Aspects of Molecular Medicine 3 (2024) 100044

Contents lists available at ScienceDirect

Aspects of Molecular Medicine

journal homepage: www.journals.elsevier.com/aspects-of-molecular-medicine

The interaction between ultra-processed foods and genetic risk score on body adiposity index (BAI), appendicular skeletal muscle mass index (ASM), and lipid profile in overweight and obese women

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ARTICLE INFO

Handling Editor: Prof A Angelo Azzi

Keywords:
Genetic risk score
Ultra-processed foods
Body composition
Body adiposity index
Appendicular skeletal muscle mass

ABSTRACT

Background & aims: Ultra-processed foods (UPF) are formulations of ingredients, resulting from a series of industrial processes. Excess intake of UPF is associated with an increased risk of obesity and chronic disease. The present study investigates the interaction between the consumption of UPF and genetic risk score with body composition, body adiposity index (BAI), and appendicular skeletal muscle mass (ASM) in overweight and obese women.

Method: The study is cross-sectional with 376 overweight and obese women aged 18–65 years. The food consumption was obtained with 147-item food frequency (FFQ), and food items were grouped according to the level of processing as per the NOVA classification. Three single nucleotide polymorphisms (SNPs), including *Caveolin_1 (Cav_1), Melanocortin4 receptor (MC4R),* and *cryptochrome circadian regulator 1 (CRY1)*, were used to calculate GRS. The individual risk allele for each SNP was calculated using the incremental genetic model. Each SNP was recoded as 0, 1, or 2 based on the number of risk alleles associated with a higher body mass index (BMI). Subsequently, the unweighted GRS was computed by summing the number of risk alleles across the three SNPs. The GRS scale spans from 0 to 6, with each point representing a risk allele.Anthropometric measurements and some blood parameters were measured by standard protocols.

Results: After controlling for confounders such as age, energy intake, and BMI a significant interaction was found for appendicular skeletal muscle mass ($\beta = -1.65$, $P = 0.04$) and appendicular skeletal muscle mass index ($\beta = -0.38$, $P = 0.07$) on the NOVA classification system and GRS.

Conclusions: The findings of this study showed a significant interaction between GRS and the NOVA classification system on some body composition, including appendicular skeletal muscle mass. A higher intake of ultra-processed foods may be associated with lower appendicular skeletal muscle mass in people with high obesity-GRS.

1. Introduction

The worldwide consumption of ultra-processed food products (UPFs) has surged dramatically. According to data from Nationwide Food Surveys, UPFs contribute to anywhere between 25% and 60% of the overall daily energy intake (Cediel et al., 2018; Moubarac et al., 2017; Marrón et al., 2018; Baraldi et al., 2018). The NOVA system is the most widely adopted and recognized among the different systems used to classify food based on their degree of processing (Martinez-Perez et al., 2021). According to the NOVA categorization, UPFs are described as food items composed mainly or entirely of less healthy constituents, featuring higher levels of unhealthy fat such as hydrogenated oil and saturated fat,

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https://doi.org/10.1016/j.amolm.2024.100044
Received 30 November 2023; Received in revised form 16 April 2024; Accepted 1 May 2024
Available online 3 May 2024

modified starch, dietary energy density (DED), sodium, and added sugar, colors, and classes of additives, while having reduced levels of different type of vitamins content and total fiber (Zinöcker et al., 2018; Pagliai et al., 2021). UPFs are characterized by their high DED, but they are lacking in essential nutrients (Haghighatdoost et al., 2023). Dependence on UPFs as a substantial part of one's daily calorie intake can potentially decrease the consumption of fresh and minimally processed foods, which can indirectly jeopardize one's health (Montero-Salazar et al., 2020). The consumption of UPFs has a substantial effect on nutrient intake and the overall quality of one's diet, and it plays a crucial role in increased risk of weight gain and health conditions like obesity (Haghighatdoost et al., 2022a). In a cross-sectional study, there is evidence to propose a gender-specific relationship between the intake of UPFs and the condition of being overweight. This particular study implies that the consumption of UPFs may be linked to an elevated risk of overweight among males with higher body mass index (BMI), waist circumference (WC), and abdominal obesity, while no such connection was observed among female (Haghighatdoost et al., 2022a). Moreover, UPFs wereassociated to lower muscle mass markers, corrected arm muscle area and arm circumference (Monteles et al., 2023). In addition, in a sample of adults that represented the entire nation, it was observed that food insecurity was linked to increased consumption of UPFs (Leung et al., 2022).

Furthermore, genetic predisposition has also been identified as a substantial contributing factor to the risk of overweight and obesity (Damavandi et al., 2022; Zhu et al., 2014; Seral-Cortes et al., 2021; Gholami et al., 2022a). Advancements in genome-wide association studies (GWAS) have enabled the exploration of genetic risk scores (GRS), which involve the assessment of each individual single nucleotide polymorphisms (SNPs) and the aggregation of risk alleles associated with them (Rasaei et al., 2023; Bauer et al., 2019; Dudbridge, 2013). Numerous studies have linked *caveolin-1 (CAV-1)* SNPs, which are prevalent in adipocytes, to the onset and progression of obesity (Thorn et al., 2003; Al et al., 2023; Nizam et al., 2018). Moreover, past research has revealed a correlation between the C allele, considered a risk variant, of the *melanocortin 4 receptor (MC4R)* rs17782313 and cardiovascular risk factors such as elevated body weight and body mass index (BMI) (Chambers et al., 2008; Xi et al., 2012). Additionally, there have been reports indicating that *cryptochromes (Cry) 1* have a significant role in the regulation of metabolism and obesity (Gholami et al., 2023; Zhang et al., 2010). As a result, the genetic variants mentioned above have previously been identified as having individual associations with overweight, obesity and cardiometabolic risk factors in specific populations (Gholami et al., 2022a; Turcot et al., 2018; Yengo et al., 2018).

After this identification, the hypothesis of "gene-environment interaction" was proposed (Garver et al., 2013). Given the roles of UPFs, along with the emerging significance of GRS in metabolic regulation, it is plausible that their interactions could play a pivotal role in determining the anthropometric and adiposity indices. Haghighatdoost et al. demonstrated that a 1-g increase in the consumption of UPFs is associated with elevated levels of transforming growth factor, an increased atherogenic coefficient, and higher levels of visceral fat (Haghighatdoost et al., 2023). An extensive review of the literature uncovered that most studies have identified strong associations between the consumption of UPFs and higher levels of body fat in children and adolescents (Costa et al., 2018). Prospective studies have indicated that the consumption of UPFs is linked to the development of abdominal obesity and alterations in anthropometric indices (Costa et al., 2019). One study's findings suggest that a heightened intake of UPFs is associated with elevated levels of excess weight, BMI, and waist circumference (WC), with a particularly pronounced connection observed among women (Juul et al., 2018).

While numerous studies have explored the link between UPFs and overweight or obesity, it is important to note that, to date, no specific study has focused on the interaction between UPFs and GRS on anthropometric indices and body composition measurements. Indeed, differences in lifestyle, dietary patterns, and the typical consumption levels of UPFs within various populations with different genetic predisposition can result in inconsistencies in the outcomes observed across different research studies. Therefore, this study aims to investigate the interaction between UPFs and GRS on adiposity indices in a cross-sectional study of Iranians.

1.1. Participants

A total of 376 participants were investigated for the current cross-sectional study conducted between April 2023 and February 2024. Study participants were recruited from overweight and obese women referred to 21 health centers of Tehran, Iran by a multistage cluster random sampling method and provided written informed consent. This cross-sectional research project included 376 women who were overweight or obese apparently healthy and ranged in age >18 years. Using PASS software and considering alpha = 0.05 and power of 0.90, the required sample size is 376. In adults, WHO defines a BMI between 25 and 29.9 as "overweight" and a BMI ≥30 as "obese". Obesity is classified into three levels in terms of severity: first-degree obesity (BMI = 30-34-9), second-degree obesity (BMI = 35–39) and third-degree obesity (BMI ≥40) (Obesity: preventing and managing the, 2000). These women were recruited from health centers located in Tehran, Iran. The participants had a BMI range of 25–40 kg/m^2. Exclusion criteria for the study encompassed various health conditions, including liver disease, kidney disease, malignancies, cancer, thyroid disease, diabetes (both type I and II), cardiovascular disease (CVD), pregnancy, lactation, menopause, smoking, any chronic or acute illnesses, the use of weight-loss medications, engagement in a weight loss diet in the past year, and the use of medications to lower glucose, lipid levels in plasma, and blood pressure. The research protocol received ethical approval from the ethics committee of Tehran University of Medical Sciences (TUMS) under the following reference number: IR.TUMS.MEDICINE.REC.1402.632. All research methods adhered to the pertinent guidelines and regulations. Prior to their inclusion in the study, all participants provided written informed consent, a process that was thoroughly reviewed and sanctioned by Tehran University of Medical Sciences (TUMS) in Tehran, Iran.

1.2. Measurement of biochemical parameters

Blood samples were systematically collected and assessed using established methodologies at the Nutrition and Biochemistry laboratory within the School of Nutritional and Dietetics at Tehran University of Medical Sciences (TUMS). Fasting venous blood samples of 12 ml were drawn from individuals who had fasted for a duration of 10–12 h, with the sampling occurring between 8:00 a.m. and 10:00 a.m. Following collection, these blood samples were promptly centrifuged, divided into smaller portions, and stored at a temperature of −80 °C. All of these samples were subsequently analyzed using a uniform assay procedure. Enzymatic colorimetric tests with Glycerol-3-phosphate oxidase Phenol 4-Aminoantipyrine Peroxidase (GPO-PAP) was used for total cholesterol (TC) levels' assessment. Direct enzymatic clearance assay was used for low-density lipoprotein (LDL) and high-density lipoprotein (HDL) cholesterol levels' assessment.

1.3. Assessment of anthropometric and body composition measures

We employed a calibrated digital scale to accurately measure and record participants' weight, rounded to the nearest 100 g, while they were wearing light clothing and not wearing shoes. Height was determined by using a measuring tape while participants were in a standard standing position. The BMI is computed by dividing a person's weight in kg by the square of their height. The technician measured HC (hip circumference) as the most prominent and distinct area around the buttocks, and WC (waist circumference) was assessed at the narrowest point of the abdomen after a natural exhale. We used elastic measuring

tape for these measurements with a precision of 0.5 cm. To minimize errors in measurement, the same technician conducted all of them. We used the bioelectrical impedance analyzer (BIA) (Inbody 770 Co., Seoul, Korea) device to assess the body composition status of female participants according to the device protocol and methodology such as visceral fat area, appendicular skeletal muscle mass, skeletal muscle mass index (SMI), and appendicular skeletal muscle mass index (ASMI) (TspBC, 2015). We assessed different body composition status by Inbody device base on Dual Energy X-ray Absorptiometry (DXA). For measuring the fat distribution, we used BAI (for women) with the following formula (Bergman et al., 2011).

$$\text{BAI} = \frac{\textit{Hip Circumference}\ (cm)}{\text{height}\ (\text{m})^{1.5}} - 18$$

$$\text{BRI}\ [36] : 364.2\text{-}\ 365.5\ *\ \sqrt{1} - \left(\frac{(WC/2\pi)2}{(0.5 * height)2}\right)$$

$$\text{AVI}\ [37] : \frac{2 * (WC)2 + 0.7 * (WC - HC)2}{1000}$$

1.4. Assessment of dietary intake and NOVA calculation

To assess the dietary habits of participants over the past year, a validated semi-quantitative Food Frequency Questionnaire (FFQ) was employed. Its validity and reliability have previously been established and approved (Mirmiran et al., 2010; Toorang et al., 2020). Trained dietitians were tasked with administering the FFQ. This particular FFQ encompassed a total of 147 food items, each standardized with a serving size. Participants evaluated their consumption frequency using four categories: daily, weekly, monthly, and infrequent. Portion sizes of the foods consumed were converted to grams using home measures (Azizi et al., 2002). Nutrient and energy intakes were computed utilizing NUTRITIONIST IV software (version 7.0; N-Squared Computing, Salem, OR). In the context of this research, the NOVA food group classification categorizes the following food and beverage items as Ultra-Processed Foods (UPFs), which were grouped into seven food categories in the Food Frequency Questionnaire (FFQ) for daily intake calculations (measured in grams) (Edalati et al., 2021).

1. Non-dairy beverages (including *coffee, cola, nectar,* and *industrial sweet drinks*).
2. Dairy beverages (including ice cream, pasteurized and non-pasteurized milk, chocolate milk, and cocoa milk).
3. Cakes and cookies (encompassing cookies, biscuits, pastries - both creamy and non-creamy, cake, pancake, industrial bread, toasted bread, noodles, and pasta).
4. Fast food and processed meat (comprising burgers, sausages, pizza, and bologna).
5. Salty snacks (including chips, crisps, crackers, and cheese puffs).
6. Oil and sauce (covering mayonnaise, margarine, and ketchup).
7. Sweets (encompassing Gaz, Sohan, Noghl, sesame halva, chocolate, candies, rock candies, jam, and sweets).

1.5. Assessment of physical activity

The physical activity status was determined using the validated International Physical Activity Questionnaire (IPAQ). Individuals' physical activity was assessed using the short-term International Physical Activity Questionnaire (IPAQ).). This questionnaire calculates the physical activity of all participants during the past 7 days. The validity and reliability of IPAQ questionnaires was assessed across 12 countries. The criterion reliability of this questionnaires had the Spearman's ρ of around 0.8. The median ρ for the validity has been reported around 0.30, which was similar to other validation studies. IPAQ is a validated self-reported seven-item measure of physical activity that showed physical activity rate (vigorous, moderate, walking, and inactive) over the last week, and then the values were multiplied by their metabolic equivalent (MET) quantities and the acquired numbers were summed together to calculate MET/min/week value.Trained professionals were responsible for administering the questionnaires and calculating the MET-min/week scores for each subject (Ainsworth et al., 2011; Hagströmer et al., 2006).

1.6. Genotyping and GRS

In whole blood DNA extraction was done. he DNA extraction process involved the use of the salting-out method (Watkins et al., 2015). Following that, the integrity of the DNA was assessed by running it through a 1% agarose gel, and the DNA concentration was quantified using a Nanodrop 8000 spectrophotometer. The genotype of SNPs was determined using the PCR-allele technique conducted with the TaqMan open array (Myakishev et al., 2001). The prior study resulted in the choice of *MC4R* gene primers (Zlatohlavek et al., 2013). For *MC4R (rs17782313)*, we employed the polymerase chain reaction (PCR) method with the following primers: the reverse primer with the sequence 5-TTCCCCCTGAAGCTTTTCTTGTCATTTTGAT-3 and the forward primer with the sequence 5-AAGTTCTACCTACCATGTTCTTGG-3. Subsequently, the fragments containing the three genotypes, TT, CT, and CC, were identified. For *CAV-1 (rs3807992)*, PCR was conducted using the following primer sequences: the reverse primer sequence was 5′-GTCTTCTGGAAAAAGCACATGA-3′ and the forward primer sequence was 5′-AGTATTGACCTGATTTGCCATG-3'. Next, the fragments containing the three genotypes, AA, GA, and GG, were identified. For *Cry1 (rs2287161)*, PCR was performed using the following primer sequences: the reverse primer sequence was 5′-GGTCCTCGGTCTCAAGAAG-3′, and the forward primer sequence was 5′-GGAACAGTGATTGGCTCTATCT-3′ and fragments containing three genotypes: GG, GC, and CC. Three single nucleotide polymorphisms (SNPs), namely *MC4R (rs17782313), CAV-1 (rs3807992),* and *Cry-1 (rs2287161)*, which had previously demonstrated associations with obesity-related traits in Genome-Wide Association Studies (GWAS) and other related research (Yengo et al., 2018; Yu et al., 2020; Yarizadeh et al., 2021a; Abaj et al., 2021a; Tangestani et al., 2021) created the GRS. Each SNP was recoded as 0, 1, or 2 based on the number of risk alleles associated with a higher BMI. Subsequently, the unweighted Genetic Risk Score (GRS) was computed by summing the number of risk alleles across the three SNPs. The GRS scale spans from 0 to 6, with each point representing a risk allele. Higher GRS scores indicate a greater genetic predisposition to higher BMI or increased body weight (Miranda et al., 2019).

1.7. Statistical analysis

The normality of the quantitative variables was assessed using the Kolmogorov–Smirnov test, with a significance level set at $P > 0.05$. Categorical data were presented as both absolute frequencies and relative frequencies, while quantitative data were presented as means along with their corresponding standard deviations (SD). To assess the disparity in mean values for quantitative variables and the distribution of categorical variables across UPF tertiles, one-way analysis of variance (ANOVA) and Pearson chi-square ($\chi 2$) tests were conducted, respectively. Additionally, analysis of covariance (ANCOVA) was employed, with adjustments made for confounding factors such as age, BMI, energy intake, physical activity. The results of this analysis were expressed in terms of β-values along with a 95% confidence interval (CI). Statistical analysis was carried out using SPSS v.26 software (SPSS Inc., IL, USA), and the significance level was established at $p < 0.05$ and marginal significance level was established at $p < 0.07$. Generalized linear models (GLMs) as linear regression was exerted to analyze the interaction between GRS and UPFs in the crude and adjusted model. The adjustment was applied based on age, BMI, energy intake, physical activity and education in Model 1. GRS was assessed base on median.

2. Result

2.1. Participant's descriptive characteristic

The present study included 376 women who were classified as overweight or obese. The mean (SD) age, body weight, height, BMI, and waist circumference of participants were 36.68 ± 9.23 years, 80.59 ± 11.27 Kg, 161.21 ± 5.78 cm, 31.02 ± 3.86 kg/m^2 and 99.21 ± 9.58 cm respectively. 48.5% of participants had a bachelor's degree or higher and most of them were married (71.7%). The mean (SD) for physical activity of subjects was 993.26(1098.67) MET/min/week.

Table 1
Mean and SD of anthropometric measurement, body composition, and lipid profile according to tertile categories of NOVA score in obese and overweight women (n = 376).

Variables†	NOVA				
	T1 N = 127	T2 N = 123	T3 N = 126	P-value	P-value [b]
Age (years)[c]	36.62 ± 9.49	36.89 ± 8.37	34.56 ± 8.31	**0.002**	**0.03**
Body weight (Kg)[d]	79.35 ± 10.93	82.80 ± 13.00	81.47 ± 12.56	0.06	**0.02**
Height (cm)	159.97 ± 6.20	161.89 ± 5.90	161.60 ± 5.37	**0.01**	0.09
BMI (Kg/m^2)	30.96 ± 3.90	31.60 ± 4.36	31.25 ± 4.61	0.48	0.16
Body composition					
WC (cm) [e]	98.27 ± 9.13	100.98 ± 10.57	99.51 ± 10.34	0.09	**0.02**[a]
BF (%)	42.18 ± 5.11	42.06 ± 5.41	42.42 ± 5.98	0.86	**0.06**[a,*]
BAI	29.25 ± 9.43	30.31 ± 5.21	29.39 ± 7.49	0.60	0.27[a]
VFA (cm2)	164.24 ± 35.01	181.76 ± 150.14	167.61 ± 41.16	0.26	0.21[a]
ASM	19.22 ± 2.65	19.72 ± 2.82	19.41 ± 2.27	0.41	0.27[a]
ASMI	7.43 ± 0.66	7.49 ± 0.74	7.39 ± 0.64	0.64	0.46[a]
SMI	0.24 ± 0.02	0.24 ± 0.02	0.24 ± 0.02	0.99	0.88[a]
BRI	19.26 ± 3.61	20.28 ± 3.60	20.02 ± 5.00	0.64	0.42[a]
AVI	19.26 ± 3.61	20.28 ± 3.60	20.02 ± 5.00	0.64	0.19[a]
Lipid profile					
Total cholesterol (g/dl)	186.50 ± 37.17	187.60 ± 39.01	180.67 ± 31.60	0.44	0.74
HDL (mg/dl)	48.17 ± 10.84	45.23 ± 12.07	46.94 ± 9.14	0.20	0.08
LDL (mg/dl)	98.85 ± 24.18	92.67 ± 25.30	93.08 ± 22.59	0.17	0.32

SD: Standard deviation; BMI: Body mass index; WC: waist circumference; WC: waist circumference; BF: body fat; VFA: visceral fat area; ASM: Appendicular skeletal muscle; ASMI: Appendicular skeletal muscle index; SMI: skeletal muscle mass index; BRI: Body Roundness Index; AVI: Abdominal volume Index; LDL: Low density lipoprotein; HDL: High density lipoprotein.
$p < 0.05$ was considered significant.
† Calculated by analysis of variance (ANOVA).
[b] Adjusted for age, BMI, physical activity, and total energy intake by analysis of covariance (ANCOVA).
[a] BMI considered as collinear and this variable adjusted for Age, physical activity, and total energy intake.
[c] Significant difference was seen between T3 and T1.
[d] Significant difference was seen between T3 and T2.
[e] Significant difference was seen between T3 and T2.
[*] $p \leq 0.07$ was considered marginally significantt

2.2. Variables mean differences among NOVA scores

The general subject's characteristics across NOVA score tertiles are depicted in Table 1. Participants in the higher tertiles of NOVA score were younger. The mean ages displayed a significant difference between tertile 3(T3) and tertile 1(T1) ($p = 0.03$). Participants with the lowest tertile of NOVA had lower mean body weight. A significant mean difference was seen between T3 and tertile 2(T2) for the mentioned variable (p = 0.02). Body fat percent (BF %) was higher in people who were categorized as T3 of the NOVA score. So, BF % displayed a marginally significant variation ($p = 0.06$). Based on the Bonferroni post-hoc test a significant difference was shown between T3 and T2 for waist circumference (WC) in the adjusted model. The average height was statistically significantly different among NOVA tertile in the crude model.

2.3. Variables mean differences based on GRS groups

The average of an anthropometric measurement, body composition, and lipid profile according to the groups of GRS are displayed in Table 2. The participants who were categorized as GRS<3 had higher mean differences for height and the p-values in both crude ($p = 0.02$) and adjusted models ($p = 0.03$) were statically significant. In the crude model for BMI, a significant difference was seen) $p = 0.01$), which after adjustment for confounding variables (age, physical activity, and total energy intake) this variation marginally remained significant ($p = 0.07$). The average Body Roundness Index (BRI) for participants in the GRS>3 group was higher than the other GRS group and significant differences were found both in crude ($p = 0.01$) and adjusted model ($p = 0.02$). Similarly, among the GRS groups, a significant mean difference was observed in the skeletal muscle mass index (SMI) variable in the crude

Table 2
Mean and SD of anthropometric measurement, body composition, and lipid profile according to median of GRS in obese and overweight women (n = 376).

Variables†	GRS<3	GRS>3	P-value	P-value [b]
Age (year)	28.54 ± 7.00	30.78 ± 8.22	0.55	
Body weight (Kg)	80.07 ± 10.83	81.44 ± 11.97	0.25	0.44
Height (cm)	161.75 ± 5.76	160.32 ± 5.72	**0.02**	**0.03**
BMI (Kg/m^2)	30.66 ± 3.74	31.62 ± 3.93	**0.01**	**0.07***
Body composition				
WC (cm)	98.64 ± 9.27	100.14 ± 10.05	0.14	0.17[a]
BF (%)	41.78 ± 5.13	42.48 ± 5.71	0.21	0.28[a]
BAI	36.89 ± 9.36	36.31 ± 9.04	**0.02**	**0.01**[a]
VFA (cm2)	170.11 ± 114.16	169.90 ± 37.81	0.98	0.97[a]
ASM	19.55 ± 2.59	19.22 ± 2.53	0.32	0.24[a]
ASMI	7.41 ± 0.67	7.46 ± 0.69	0.56	0.93[a]
SMI	0.247 ± 0.02	0.240 ± 0.02	**0.01**	**0.02**[a]
BRI	5.71 ± 1.30	6.06 ± 1.39	**0.01**	**0.02**[a]
AVI	19.27 ± 3.61	20.10 ± 3.60	0.18	0.17[a]
Lipid profile				
Total cholesterol (g/dl)	186.17 ± 36.22	179.23 ± 35.01	0.15	0.19
HDL (mg/dl)	47.46 ± 10.82	45.06 ± 9.98	0.09	0.22
LDL (mg/dl)	96.38 ± 23.43	90.39 ± 24.38	0.06	0.10

SD: Standard deviation; GRS: Genetic risk score; BMI: Body mass index; WC: waist circumference; VFA: visceral fat area; ASM: Appendicular skeletal muscle; ASMI: Appendicular skeletal muscle index; SMI: skeletal muscle mass index; BRI: Body Roundness Index; AVI: Abdominal volume Index; LDL: Low density lipoprotein; HDL: High density lipoprotein.
$p < 0.05$ was considered significant.
† Calculated by analysis of variance (ANOVA).
[b] Adjusted for age, BMI, physical activity, and total energy intake, by analysis of covariance (ANCOVA).
[a] BMI considered as collinear and this variable adjusted for Age, physical activity, and total energy intake.
[*] $p \leq 0.07$ was considered marginally significant.

model and after controlling confounding factors ($p = 0.02$). Therefore, the result show that the participants in the GRS>3 group had lower SMI in comparison to the other GRS group.

2.4. Dietary intake across the UPF consumption tertiles

The dietary intakes of all the individuals across the UPF consumption tertiles are presented in Table 3. The mean intake of non-dairy beverages ($p = 0.00$), cookies-cakes ($p = 0.00$), dairy beverages ($p = 0.00$), potato chips-salty ($p = 0.00$), processed meat-fast food ($p = 0.00$), Oil_ Sauce ($p = 0.00$), and Sweet ($p = 0.01$) had significant variation across UPF consumption tertiles. It should be noted that the average intakes in the third tertile were higher than the two others. In addition, with increasing UPF consumption, all the mentioned components have increased in both models. Although significant differences were observed for energy intake among UPF consumption tertiles ($p = 0.00$). In the food group category, refined grains ($p = 0.00$), fruits ($p = 0.003$), eggs ($p = 0.05$), dairy ($p = 0.009$), and red meat ($p = 0.001$) were statically significant in the crude model and after adjustment for energy intake as a confounding. only the vegetable group remained significant in the adjusted model($p = 0.00$). All of the mean nutrient intakes such as protein, carbohydrate, total fat, etc. had significant variations in the crude model, but two of them including potassium ($p = 0.01$) and total fiber ($p = 0.00$) remained significant after adjustment.

2.5. Interaction between GRS and NOVA scores on anthropometric measurement, body composition, and lipid profile

Interaction between GRS and NOVA scores for anthropometric measurement, body composition, and lipid profile variables, based on using GLM, are displayed in Table 4. Significant interaction was reported between GRS and NOVA scores on ASM; moderate (ß = −1.65, CI -3.29 to −0.02, $p = 0.04$) NOVA adherence was more associated with lower levels of ASM among participants with GRS>3 compared to reference group in a multivariate-adjusted model and marginally in the crude model ($p = 0.06$). Also, in the adjusted model for confounding factors including age, energy intake, physical activity, and education, there were borderline significant GRS- NOVA interactions on ASMI; which means that moderate (ß = −0.38 CI -0.80 to 0.04, $p = 0.07$) NOVA score is related to lower ASMI across participants in the GRS>3 group when compared to the reference value.

3. Discussion

We found, that participants with greater NOVA scores were younger. In addition, greater tertile of NOVA score marginally related to greater BF %. Furthermore, upper GRS is related to lower SMI, but greater BRI. GRS modulates the association between NOVA scores and ASM/ASMI.

The NOVA scores were associated with BF% positively in our study. In line with our findings, previous studies indicated higher consumption of ultra-process foods related to greater BF% in American adults (Liu et al., 2023), and Brazilian women (Rudakoff et al., 2022). Although, Haghighatdoost et al. indicated intake of ultra-process food was not related to BMI among Iranian women but was related to higher BMI among Iranian men (Haghighatdoost et al., 2022b). In our study, NOVA scores were not associated with BAI, VFA, ASM, ASMI, SMI, BRI, AVI, and lipid profiles. In contrast, a gram increase in intake of UPFs was associated with an increase in atherogenic coefficient (calculated by a formula based on the lipid profiles) and visceral fat level (VFL) among obese and overweight women (Hosseininasab et al., 2022a). Higher consumption of UPF was related to a higher risk of premature coronary artery disease(Ansari et al., 2023). Also, Beslay et al. showed that higher consumption of UPF was associated with higher risks of overweight and obesity and greater change in BMI in a large prospective study(Beslay et al., 2020). Moreover, greater UPF consumption was related to a higher risk of all-cause mortality in a prospective study design(Schnabel

Table 3
Nutrient intake according to tertile categories of NOVA score in overweight and obese women.

Variables†	UPF consumption tertiles				
	T1 (n = 127)	T2(n = 123)	T3(n = 126)	P-value	P-value [b]
Energy intake	2128.15 ± 554.18	2629.55 ± 683.20	3146.02 ± 824.89	**0.00**	
NOVA score components					
Nondairy beverages (g/d)	145.22 ± 24.88	148.73 ± 41.38	238.34 ± 135.33	**0.00**	**0.00**
Cookies-cakes (g/d)	82.08 ± 20.95	93.04 ± 31.00	121.74 ± 60.46	**0.00**	**0.00**
Dairy beverages (g/d)	37.89 ± 13.19	48.62 ± 23.86	57.05 ± 37.82	**0.00**	**0.00**
Potato chips-salty	19.92 ± 7.48	19.77 ± 8.40	26.63 ± 20.62	**0.00**	**0.00**
Processed meat-fast food (g/d)	34.85 ± 11.20	36.97 ± 16.23	51.62 ± 37.36	**0.00**	**0.00**
Oil_ Sauce (g/d)	16.55 ± 4.87	17.66 ± 7.68	20.59 ± 11.76	**0.001**	**0.00**
Sweet (g/d)	33.17 ± 10.66	36.75 ± 18.79	40.68 ± 35.41	**0.04**	**0.01**
Food groups					
Refined grains (g/d)	333.27 ± 129.88	461.99 ± 227.66	509.16 ± 250.80	**0.00**	0.12
Whole grains (g/d)	7.94 ± 10.12	7.27 ± 9.73	7.53 ± 11.50	0.89	0.24
Nuts (g/d)	11.70 ± 12.30	14.83 ± 18.96	16.80 ± 16.34	0.08	0.23
Legumes (g/d)	51.40 ± 45.18	51.55 ± 40.49	55.39 ± 37.77	0.75	0.39
Fruits (g/d)	450.60 ± 291.35	529.12 ± 332.17	615.64 ± 373.80	**0.003**	0.16
Vegetable oils	20.85 ± 22.26	26.06 ± 24.07	23.20 ± 17.45	0.23	0.22
Vegetables(g/d)	447.74 ± 283.68	411.84 ± 239.34	442.22 ± 266.65	0.58	**0.00**
Eggs (g/d)	19.10 ± 11.40	22.25 ± 12.37	23.92 ± 18.02	**0.05***	0.85
Dairy (ml/d)	340.60 ± 223.67	378.20 ± 226.50	449.35 ± 279.16	**0.009**	0.44
Fish and seafood (g/d)	11.44 ± 11.39	9.79 ± 9.41	13.18 ± 15.21	0.15	0.20
Meats (g/d)	53.81 ± 35.89	59.61 ± 33.78	82.07 ± 70.84	0.00	0.33
Red meat (g/d)	16.36 ± 12.94	22.17 ± 21.20	26.38 ± 19.27	**0.001**	0.91
Nutrient intake					
Protein (g/d)	76.48 ± 23.62	90.21 ± 26.86	107.35 ± 34.98	**0.00**	0.39
Carbohydrate (g/d)	301.53 ± 89.15	372.31 ± 111.97	444.05 ± 126.91	**0.00**	0.77
Total fat	75.91 ± 26.81	95.26 ± 31.49	114.38 ± 35.70	**0.00**	0.76
PUFA (g/d)	16.68 ± 8.58	20.45 ± 9.73	23.12 ± 9.29	**0.00**	0.40
SFA (mg/d)	22.48 ± 8.30	28.34 ± 10.57	34.44 ± 12.21	**0.00**	0.56
Sodium (mg/d)	3743.701 ± 1161.83	4564.07 ± 1663.29	5146.17 ± 2051.55	**0.00**	0.64
Potassium (mg/d)	3911.99 ± 1516.27	4443.86 ± 1591.83	5178.20 ± 1830.30	**0.00**	**0.01**
Calcium (mg/d)	1088.19 ± 467.38	1267.08 ± 505.01	1451.97 ± 567.56	**0.00**	0.15
Vitamin C (μmol/L)	163.27 ± 94.81	183.57 ± 104.03	218.57 ± 140.55	**0.001**	0.26
Total fiber (g/d)	41.73 ± 20.90	48.82 ± 19.78	51.52 ± 22.26	**0.001**	**0.00**

PUFA: polyunsaturated fatty acid; SFA: Saturated Fatty Acid, Data are mean ± SD.

$p < 0.05$ was considered significant.

† Calculated by analysis of variance (ANOVA).

[b] Adjusted for energy intake, by analysis of covariance (ANCOVA).

* $p \leq 0.07$ was considered marginally significant.

Table 4
The interaction between GRS and NOVA score on anthropometric measurement, body composition, and lipid profile in obese and overweight women (n = 376).

Variable	GRS	T1	T2						T3					
			Crude			Model 1			Crude			Model 1		
			B	CI	P	B	CI	P	B	CI	P	B	CI	P
BMI (Kg/m^2)	**<3**	Reference	Reference						Reference					
	>3		0.28	−1.77 to 2.33	0.78	0.20	−1.76 to 2.17	0.83	0.84	−1.26 to 2.95	0.43	1.05	−0.96 to 3.07	0.30
Body composition														
WC (cm)	**<3**	Reference	Reference						Reference					
	>3		0.52	−4.54 to 5.58	0.84	0.37	−4.60 to 5.35	0.88 [a]	−0.005	−5.20 to 5.19	0.99	0.31	−4.79 to 5.42	0.90
BF (%)	**<3**	Reference	Reference						Reference					
	>3		1.15	−1.7 to 4.04	0.43	1.19	−1.68 to 4.06	0.41[a]	−1.14	−4.11 to 1.82	0.45	−0.93	−3.87 to 2.01	0.53
BAI	**<3**	Reference	Reference						Reference					
	>3		−0.48	−5.22 to 4.26	0.84	−0.77	−5.50 to 3.94	0.74	1.90	−3.06 to 6.87	0.45	2.51	−2.43 to 7.46	0.31
VFA (cm2)	**<3**	Reference	Reference						Reference					
	>3		−17.29	−70.92 to 36.33	0.52	−19.26	−72.69 to 34.16	0.48[a]	2.63	−52.40 to 57.67	0.92	3.78	−50.97 to 58.53	0.89
ASM	**<3**	Reference	Reference						Reference					
	>3		−1.54	−3.19 to 0.10	**0.06**[*]	−1.65	−3.29 to −0.02	**0.04**[a]	−0.77	−2.48 to 0.94	0.37	−0.73	−2.43 to 0.96	0.39
ASMI	**<3**	Reference	Reference						Reference					
	>3		−0.35	−0.078 to 0.08	0.11	−0.38	−0.80 to 0.04	**0.07**[*,a]	−0.02	−0.48 to 0.43	0.91	−0.04	−0.04 to 0.39	0.83
SMI	**<3**	Reference	Reference						Reference					
	>3		−0.00	−0.02 to 0.00	0.28	−0.00	−0.02 to 0.00	0.23[a]	0.00	−0.01 to 0.01	0.63	0.00	−0.01 to 0.01	0.63
BRI	**<3**	Reference	Reference						Reference					
	>3		0.00	−0.00 to 0.00	0.63	0.00	−0.00 to 0.00	0.56[a]	0.00	−0.00 to 0.00	0.60	0.00	−0.00 to 0.00	0.39
AVI	**<3**	Reference	Reference						Reference					
	>3		−547.40	−3392.90 to 2298.08	0.70	−747.75	−3511.46 to 2015.94	0.59[a]	449.57	−2658.62 to 3557.76	0.77	160.37	−2862.78 to 3183.52	0.91
Lipid profile														
Total cholesterol (g/dl)	**<3**	Reference	Reference						Reference					
	>3		−6.30	−30.94 to 18.35	0.61	−7.14	−30.11 to 15.82	0.54	−6.02	−32.44 to 20.40	0.65	−7.34	−31.87 to 17.18	0.55
LDL (mg/dl)	**<3**	Reference	Reference						Reference					
	>3		−3.11	−19.20 to 12.98	0.70	−3.38	−18.94 to 12.18	0.67	−8.54	−25.80 to 8.71	0.32	−6.72	−23.34 to 9.89	0.42
HDL (mg/dl)	**<3**	Reference	Reference						Reference					
	>3		1.38	−5.60 to 8.36	0.69	1.38	−5.73 to 8.49	0.70	6.16	−1.32 to 13.65	0.10	6.32	−1.26 to 13.92	0.10

T: tertile; SD: Standard deviation; GRS: Genetic risk score; BMI: Body mass index; WC: waist circumference; BF: body fat; VFA: visceral fat area; LDL: Low density lipoprotein; HDL: High density lipoprotein; ASM: Appendicular skeletal muscle; ASMI: Appendicular skeletal muscle index; SMI: skeletal muscle mass index; BRI: Body Roundness Index; AVI: Abdominal volume Index; LDL: Low density lipoprotein; HDL: High density lipoprotein.

GLM was performed to identify the interaction between GRS and NOVA scores on anthropometric measurement, body composition, and lipid profile.

Model 1 = adjusted for potential confounding factors including (age, energy intake, physical activity, education).

$p < 0.05$ was considered significant.

[a] BMI considered as collinear and this variable adjusted for Age, physical activity, and total energy intake.

[*] $p \leq 0.07$ was considered marginally significant.

et al., 2019). UPF are calorie-dense products that are usually consumed in large portion sizes. Furthermore, they are related to poorer diet quality, and lower nutrient intake (Haghighatdoost et al., 2022c). However, higher sugars (sugar-sweetened beverages) which are used in UPF products, may lead to a delay in satiety signal (Benelam, 2009). Firstly, they are rich in refined carbohydrates that can change insulin response and improve shuttling excess macro/micronutrients away from oxidation towards storage in adipose tissue, secondly, they could act in addictive-like eating behaviours (Schulte et al., 2015). Thirdly, they altered gut microbiota (Miclotte et al., 2020) which all of these causes could result in overweight and obesity.

GRS showed a positive association with BRI in the current study. BRI showed a significant relationship to cardio-metabolic risk factors among overweight and obese adults (Li et al., 2020) and is known as a severe potential marker to detect insulin resistance among non-diabetics (Ramos-Lopez et al., 2019). We did not find any research that assessed the association between GRS and BRI. Although GRS, *MC4R (rs17782313), CAV-1 (rs38 07992)* (Gholami et al., 2022b, 2022c), 29 single-nucleotide polymorphisms(Walter et al., 2016), were related to obesity indices like BMI, WC, and BF% (Gholami et al., 2022c) in previous research. We do not find any significant associations between GRS and obesity indices like BMI, and WC. Similar to our result GRS did not show any significant associations with BMI and WC (Gholami et al., 2022b). We found GRS is inversely related to SMI. GRS involved *MC4R, CAV-1,* and *Cry-1* related to increased obesity and disruption of *MC4R* related to hyperplasia, and weight gain (Farooqi et al., 2003). A significant difference between *MC4R* genotypes (based on rs17782313) and body mineral content and bone mineral content were found (Yarizadeh et al., 2021b). It could modulate stress response, and eating behaviors (Micioni et al., 2020). In addition, *CAV-1* plays a major regulatory role in fat distribution and genetic lipodystrophies in obese women (Abaj et al., 2021b). According to previous study in caveolin-deficient mice, *CAV-1* has shown an association with chronic diseases like diabetes, atherosclerosis, and a variety of degenerative muscular dystrophies (Cohen et al., 2004). Furthermore, *Cry-1* plays a role in promoting skeletal muscle growth and protecting against sarcopenia (Vitale et al., 2019). It seems GRS could affect body composition because of these roles.

UPF consumption positively related to non-dairy beverages, cookies-cakes, dairy beverages, potato chips-salty, processed meat-fast food, oil_sauce, and sweet in both models. However, higher UPF consumption was associated with lower vegetables in the energy adjustment model. Furthermore, higher tertile of UPF consumption was related to greater potassium and total fiber. In line with our results, UPF related to exceeding added sugar, energy intake (Martínez et al., 2016; Louzada et al., 2015), higher fat intake, saturated fat, trans fatty acid, PUFA, and SAFA (Louzada et al., 2015; Correa-Madrid et al., 2023), soft drinks, bread (Ansari et al., 2023), refined starch, ultra-process food (Correa--Madrid et al., 2023; Monteiro et al., 2017), sodium (Correa-Madrid et al., 2023; Vellinga et al., 2022) and lower vegetable intake (Ansari et al., 2023). In contrast to our finding, UPF indicated an inverse association with fibre intake (Costa et al., 2015). NOVA scores were associated with energy intake of ultra-process foods, fat, sodium, PUFA, and SAFA (Correa-Madrid et al., 2023). High glycaemic index foods resulted in a spike in plasma glucose concentration, then by an insulin-mediated decline, precipitating an increase in hunger (Chapman et al., 1998). It seems intake of these energy-dense foods may promote weight gain or obesity (Costa et al., 2018).

The interaction between NOVA scores (T2) and GRS on ASM was found. Moreover, there was a borderline significant interaction between NOVA score and GRS on ASMI. Since, ASMI is a more sensitive biomarker than BMI in adults (Hou et al., 2019). Raised in NOVA score and GRS deteriorates skeletal muscle indices. Increased Nova scores relate to greater obesity indices in previous studies (Liu et al., 2023; Rudakoff et al., 2022; Hosseininasab et al., 2022a; Beslay et al., 2020). Although there were few studies that assessed the interaction of dietary intake and GRS on obesity indices (Gholami et al., 2022b; Hosseininasab et al., 2022b; Seral-Cortes et al., 2020), insulin resistance (Ramos-Lopez et al., 2019), cardiometabolic (Gholami et al., 2022b). Ortega-Azorín and et, al. assessed 7052 high cardiovascular risk subjects (type 2 diabetes/non-diabetic subjects) with no differences in BMI in a Case-control study, GRS modulated association between Mediterranean dietary pattern and metabolic syndrome. It indicated that low adherence to the Mediterranean diet when subject's carriers of the variant alleles (*FTO* rs9939609 and *MC4R-rs17782313*) had a higher risk for diabetes. However, high adherence to the Mediterranean diet by this allele led to the disappearance of this association (Seral-Cortes et al., 2020). A cross-sectional study showed,Healthy Beverage Index (HBI) scores, involved water, tea and coffee, low fat milk, full fat milk, fruit juice, alcohol, Sugar-sweetened beverages, and total beverages, interactionally GRS *MC4R (rs17782313), CAV-1 (rs38 07992),* and *Cry1 (rs2287161)* related to lower WHR and WC, so HBI according to genetics could protect against abdominal obesity (Gholami et al., 2022b). However, the interaction between macronutrients and energy intake and obesity by 16 genome-wide was investigated among 29480 adults, the results indicated only BDNF rs4923461 modulated the association between protein intake on BMI and *NEGR1* rs2815752 related to fat, carbohydrate and fiber of diet (Rukh et al., 2013). Yarizadeh and et al. indicated *(MC4R) rs17782313* modulated association between dietary inflammatory scores and body composition indices, adherence to a pro-inflammatory diet was associated with a reduction of skeletal muscle mass and total body mineral content in *MC4R* risk allele carriers (Yarizadeh et al., 2021b). Also, an inverse association between UPF intake and muscle mass markers, arm and corrected arm muscle area in participants aged 36–59 years, were observed but interaction was not assessed (Monteles et al., 2023). Another study showed, a significant negative interaction between a modified Nordic-style diet (involved six food groups; rye and wholegrain bread, oatmeal, vegetables and cabbages, pears, apples, and high antioxidant fruits, root vegetables, and fish) and *MC4R* gene rs17782313 polymorphism on VFL (Hosseininasab et al., 2022b).

On the one hand, it seems higher intake of healthy food groups, gene variants, and their interaction could protect against some obesity indices. On the other hand, higher adherence to unhealthy food like UPF based on gene variants, and their interaction could deteriorate health outcomes.

The main strength of the current study is that we used obesity related-GRS rather than a particular single SNP. However, the interaction between *MC4R, CAV-1 (rs38 07992),* and *Cry1 (rs2287161)* and diet were assessed previously (Gholami et al., 2022b; Yarizadeh et al., 2021b; Seral-Cortes et al., 2020). The investigations which have been conducted to assess the interaction between NOVA scores and GRS *MC4R (rs17782313), CAV-1 (rs38 07992), Cry-1 (rs2287161)* polymorphism on obesity indices was not found. we provide novel findings of gene-diet interactions, although there are some limitations in this study. We conducted a cross-sectional study; we cannot show the causal relationship. Furthermore, even though we applied a validated FFQ, there is a possibility of measurement errors (Freedman et al., 2015). Also, present study only included overweight or obese women, thus, the results cannot generalizable to all population.

4. Conclusion

The study suggests that individuals with a higher genetic predisposition to obesity, as indicated by their genetic risk score (GRS), may be more susceptible to the negative effects of consuming UPF on their appendicular skeletal muscle. This implies that the detrimental impact of UPF on muscle mass could be exacerbated in individuals who already have a genetic predisposition to obesity. Further research in this area could include larger and more diverse study populations, longitudinal studies to explore causality and temporal relationships between UPF with additional genetic factors that may influence body composition and metabolic health.

Ethics approval and consent to participate

The present study was carried out in accordance to the ethical standards laid down in the 1964 Declaration of Helsinki. This investigation was also approved by the Ethics Committee of Tehran University of Medical Sciences, Tehran, Iran (with ethics number: IR.TUMS.MEDICINE.REC.1402.632). All of the study participants signed a written consent form related to this study. Each individual was informed completely regarding the study protocol and provided a written and informed consent form before taking part in the study.

Consent for publication

Not applicable.

Availability of data and materials

The datasets used and/or analyzed during the current study are available from the Khadijeh Mirzaei on reasonable request.

Funding

This study was supported by the Tehran University of Medical Sciences (TUMS), Tehran, Iran (code 970316141144).

CRediT authorship contribution statement

Fatemeh Gholami: Conceptualization, Supervision, Writing – original draft. **Azadeh Lesani:** Investigation, Writing – original draft, Writing – review & editing. **Neda Soveid:** Data curation, Formal analysis, Writing – original draft, Writing – review & editing. **Niloufar Rasaei:** Writing – original draft. **Mahsa Samadi:** Methodology, Writing – original draft, Writing – review & editing. **Niki Bahrampour:** Project administration, Visualization, Writing – review & editing. **Gholamali Javdan:** Supervision. **Khadijeh Mirzaei:** Funding acquisition, Supervision, Validation.

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Acknowledgements

We would like to acknowledge the Tehran University of Medical Sciences, Tehran, Iran, for the fund.

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