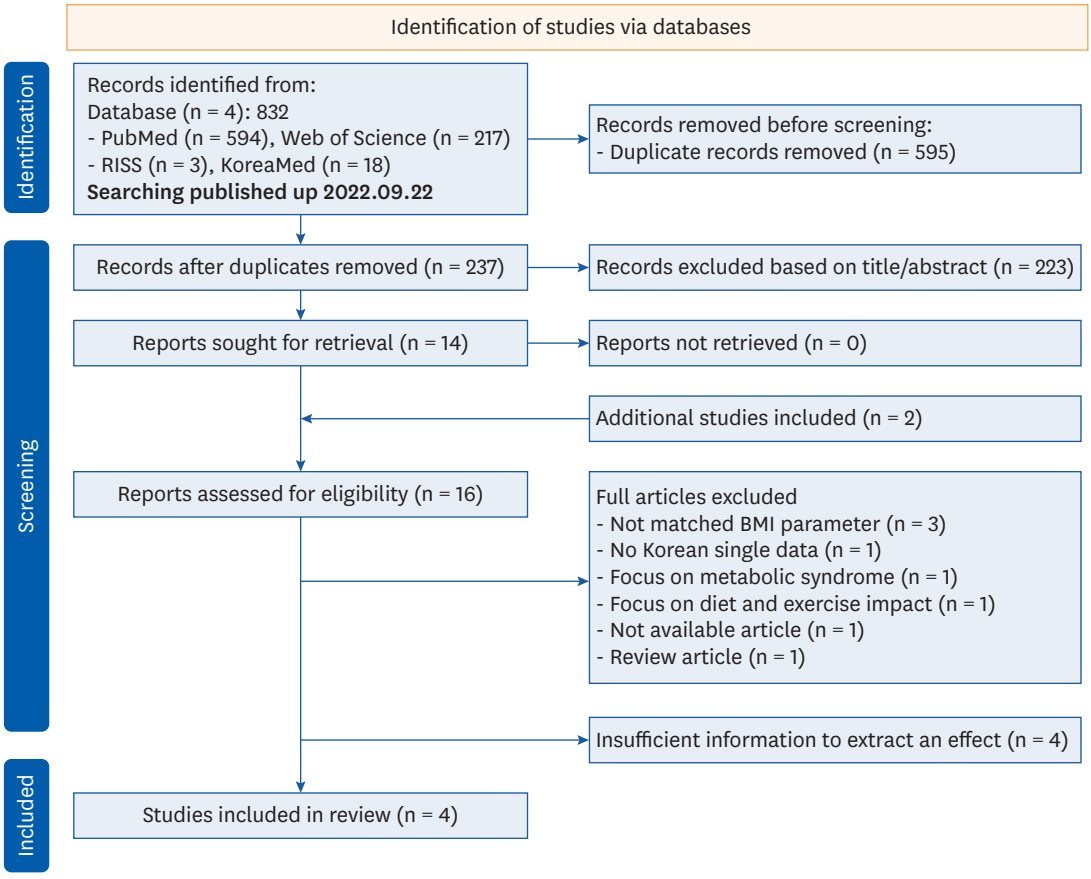

Fig. 1. PRISMA flow diagram of studies in the meta-analysis.
PRISMA, Preferred Reporting Items for Systematic review and Meta-Analysis; RISS, Research Information Sharing Service; BMI, body mass index.

literature in the meta-analysis. The analysis was conducted based on the Preferred Reporting Items for Systematic review and Meta-Analysis (PRISMA) protocol 2020 [24].

Data extraction

Data extraction was conducted preliminarily by one researcher. The following information was extracted: 1) first study author; 2) publication year; 3) cohort information in the study; 4) study design and sample size; 5) *FTO* SNPs with the rs number and minor allele frequency (MAF); 6) subject and sex distribution; 7) age (yrs) and BMI (kg/m^2); 8) BMI as an obesity parameter being indicated to the effect size under an additive model; and 9) adjustment for covariants. The BMI was used as a parameter of obesity in the analysis because there is a lack of evidence of Korean using other obesity indicators. The other researcher confirmed the extracted data. The information that needed to be confirmed while extracting the data was discussed by the 2 researchers.

RoB assessment

The RoB was assessed by Strengthening the Reporting of Observational Studies in the Epidemiology (STROBE) checklist [25]. The checklist was used for cross-sectional studies in the STROBE tool. This tool consisted of 22 items, based on "title and abstract", "introduction", "method", "results", "discussion", and "other information". Overall, RoB in each article was calculated based on the STROBE checklist criteria. The reporting bias was assessed by judging the consistency between results in the method section of the publication and the protocol.

https://doi.org/10.4162/nrp.2023.17.1.62

Statistical analysis

In all studies, the association between *FTO* SNPs and BMI was estimated by β ± SE under an additive model adjusted for the covariant. Therefore, the odds ratio (OR) and 95% confidence intervals (CIs) were conducted by generic inverse variance methods. The heterogeneity among the studies was investigated using an I^2 test. A random effects model was used because the value was more than 50%, and the number of studies included in the analysis was small. Sub-analyses were conducted according to the following SNPs: the *FTO* rs9939609 T>A and the other SNPs, respectively. The funnel plot of publication bias was assessed using an Egger's test. The overall effect and subgroup analysis between the *FTO* SNPs and BMI increment under an additive model was indicated through a forest plot. Data analysis was performed using R software version 4.2.0 (R Foundation for Statistical Computing, Vienna, Austria). The RoB assessment was performed using Review Manager 5.4 with the STROBE checklist (The Nordic Cochrane Centre, Copenhagen, Denmark).

RESULTS

Results of the literature search

Based on the search strategy, 832 articles were identified in the four databases (594 from PubMed, 217 from Web of Science, three from RISS, and 18 from KoreaMed with duplicates of 595 articles). After removing duplicates, 237 articles were screened based on the title and abstract. Fourteen articles that passed the screening were included for screening the full-text article together with an additional two articles that were cited as references. Among the 16 articles, eight articles were excluded for the following reasons: unmatched BMI parameters (unavailable for the relationship between the *FTO* SNPs and obesity-related parameters to be expressed as OR or β effect size) (n = 3), no single data from Koreans with obesity-related parameters (n = 1), data focusing on metabolic syndrome (n = 1) or the effect of diet and exercise (n = 1), full-text unavailable (n = 1), and review article (n = 1). Among the eight articles corresponding to the inclusion criteria, four were also excluded because they had not satisfied the criteria for calculating the effect size for meta-analysis. Finally, the remaining four articles were eligible and included in the meta-analysis (**Fig. 1**).

Characteristics of included studies

Table 1 lists the characteristics of the data among the four articles. All the studies were population-based cross-sectional studies performed on Koreans. As the Korea Association REsource (KARE) cohort was used in all four studies, the most recent data were only included in the analysis if the same cohort and *FTO* SNPs were included. On the other hand, the cases examined by different SNPs in the *FTO,* even from the same cohort, were included in the analysis. The cohort data included in the analysis are marked in bold in **Table 1**. Therefore, a meta-analysis was performed by extracting seven data from four articles. The sample size ranged from 2,281 to 8,840, and the age ranged from 30 to 69 showing similar patterns among the studies. In addition, the average BMI was 23.4–24.7 kg/m^2. Five kinds of *FTO* SNPs (rs9939609 T>A, rs7193144 T>C, rs9940128 G>A, rs8050136 C>A, and rs9926289 G>A) were invested among the four studies. Except for *FTO* SNPs, rs7193144 T>C and rs9940128 G>A, the MAF of rs9939609 T>A, rs8050136 C>A, and rs9926289 G>A for Korean were 12.5–18% with similarity. All studies indicated the relationship between the *FTO* SNPs and BMI by effect size (β) ± SE. The *P*-values were also calculated by linear regression under an additive model adjusted for covariants, such as age, sex, and area. **Fig. 2** gives a summary of the RoB assessment (STROBE). All 4 articles categorized as "low" risk of bias were finally included in the meta-analysis.

https://doi.org/10.4162/nrp.2023.17.1.62

Table 1. Characteristics of the studies included in the meta-analysis

Study (Author)	Year	Cohort*	Study design	Sample size	*FTO* SNP	MAF	Age (yrs) Mean ± SD (range)	Sex (M/F)	BMI (kg/m²) Mean ± SD	Effect size (β)	SE	*P*-value†	Adjustment
Cho *et al.*	2009	KARE, **Health2**	Population-based	7,861	rs9939609 T>A	0.18 (Total)	56.58 ± 7.85 (40–69 yrs)	3,214/4,647	24.49±3.18	0.123	0.054	2.2E−02	Age, sex, area
Cho *et al.*	2020	KARE	Population-based	8,840	rs9939609 T>A	0.1262 (Total)	52.22 ± 8.91 (40–69 yrs)	4,182/4,658	24.58±3.13	0.334	0.07	$1.76^{*}10^{-6}$	Age, sex, area
				8,840	rs7193144 T>C	NA	52.22 ± 8.91 (40–69 yrs)	4,182/4,658	24.58±3.13	0.328	0.07	$2.80^{*}10^{-6}$	Age, sex, area
				8,840	rs9940128 G>A	NA	52.22 ± 8.91 (40–69 yrs)	4,182/4,658	24.58±3.13	0.205	0.063	$1.12^{*}10^{-3}$	Age, sex, area
Lee *et al.*	2011	**KARE**, Health2	Population-based	6,742	rs8050136 C>A	0.125 (Total)	48.3 ± 6.06 (40–60 yrs)	3,275/3,467	24.7±3.07	0.379	0.078	1.37E-06	Age, sex, area
				6,742	rs9926289 G>A‡	0.126 (Total)	48.3 ± 6.06 (40–60 yrs)	3,275/3,467	24.7±3.07	0.373	0.079	2.07E-06	Age, sex, area
Sull *et al.*	2013	**Bundang-gu**, KARE	Population-based & Meta-analysis	2,281	rs9939609 T>A	0.127 (Total)	42.9 ± 7.8 (30–59 yrs)	1,256/1,025	23.4±3.0	0.15	0.12	0.223	Age, sex

FTO, fat mass and obesity-related gene; SNP, single nucleotide polymorphism; MAF, minor allele frequency; BMI, body mass index; NA, no available.
*Studies included in the current meta-analysis are shown in bold. †Main results under an additive model. ‡Original article, *FTO* polymorphism data was rs9926289 C>T.

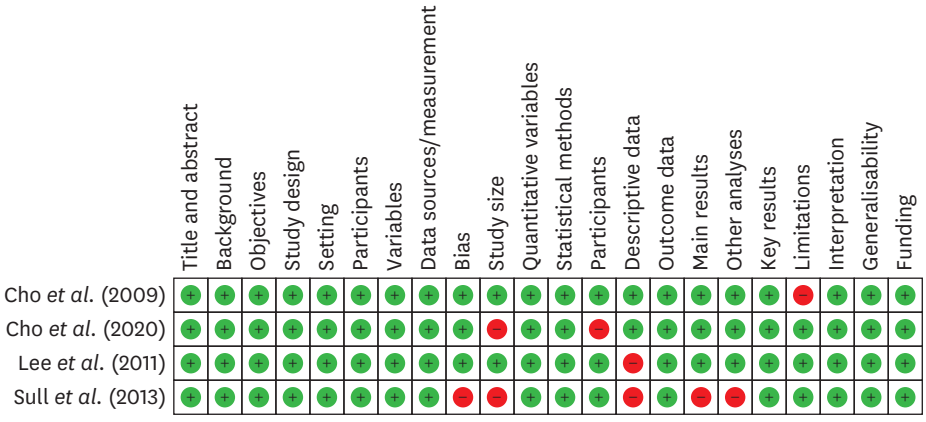

Fig. 2. Summary for the risk of bias assessment (STROBE).
STROBE, Strengthening the Reporting of Observational Studies in Epidemiology.

Outcomes of meta-analysis

Fig. 3 shows the Forest plot for the overall effect of *FTO* SNPs on BMI. From the seven datasets, the minor alleles of *FTO* SNPs were significantly associated with the increased BMI under an additive model adjusted for covariants (OR, 1.31; 95% CIs, 1.21–1.42). Moderate-substantial heterogeneity was noted (I^2 = 59%; *P* = 0.02). Publication bias was evaluated using funnel plots (**Fig. 4**). Dissymmetry was not observed in the funnel plot according to the Egger's test (*P* = 0.4019). That is, there was no publication bias in this meta-analysis that examined the effects of minor alleles in *FTO* SNPs on the risk of obesity.

In addition, sub-group analysis was performed according to *FTO* SNPs (rs9939609) and the other SNPs. **Fig. 5** presents a forest plot by sub-group analysis. Precisely, *FTO* rs9939609 T>A was analyzed in the data from the three articles and found to be significantly associated with the BMI under an additive model adjusted for covariant (OR, 1.23; 95% CI, 1.06–1.42). The other *FTO* SNPs were also analyzed in the data from the two articles and showed a significant association with the BMI under an additive model adjusted for covariant (OR, 1.37; 95% CI, 1.25–1.49). On the other hand, the heterogeneity for the sub-analysis was different between the FTO rs9939609 T>A group (I^2 = 66%; *P* = 0.05) and the other *FTO* SNPs group (I^2 = 30%; *P* = 0.23).

https://doi.org/10.4162/nrp.2023.17.1.62

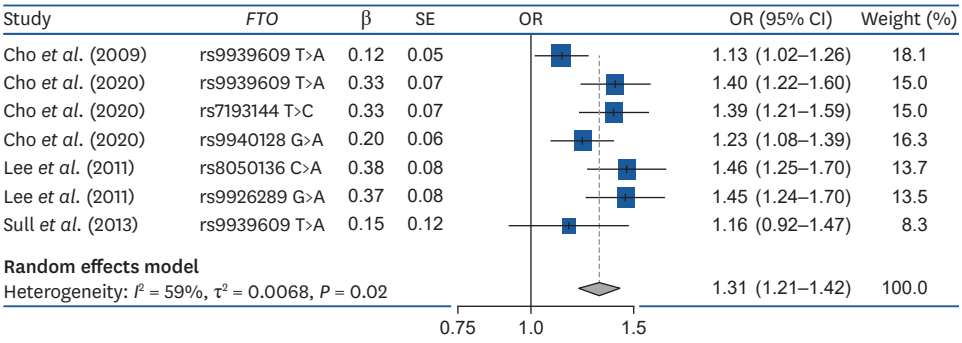

Fig. 3. Association between *FTO* polymorphism and BMI under an additive genetic model adjusted for covariant. Effect size combined using the random-effects meta-analysis. Meta-analysis using generic inverse variance methods. *FTO*, fat mass and obesity-related gene; BMI, body mass index; OR, odds ratio; CI, confidence interval.

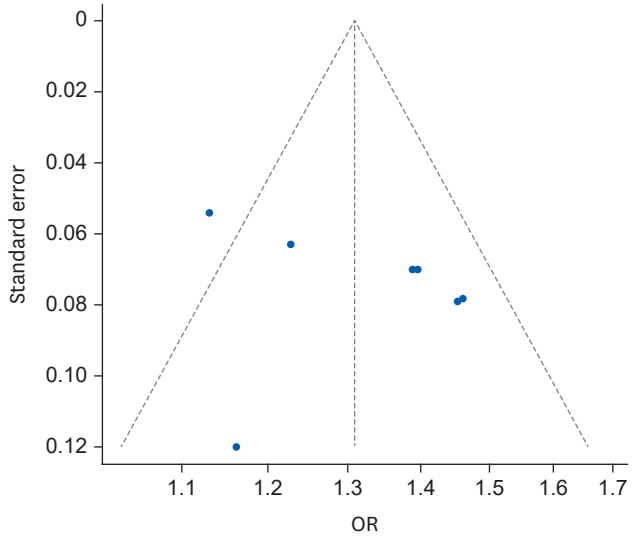

Fig. 4. Egger's funnel plot for publication bias in an additive model.
OR, odds ratio.

DISCUSSION

This report is the first meta-analysis to show that minor alleles in the *FTO* SNPs contribute significantly to the increased risk of obesity among Korean adults using data from only the Korean population. Minor alleles in the 5 SNPs at *FTO* (rs9939609 T>A, rs7193144 T>C, rs9940128 G>A, rs8050136 C>A, and rs9926289 G>A) were associated with the increased BMI among Korean adults.

The association between the *FTO* SNPs and increased BMI observed in this study was similar to those observed in the diverse East Asian population [16,17,26-28]. An obesity case-control study performed in the Chinese population showed that the *FTO* SNP was related to the risk of obesity [17,26,27]. The A allele at the rs9939609 in the *FTO* was significantly associated with obesity compared to the major T allele (OR, 1.447; 95% CI, 1.104–1.896) [26]. The A allele at the *FTO* SNP rs9939609 was also associated with increased BMI (P = 0.0024) and obesity (OR, 1.43; 95% CI, 1.16–1.75) [17]. Furthermore, a meta-analysis of the Chinese population showed that minor alleles at the *FTO* SNPs, including rs9939609, rs6499640, rs8050136, and rs1558902 were related to the risk of obesity in children, adolescents, and adults. In

https://doi.org/10.4162/nrp.2023.17.1.62

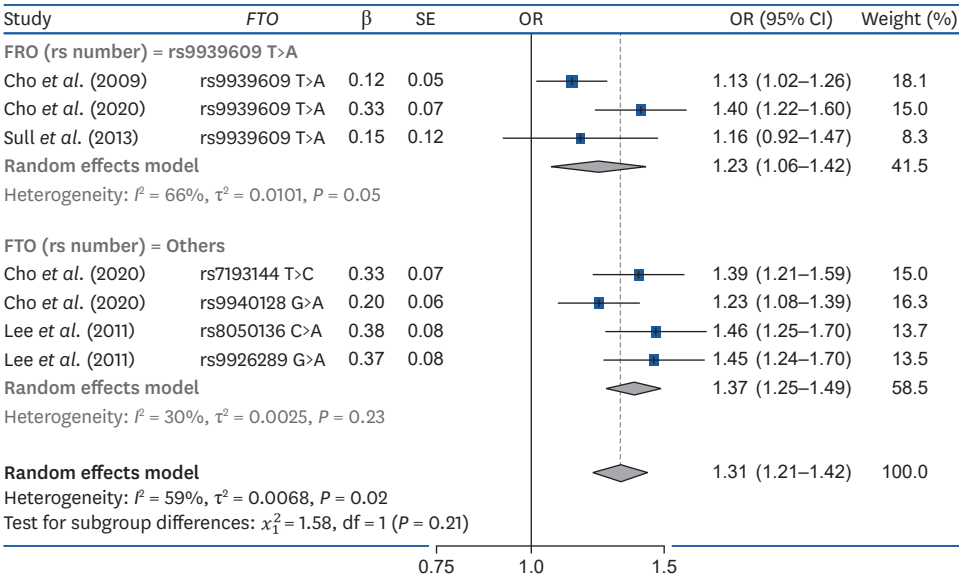

Fig. 5. Sub-group analysis of the association between *FTO* polymorphism (rs number) and BMI under an additive model adjusted for covariant. Effect size combined using random-effects meta-analysis. Meta-analysis using generic inverse variance methods.
FTO, fat mass and obesity-related gene; BMI, body mass index; OR, odds ratio; CI, confidence interval.

particular, the association between *FTO* SNPs (rs9939609 or its proxy) and obesity risk under an additive model observed in the Chinese population (OR, 1.20; 95% CI, 1.03–1.40) was similar to the results in the present study [27]. Japanese population studies also showed a significant association between *FTO* SNP and obesity [16,28]. The case-control association study showed that the AA genotype in the *FTO* SNP rs9939609 was significantly associated with obesity (OR, 1.53; 95% CI, 1.04–2.24) [16]. Similarly, another *FTO* SNP rs11558902 was significantly related to obesity under an additive model adjusted for age and gender (OR, 1.41; 95% CI, 1.22–1.62) [28].

The size of the MAFs in *FTO* SNPs supposed to be contributing to the increased BMI was reported to be much higher in Europeans (up to 42%) than in East Asia (12–20%) [29]. In this study, MAFs of rs9939609 T>A, rs8050136 C>A, and rs9926289 G>A for Korean were 12.5–18%, which were similar to the others. East Asians had a lower MAF of BMI-associated alleles at the SNPs in the *FTO* than Europeans but showed a similar pattern on the risk of obesity (OR per allele) shown in both ethnics (European, 1.20; East Asian, 1.27) [29]. This result may be related to the difference in the BMI cut-off point defining obesity between Western and Asian populations [30,31]. WHO defined BMI ≥ 30 kg/m^2 as obesity and 25 kg/m^2 ≤ BMI < 30 kg/m^2 as overweight [30]. On the other hand, East Asians, including Koreans, used the Asia-Pacific criteria of the WHO guideline defining obesity as BMI ≥ 25 kg/m^2 [30]. The difference in criteria for obesity is supported by the evidence that compared with the Western and Asian populations are more likely to be exposed to the risk of comorbidities, such as CVD and T2DM, even though they are below 25 kg/m^2 of BMI, which may be related to the differences in the endocrine metabolism between populations [31]. According to the pattern analysis of linkage disequilibrium (LD) from HapMap DB, *FTO* SNPs rs9939609 and rs8050136 were strongly associated with Caucasian, Asian (Chinese and Japanese), and South American, but *FTO* SNPs rs8050136 did not affect the risk of obesity in Asian [32]. These results might be due to the differences in LD patterns or MAF across different ethnic populations. Therefore, further studies will be needed to suggest the appropriate evidence

https://doi.org/10.4162/nrp.2023.17.1.62

for the association between *FTO* SNPs and obesity risk according to racial characteristics. In this aspect, this meta-analysis study provides additional evidence to identify the effect of *FTO* SNPs on the risk of obesity among Koreans.

Several studies performed in the Western population reported that *FTO* SNPs and environmental parameters might affect the BMI changes interactively [33-38]. For example, the minor allele effect of the *FTO* SNPs on the increased BMI was highly observed in the subjects consuming the high-fat diet or those with low physical activity [33,34]. In addition, increased physical activity weakened the effects of *FTO* SNPs on obesity by reducing the genetic susceptibility [37,38]. On the other hand, some studies did not find an interaction effect of *FTO* SNPs and physical activity on obesity [39,40]. This result may be due to the differences in physical activity intensity, participant characteristics, study design, and study period. *FTO* SNPs were also reported to affect the metabolic status, such as insulin metabolism and circulating high-density lipoprotein cholesterol levels, and are involved in diminished satiety and its genetic susceptibility to obesity by macronutrient composition in the diet consumed [41-46]. On the other hand, environmental parameters, such as physical activity and dietary nutrient composition, could not be considered in the meta-analysis because the number of publications on the association between *FTO* SNPs and obesity among Korean adults was very small and did not have sufficient information on the environmental parameters mentioned above. Therefore, further studies investigating the interaction between *FTO* SNPs and environmental parameters affecting obesity and the related metabolic status among Koreans are needed.

This meta-analysis study had several limitations. First, the association between the *FTO* SNPs and obesity-related traits was confirmed in Koreans. On the other hand, it was difficult to compare them due to the small number of papers and the differences in the study characteristics. Second, most studies used the big data of the KARE cohort. Therefore, extracted data overlapped among studies. Moreover, the causality between *FTO* SNPs and obesity risk could not be suggested because of all studies with cross-sectional design. Hence, many kinds of gene-based research must be performed by the life cycle (adults, children, elderly, and patients). Third, this meta-analysis could not analyze a single *FTO* SNP due to the limited literature. *FTO* SNP rs9939609 focused on obesity risk due to much evidence without racial differences because LD pattern analysis of five *FTO* SNPs on Korean was unavailable.

Despite some limitations, this study is the first meta-analysis study identifying that minor alleles in the *FTO* SNPs are associated with the increased risk of obesity among Korean adults using the data from only a Korean population. These results provide evidence that *FTO* is suitable for the DTC genetic test predicting the risk of obesity in Koreans. The prospective or retrospective studies examining whether the prevalence of obesity or BMI increase for a certain period (i.e., for 10 years) is associated with *FTO* SNPs should be performed to elucidate the relationship.

REFERENCES

1. Misra A, Khurana L. Obesity-related non-communicable diseases: South Asians vs White Caucasians. Int J Obes 2011;35:167-87.
PUBMED | CROSSREF
2. Korean National Health and Nutrition Survey. National health and nutrition survey 8th 2nd year (2020). Prevalence of chronic disease [Internet]. Cheongju: Korea Disease Control and Prevention Agency; 2022 [cited 2022 September 29]. Available from: https://knhanes.kdca.go.kr/knhanes/sub01/sub01_05.do#s50201.

3. Yang YS, Han BD, Han K, Jung JH, Son JW; Taskforce Team of the Obesity Fact Sheet of the Korean Society for the Study of Obesity. Obesity fact sheet in Korea, 2021: Trends in obesity prevalence and obesity-related comorbidity incidence stratified by age from 2009 to 2019. J Obes Metab Syndr 2022;31:169-77.
PUBMED | CROSSREF
4. Lazarus JV, Mark HE, Anstee QM, Arab JP, Batterham RL, Castera L, Cortez-Pinto H, Crespo J, Cusi K, Dirac MA, et al. Advancing the global public health agenda for NAFLD: a consensus statement. Nat Rev Gastroenterol Hepatol 2022;19:60-78.
PUBMED | CROSSREF
5. Laddu D, Dow C, Hingle M, Thomson C, Going S. A review of evidence-based strategies to treat obesity in adults. Nutr Clin Pract 2011;26:512-25.
PUBMED | CROSSREF
6. An J, Yoon SR, Lee JH, Kim H, Kim OY. Importance of adherence to personalized diet intervention in obesity related metabolic improvement in overweight and obese Korean adults. Clin Nutr Res 2019;8:171-83.
PUBMED | CROSSREF
7. Kim H, Yoon E, Kim OY, Kim EM. Short-term effects of eating behavior modification on metabolic syndrome-related risks in overweight and obese Korean adults. J Obes Metab Syndr 2022;31:70-80.
PUBMED | CROSSREF
8. Kim OY, Chung JY, Song J. Effect of resveratrol on adipokines and myokines involved in fat browning: perspectives in healthy weight against obesity. Pharmacol Res 2019;148:104411.
PUBMED | CROSSREF
9. Shin MJ, Jang Y, Koh SJ, Chae JS, Kim OY, Lee JE, Ordovas JM, Lee JH. The association of SNP276G>T at adiponectin gene with circulating adiponectin and insulin resistance in response to mild weight loss. Int J Obes 2006;30:1702-8.
PUBMED | CROSSREF
10. Frayling TM, Timpson NJ, Weedon MN, Zeggini E, Freathy RM, Lindgren CM, Perry JR, Elliott KS, Lango H, Rayner NW, et al. A common variant in the *FTO* gene is associated with body mass index and predisposes to childhood and adult obesity. Science 2007;316:889-94.
PUBMED | CROSSREF
11. Scuteri A, Sanna S, Chen WM, Uda M, Albai G, Strait J, Najjar S, Nagaraja R, Orrú M, Usala G, et al. Genome-wide association scan shows genetic variants in the *FTO* gene are associated with obesity-related traits. PLoS Genet 2007;3:e115.
PUBMED | CROSSREF
12. Dina C, Meyre D, Gallina S, Durand E, Körner A, Jacobson P, Carlsson LM, Kiess W, Vatin V, Lecoeur C, et al. Variation in *FTO* contributes to childhood obesity and severe adult obesity. Nat Genet 2007;39:724-6.
PUBMED | CROSSREF
13. Prakash J, Mittal B, Srivastava A, Awasthi S, Srivastava N. Association of *FTO* rs9939609 SNP with obesity and obesity- associated phenotypes in a north Indian population. Oman Med J 2016;31:99-106.
PUBMED | CROSSREF
14. Ağagündüz D, Gezmen-Karadağ M. Association of *FTO* common variant (rs9939609) with body fat in Turkish individuals. Lipids Health Dis 2019;18:212.
PUBMED | CROSSREF
15. Mehrdad M, Fardaei M, Fararouei M, Eftekhari MH. The association between *FTO* rs9939609 gene polymorphism and anthropometric indices in adults. J Physiol Anthropol 2020;39:14.
PUBMED | CROSSREF
16. Karasawa S, Daimon M, Sasaki S, Toriyama S, Oizumi T, Susa S, Kameda W, Wada K, Muramatsu M, Fukao A, et al. Association of the common fat mass and obesity associated (*FTO*) gene polymorphism with obesity in a Japanese population. Endocr J 2010;57:293-301.
PUBMED | CROSSREF
17. Chang YC, Liu PH, Lee WJ, Chang TJ, Jiang YD, Li HY, Kuo SS, Lee KC, Chuang LM. Common variation in the fat mass and obesity-associated (*FTO*) gene confers risk of obesity and modulates BMI in the Chinese population. Diabetes 2008;57:2245-52.
PUBMED | CROSSREF
18. Bressler J, Kao WH, Pankow JS, Boerwinkle E. Risk of type 2 diabetes and obesity is differentially associated with variation in *FTO* in whites and African-Americans in the ARIC study. PLoS One 2010;5:e10521.
PUBMED | CROSSREF
19. Vasan SK, Karpe F, Gu HF, Brismar K, Fall CH, Ingelsson E, Fall T. *FTO* genetic variants and risk of obesity and type 2 diabetes: a meta-analysis of 28,394 Indians. Obesity (Silver Spring) 2014;22:964-70.
PUBMED | CROSSREF

20. Li H, Kilpeläinen TO, Liu C, Zhu J, Liu Y, Hu C, Yang Z, Zhang W, Bao W, Cha S, et al. Association of genetic variation in *FTO* with risk of obesity and type 2 diabetes with data from 96,551 East and South Asians. Diabetologia 2012;55:981-95.
PUBMED | CROSSREF
21. Liu C, Mou S, Cai Y. *FTO* gene variant and risk of overweight and obesity among children and adolescents: a systematic review and meta-analysis. PLoS One 2013;8:e82133.
PUBMED | CROSSREF
22. Cha SW, Choi SM, Kim KS, Park BL, Kim JR, Kim JY, Shin HD. Replication of genetic effects of *FTO* polymorphisms on BMI in a Korean population. Obesity (Silver Spring) 2008;16:2187-9.
PUBMED | CROSSREF
23. Ministry of Health and Welfare. Partial revision of regulations on genetic testing items that can be directly conducted by genetic testing institutions other than medical institutions [Internet]. Sejong: Ministry of Health and Welfare; 2020 [cited 2022 October 26]. Available from: https://www.mohw.go.kr/react/jb/sjb0406vw.jsp.
24. Page MJ, McKenzie JE, Bossuyt PM, Boutron I, Hoffmann TC, Mulrow CD, Shamseer L, Tetzlaff JM, Akl EA, Brennan SE, et al. The PRISMA 2020 statement: an updated guideline for reporting systematic reviews. BMJ 2021;372:n71.
PUBMED | CROSSREF
25. von Elm E, Altman DG, Egger M, Pocock SJ, Gøtzsche PC, Vandenbroucke JP; STROBE Initiative. The Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) statement: guidelines for reporting observational studies. Ann Intern Med 2007;147:573-7.
PUBMED | CROSSREF
26. Li X, Song F, Jiang H, Zhang M, Lin J, Bao W, Yao P, Yang X, Hao L, Liu L. A genetic variation in the fat mass- and obesity-associated gene is associated with obesity and newly diagnosed type 2 diabetes in a Chinese population. Diabetes Metab Res Rev 2010;26:128-32.
PUBMED | CROSSREF
27. Zhao NN, Dong GP, Wu W, Wang JL, Ullah R, Fu JF. *FTO* gene polymorphisms and obesity risk in Chinese population: a meta-analysis. World J Pediatr 2019;15:382-9.
PUBMED | CROSSREF
28. Hotta K, Nakata Y, Matsuo T, Kamohara S, Kotani K, Komatsu R, Itoh N, Mineo I, Wada J, Masuzaki H, et al. Variations in the *FTO* gene are associated with severe obesity in the Japanese. J Hum Genet 2008;53:546-53.
PUBMED | CROSSREF
29. Loos RJ, Yeo GS. The bigger picture of *FTO*: the first GWAS-identified obesity gene. Nat Rev Endocrinol 2014;10:51-61.
PUBMED | CROSSREF
30. World Health Organization. Fact sheets of obesity and overweight [Internet]. Geneva: World Health Organization; 2021 [cited 2022 October 26]. Available from: https://www.who.int/news-room/fact-sheets/detail/obesity-and-overweight.
31. Expert Consultation WH; WHO Expert Consultation. Appropriate body-mass index for Asian populations and its implications for policy and intervention strategies. Lancet 2004;363:157-63.
PUBMED | CROSSREF
32. Peng S, Zhu Y, Xu F, Ren X, Li X, Lai M. *FTO* gene polymorphisms and obesity risk: a meta-analysis. BMC Med 2011;9:71.
PUBMED | CROSSREF
33. Sonestedt E, Roos C, Gullberg B, Ericson U, Wirfält E, Orho-Melander M. Fat and carbohydrate intake modify the association between genetic variation in the *FTO* genotype and obesity. Am J Clin Nutr 2009;90:1418-25.
PUBMED | CROSSREF
34. Rampersaud E, Mitchell BD, Pollin TI, Fu M, Shen H, O'Connell JR, Ducharme JL, Hines S, Sack P, Naglieri R, et al. Physical activity and the association of common *FTO* gene variants with body mass index and obesity. Arch Intern Med 2008;168:1791-7.
PUBMED | CROSSREF
35. Leońska-Duniec A, Jastrzębski Z, Zarębska A, Maciejewska A, Ficek K, Cięszczyk P. Assessing effect of interaction between the *FTO* A/T polymorphism (rs9939609) and physical activity on obesity-related traits. J Sport Health Sci 2018;7:459-64.
PUBMED | CROSSREF
36. Liaw YC, Liaw YP, Lan TH. Physical activity might reduce the adverse impacts of the *FTO* gene variant rs3751812 on the body mass index of adults in Taiwan. Genes (Basel) 2019;10:354.
PUBMED | CROSSREF

37. Vimaleswaran KS, Li S, Zhao JH, Luan J, Bingham SA, Khaw KT, Ekelund U, Wareham NJ, Loos RJ. Physical activity attenuates the body mass index-increasing influence of genetic variation in the *FTO* gene. Am J Clin Nutr 2009;90:425-8.
PUBMED | CROSSREF

38. Andreasen CH, Stender-Petersen KL, Mogensen MS, Torekov SS, Wegner L, Andersen G, Nielsen AL, Albrechtsen A, Borch-Johnsen K, Rasmussen SS, et al. Low physical activity accentuates the effect of the *FTO* rs9939609 polymorphism on body fat accumulation. Diabetes 2008;57:95-101.
PUBMED | CROSSREF

39. Cho YS, Go MJ, Kim YJ, Heo JY, Oh JH, Ban HJ, Yoon D, Lee MH, Kim DJ, Park M, et al. A large-scale genome-wide association study of Asian populations uncovers genetic factors influencing eight quantitative traits. Nat Genet 2009;41:527-34.
PUBMED | CROSSREF

40. Huang W, Sun Y, Sun J. Combined effects of *FTO* rs9939609 and MC4R rs17782313 on obesity and BMI in Chinese Han populations. Endocrine 2011;39:69-74.
PUBMED | CROSSREF

41. Kim YJ, Lee HS, Kim YK, Park S, Kim JM, Yun JH, Yu HY, Kim BJ. Association of metabolites with obesity and type 2 diabetes based on *FTO* genotype. PLoS One 2016;11:e0156612.
PUBMED | CROSSREF

42. den Hoed M, Westerterp-Plantenga MS, Bouwman FG, Mariman EC, Westerterp KR. Postprandial responses in hunger and satiety are associated with the rs9939609 single nucleotide polymorphism in *FTO*. Am J Clin Nutr 2009;90:1426-32.
PUBMED | CROSSREF

43. Wardle J, Carnell S, Haworth CM, Farooqi IS, O'Rahilly S, Plomin R. Obesity associated genetic variation in *FTO* is associated with diminished satiety. J Clin Endocrinol Metab 2008;93:3640-3.
PUBMED | CROSSREF

44. de Luis DA, Aller R, Izaola O, Primo D, Urdiales S, Romero E. Effects of a hgh-protein/low-carbohydrate diet versus a standard hypocaloric diet on weight and cardiovascular risk factors: role of a genetic variation in the rs9939609 *FTO* gene variant. J Nutrigenet Nutrigenomics 2015;8:128-36.
PUBMED | CROSSREF

45. Qi Q, Kilpeläinen TO, Downer MK, Tanaka T, Smith CE, Sluijs I, Sonestedt E, Chu AY, Renström F, Lin X, et al. *FTO* genetic variants, dietary intake and body mass index: insights from 177,330 individuals. Hum Mol Genet 2014;23:6961-72.
PUBMED | CROSSREF

46. Lee HJ, Kim IK, Kang JH, Ahn Y, Han BG, Lee JY, Song J. Effects of common *FTO* gene variants associated with BMI on dietary intake and physical activity in Koreans. Clin Chim Acta 2010;411:1716-22.
PUBMED | CROSSREF