The relationship between ultra-processed food intake and cardiometabolic risk factors in overweight and obese women: A cross-sectional study

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Background: Cardiovascular diseases (CVDs) are the leading cause of death globally. Based on recent studies, one of the factors that can have detrimental effects on CVD is the consumption of ultra-processed foods (UPFs). The current study investigated the relationship between UPF intake and cardiometabolic risk factors among Iranian women.

Methods: The current cross-sectional study was conducted on 391 women aged 18–65 years with a body mass index (BMI) ≥ 25 kg/m². Dietary intake was assessed using a 147-item food frequency questionnaire (FFQ). Anthropometric and biochemistry parameters were also collected. UPFs were identified using the NOVA classification.

Results: In the present study, women had a mean (standard deviation) age of 36.67 (9.10) years and the mean BMI of 31.26 (4.29) kg/m². According to our findings, there was a significant association between UPF consumption and transforming growth factor (TGF) (β: 0.101, 95% CI: 0.023, 0.180, p = 0.012), atherogenic coefficient (AC) (β: 0.011, 95% CI: 0.001, 0.032, p = 0.034), visceral fat level (VFL) (β: 0.006, 95% CI: −0.017, 0.029, p = 0.076), and the quantitative insulin sensitivity check index (QUICKI) (β: −3.775, 95%CI: 0.001, 0.001, p = 0.042).

Conclusion: In conclusion, an increase in consumption of one gram of UPFs is associated with an increase in TGF, AC, and VFL but with a decrease in QUICKI. Despite this, further experimental studies are necessary to draw a more definite conclusion and disentangle the mechanisms by which UPFs may affect health.

KEYWORDS
ultra-processed food, cardiovascular diseases, obesity, overweight, cardiometabolic risk
Introduction

Cardiovascular diseases (CVDs) are the leading cause of death globally; an estimated 17.9 million people died from CVDs in 2019, representing 32% of all global deaths (1). About 85% of the deaths were due to heart attack and stroke (1). According to previous studies conducted in 2016 and 2017, CVD has been the major cause of mortality in Iran, accounting for 46% of all deaths and 20–23% of the disease burden (2, 3).

The global consumption of ultra-processed foods (UPF) has risen exponentially. UPFs account for between 25 and 60% of total daily energy consumption, according to the Nationwide Food Surveys (4–14). According to the NOVA classification system, UPFs are defined as foods made up entirely or predominantly from unhealthy components containing higher levels of total fat, saturated fat, added sugar, energy density, and salt, and lower quantities of fiber and vitamin density (15). UPF packaging contains materials that come into contact with food, such as Bisphenol A, which, according to a meta-analysis of observational studies, may increase the risk of cardiometabolic disorders, even though prospective cohort studies are still limited (16, 17). Some studies reported that consumption of UPF is associated with adverse health outcomes, including CVDs, and obesity (18–20). Srour et al. reported a higher risk of CVD associated with the consumption of ultra-processed foods (21).

Given the high prevalence of CVDs in Iran, it is necessary to find dietary factors that may associate with the disease (22). The main objective of this study was to investigate the relationship between UPF intake and cardiometabolic risk factors among Iranian women, and the secondary objectives were to exhibit the association between UPF consumption, food groups, and demographic variables.

Methods

Study population

The research was conducted in Tehran, Iran, using a multi-stage cluster random sampling procedure on 391 overweight and obese women with a body mass index (BMI) ranging from 25 to 40 kg/m² and aged 18–48 years, recruited from the community health center of the Tehran University of Medical Sciences (TUMS) in 2018. We used the sample size formula $N = \left( \frac{Z_{1-\alpha} Z_{1-\beta}}{\sqrt{1 - r^2}} \right)^2 + 2$, $\beta = 95\%$, and $\alpha = 0.05$, $r = 0.25$. Participants were excluded if they reported a total daily energy intake outside of 800–4,200 kcal (17,556–3,344 kJ) (23) or if they reported a history of diseases such as CVD, diabetes, cancer, kidney disease, thyroid disease, menopause, pregnancy, and breastfeeding. In addition, individuals on lipid-lowering agents, individuals on blood glucose-lowering agents, and those who consumed alcohol or smoked were excluded from the study. Furthermore, the food frequency questionnaire (FFQ) did not include individuals who did not respond to more than 70 questions and had significant fluctuations in their weight over the past year. After learning about the study’s objectives, all the participants signed an informed consent form. The Human Ethics Committee of Tehran University of Medical Sciences approved the study protocol (Ethics number: IR.TUMS.VCR.REC.1398.142, Date of reference number: 5 April 2019).

Dietary assessment and NOVA calculation

To evaluate the food consumption of participants during the previous year, we used a validated semi-quantitative FFQ, whose validity and reliability have already been authorized (24, 25). Trained dietitians were responsible for applying the FFQ. In total, one hundred forty-seven food items were included in this FFQ with a standard serving size, and participants assessed their consumption frequency according to four categories: daily, weekly, monthly, and infrequent. Using home measures, the portion sizes of the consumed foods were converted to grams (23). Nutrient and energy intakes were calculated using NUTRITIONIST IV software (version 7.0; N-Squared Computing, Salem, OR). The following food and beverage items are classified as UPFs in the NOVA food group classification, which is the subject of this research, and are grouped into the FFQ into seven food groups (daily intake was calculated as grams): (1) Non-dairy beverages (coffee, cola, nectar, and industrial sweet drink), (2) dairy beverages (ice cream, pasteurized and non-pasteurized, chocolate milk, and cocoa milk), (3) cakes and cookies (cookies, biscuits, pastries (creamy and non-creamy), cake, pancake, industrial bread, toasted bread, noodles, and pasta), (4) fast food and processed meat (burger, sausage, pizza, and bologna), (5) salty snacks (chips, crisps, crackers, and cheese puff), (6) oil and sauce (mayonnaise, margarine, and ketchup), (7) sweets (Gaz, Sohan, Noghli, sesame halva, chocolate, candies, rock candies, jam, and sweets) (26). All the NOVA components were adjusted for energy intake.

Anthropometry and body composition

Participants were advised to fast for 12 h the night before the assessment and avoid unusual physical activity for 72 h before the anthropometrics and body composition assessments. A digital stadiometer (Seca) was used to measure height (m) with a precision of 0.5 cm. The waist circumference (WC) (cm) and hip circumference (HC) (cm) with an accuracy of 0.5 cm were measured within the largest and the littlest circumference separately. The waist-to-hip ratio (WHR) was computed as WC (cm)/HC (cm).
A multi-frequency bioelectric impedance analyzer (BIA) (Inbody Co., Seoul, Korea) scanner evaluated body composition. This electrical impedance analyzer measures the resistance of body tissues to the passage of an electrical signal given through the feet and hands. The body composition analyzer was used to assess the individuals’ weight, BMI, fat mass (FM), fat-free mass (FFM), body fat percentage (%), and the others, according to a predetermined methodology. The participants were instructed to urinate before measuring their body composition according to the fabricant recommendations.

**Biochemical assessment**

The blood samples were obtained between 8:00 and 10:00 a.m. at the Nutrition and Biochemistry lab of the School of Nutritional Sciences and Dietetics, TUMS, after an overnight fast and deposited in tubes containing 0.1 percent ethylenediaminetetraacetic acid (EDTA). The serum was centrifuged, aliquoted, and stored at −70°C. The glucose oxidase phenol 4-aminoantipyrine peroxidase (GOD/PAP) technique determined fasting blood glucose levels (FBG). To evaluate blood triglyceride (TG) levels, enzyme colorimetric assays with GPO–PAP were utilized. Total cholesterol was assessed using phenol 4-aminoantipyrine peroxidase (CHOD–PAP), low-density lipoprotein (LDL), and high-density lipoprotein (HDL) were measured using the direct approach (Human PAI-1, Zell Bio GmbH, Germany, assay range: 5 ng/L to 1,500 ng/L, sensitivity: 2.4 ng/L, CV10 percent inter-assay variability). All of the kits were used to quantify serum MCP-1 levels (Zell Bio GmbH, Germany, assay range: 5 ng/L to 1,500 ng/L, sensitivity: 2.4 ng/L, CV10 percent inter-assay variability). The serum insulin concentrations were determined using the enzyme-linked immunosorbent assay (ELISA kit). The ELISA kit was also used to quantify serum MCP-1 levels (Zell Bio GmbH, Germany, assay range: 5 ng/L to 1,500 ng/L, sensitivity: 2.4 ng/L, CV10 percent inter-assay variability). All of the kits were given by Pars Azmoon (Pars Azmoon Inc. Tehran, Iran). Insulin resistance was assessed using a homeostasis model (HOMA–IR). The index was computed using the algorithm (plasma glucose mmol/ l / fasting plasma insulin miU/ l)/22.5 (27). The quantitative insulin sensitivity check index (QUICKI) was also used to evaluate insulin resistance through the formula 1/[log (fasting insulin) + log (fasting glucose)] (27). From biochemical parameters, FBG, TG, HDL, LDL, hs-CRP, and IL_1β variables are considered as CVD risk factors in this study.

The atherogenic index of plasma (AIP) was calculated using the logarithmic of (TG/HDL-C). TC/HDL, LDL/HDL, and (TC-HDL)/LDL were used to determine castelli’s risk index 1 (CRI-I), castelli’s risk index 2 (CRI-II), and atherogenic coefficient (AC), respectively. The following formula was used to compute CHOLIndex: \[ \text{CHOLIndex} = \text{LDL-C} - \text{HDL-C} \times (\text{TG} < 400) = \text{LDL-C} - \text{HDL-C} + 1/5 \times (\text{TG} > 400). \] (28). Ln (FBG (mg/dl)) * TG (mg/dl)/2) was used to determine triglyceride–glucose index (TyG index) (29). The terms triglyceride glucose-waist circumference (TyG–WC) and triglyceride glucose–body mass index (TyG–BMI) were obtained through the formulas: [Ln (FBG (mg/dl)) * TG (mg/dl)/2] * WC and [Ln (FBG (mg/dl)) * TG (mg/dl)/2)] * BMI, respectively (30).

**Blood pressure assessment**

Blood pressure was measured using an automated sphygmomanometer according to standard procedures (OMRON, Germany).

**Other collected data**

General information about the participants, such as their age, job status (employed, unemployed), education level (illiterate, under diploma, diploma, and bachelor and higher) (what are the categories? Detail the methodology here, as well as the other variables), marital status (single and married), economic status (low, middle, and high class), standard questionnaires, were collected. The physical activity status was obtained using the validated International Physical Activity Questionnaire (IPAQ). Afterward, metabolic equation hours per day (MET-min/week) was calculated for each subject. After that, each subject’s metabolic equation hours per day score (MET-min/week) was calculated. Trained professionals were responsible for applying the questionnaires (31, 32).

**Statistical analyses**

The Kolmogorov–Smirnov test was used to check the quantitative variable’s normality (P > 0.05). Categorical data were reported as absolute and relative frequencies, and quantitative data were reported as means and standard deviation (SD). According to the NOVA score, the participants were categorized into tertiles of UPF consumption in grams. To compare the mean difference of quantitative and frequency of categorical variables across UPF tertiles, a one-way analysis of variance (ANOVA) and Pearson chi-square (χ²) tests were performed, respectively. Analysis of covariance (ANCOVA) adjusted for potential confounders (age, BMI, energy intake, and physical activity) and considering BMI as a collinear variable for anthropometrics and body composition variables were performed. The Bonferroni post-hoc test was used to detect the statistically significant difference among UPF tertiles. Linear regression was performed to evaluate the association of the UPF consumption (independent variable) with cardiometabolic risk factors (dependent variable). Model 1 was adjusted for age, BMI, physical activity, total energy

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**TABLE 1** General characteristics among tertiles of NOVA score in obese and overweight women (n = 391).

| Quantitative variables | NOVA tertiles | P-value | P-value* |
|------------------------|---------------|---------|---------|
|                        | T1            | T2      | T3      |
| Age (year)             | 36.480 ± 9.138 | 38.759 ± 8.77 | 34.860 ± 9.352 | 0.003 | 0.004 |
| PA (MET-min -week)     | 1,465.171 ± 231.881 | 834.995 ± 235.775 | 1,353.665 ± 254.709 | 0.098 | 0.154 |
| Weight (kg)            | 81.958 ± 12.382 | 79.884 ± 10.975 | 81.669 ± 13.320 | 0.337 | 0.365 |
| Height (cm)            | 161.574 ± 5.888 | 160.115 ± 5.881 | 161.763 ± 5.796 | 0.047 | 0.869 |
| BMI (kg/m²)            | 31.141 ± 0.440 | 30.847 ± 0.449 | 30.459 ± 0.483 | 0.946 | 0.576 |
| WC (cm)                | 113.163 ± 8.516 | 113.638 ± 7.477 | 116.295 ± 13.657 | 0.247 | 0.592 |
| BMC (Kg)               | 2.676 ± 0.376 | 2.622 ± 0.342 | 2.661 ± 0.330 | 0.445 | 0.643 |
| SMM (Kg)               | 25.954 ± 3.281 | 25.347 ± 3.300 | 25.333 ± 3.4205 | 0.247 | 0.311 |
| SLM (Kg)               | 44.083 ± 5.759 | 43.585 ± 5.126 | 43.587 ± 5.317 | 0.693 | 0.454 |

| Categorical variables |
|-----------------------|
| Supplementation intake n (%) | 0.311 | 0.057 |
| Yes %                 | 58 (36.7) | 47 (29.7) | 53 (33.5) |
| No %                  | 51 (32.0) | 61 (34.7) | 64 (36.4) |
| Income status n (%)   | 0.582 | 0.185 |
| Low class             | 33 (37.5) | 31 (35.2) | 24 (27.3) |
| Middle class          | 60 (33.0) | 61 (33.5) | 61 (33.5) |
| High class            | 35 (32.7) | 31 (29.0) | 41 (38.3) |
| Marital status n (%)  | 0.275 | 0.880 |
| Single                | 35 (32.1) | 31 (28.4) | 43 (39.4) |
| Married               | 92 (33.6) | 96 (35) | 86 (31.4) |
| Job status n (%)      | 0.137 | 0.073 |
| Unemployed            | 2 (100) | 0 (0) | 0 (0) |
| Employed              | 128 (33.2) | 129 (33.5) | 128 (33.2) |
| Educational status n (%) | 0.753 | 0.744 |
| Illiterate            | 1 (25) | 1 (25) | 2 (50) |
| Under diploma         | 12 (26.1) | 17 (37) | 17 (37) |
| Diploma               | 46 (30.9) | 54 (36.2) | 49 (32.9) |
| Bachelor and higher   | 68 (37) | 55 (29.9) | 61 (33.2) |

PA, physical activity; BMI, body mass index; WC, waist circumference; BMC, bone mineral content; SMM, skeletal muscle mass; SLM, soft lean mass.

Values are represented as means and SD and number (%) for categorical variables.

**ANCOVA (P-value*)** was performed to adjust potential confounding factors; age, energy intake, PA, BMI. BMI consider as the collinear variable for body composition, and anthropometric measurements.

p < 0.05 were considered as significant.

*significant difference was seen between T3 and T2.

A p < 0.05 were considered as significant and p-values of 0.05, 0.06, and 0.07 were considered as marginally significant.

Results

A total of 391 participants were included in the present study. Women had a mean (SD) age of 36.67 (9.10) years and a mean BMI of 31.26 (4.29) kg/m². The majority of women were employed (97%), 47% were highly educated (bachelor's degree...
and higher), and 45.5% had a middle income. The mean of UPF intake in our sample was 442.47 (127.91) g or 96.8%.

The general characteristics of participants among UPF tertiles are presented in Table 1. The average UPF consumption in tertile 1 was <383.681 g, in tertile 2 was from 383.681 g to 467.713 g, and in tertile 3 was >467.713 g. The mean of age (P = 0.003) was statistically different between UPF tertiles in the crude model and after controlling for confounding variables. The mean height (P = 0.047) was statistically different between UPF tertiles in the crude model. According to the Bonferroni’s post-hoc test, the significant mean difference in age was between T2 and T3, and the mean difference was higher in T2 than in T3.

In the categorical variables, the supplementation intake (P = 0.057) and job status (P = 0.073) were marginally significant between UPF tertiles after controlling for confounders. There was no significant difference for other variables (Table 1).

### Dietary intakes among the UPF tertiles

Dietary intakes of all the participants among tertiles of UPF consumption are presented in Table 2. The mean of non-dairy beverages (P = 0.001), dairy beverages (P = 0.001), cookies (cakes) (P = 0.001), potato chips (salty) (P = 0.001),

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**Table 2** Dietary intakes among tertiles of the NOVA score in obese and overweight women (n = 391).

| NOVA score components | Total | T1 (n = 131) | T2 (n = 130) | T3 (n = 130) | P-value | P-value* |
|-----------------------|-------|--------------|--------------|--------------|---------|----------|
|                       |       | <383.681     | 383.681-467.713 | >467.713    |         |          |
| Nondairy beverages (g/d) | 177.351 ± 90.232 | 124.069 ± 25.540 | 157.152 ± 27.648 | 251.242 ± 126.711 | 0.001 | 0.001 |
| Cookies-cakes (g/d)     | 98.913 ± 44.205 | 75.570 ± 25.626 | 97.288 ± 28.007 | 124.061 ± 57.167  | 0.001 | 0.001 |
| Dairy beverages (g/d)    | 47.833 ± 27.952 | 37.472 ± 18.4894 | 46.629 ± 22.117 | 59.479 ± 35.795   | 0.001 | 0.001 |
| Potato chips- salty      | 22.106 ± 13.893 | 17.354 ± 9.094  | 22.652 ± 10.166 | 26.348 ± 18.853   | 0.001 | 0.001 |
| Processed meat- fast food (g/d) | 41.138 ± 25.424 | 28.402 ± 12.600 | 40.230 ± 14.202 | 54.881 ± 35.167   | 0.001 | 0.001 |
| Oil, Sauce (g/d)         | 18.269 ± 8.727  | 16.764 ± 8.5494 | 17.861 ± 7.4184 | 20.194 ± 9.766    | 0.005 | 0.005 |
| Sweet (g/d)              | 36.861 ± 24.0635| 30.679 ± 15.1176| 36.916 ± 17.858 | 43.037 ± 33.8778  | 0.001 | 0.001 |

**Food groups**

| Refined grains (g/d) | 432.348 ± 220.133 | 474.142 ± 191.103 | 380.801 ± 207.529 | 444.129 ± 253.512 | 0.008 | 0.969 |
| Whole grains (g/d)    | 7.586 ± 10.410   | 9.144 ± 11.2396   | 6.769 ± 9.0196    | 6.746 ± 10.831    | 0.177 | 0.361 |
| Fruits (g/d)          | 528.904 ± 338.1681| 605.778 ± 317.153 | 466.287 ± 317.377 | 513.252 ± 370.044 | 0.011 | 0.340 |
| Vegetables (g/d)      | 433.577 ± 263.259| 526.618 ± 264.203 | 382.927 ± 226.814 | 385.498 ± 275.073 | 0.001 | 0.003 |
| Nuts (g/d)             | 14.370 ± 16.1866 | 17.821 ± 17.786   | 11.449 ± 14.354   | 13.795 ± 15.697   | 0.018 | 0.518 |
| Legumes (g/d)         | 52.691 ± 41.7288 | 63.432 ± 49.5718  | 45.834 ± 35.5690  | 48.313 ± 34.0807  | 0.005 | 0.045 |
| Dairys (g/d)          | 387.451 ± 246.357| 438.192 ± 267.952 | 330.196 ± 224.147 | 394.927 ± 233.413 | 0.007 | 0.769 |
| Eggs (g/d)            | 21.687 ± 14.174 | 22.105 ± 12.3656 | 21.235 ± 12.394  | 21.732 ± 17.7520  | 0.909 | 0.569 |
| Fish and seafood (g/d) | 11.408 ± 12.1569 | 12.086 ± 11.932  | 10.743 ± 11.2257 | 11.399 ± 13.4774  | 0.735 | 0.990 |
| Meats (g/d)           | 64.571 ± 50.1758 | 67.371 ± 40.9762  | 54.081 ± 41.6793  | 73.518 ± 65.0100  | 0.022 | 0.250 |
| Red meat (g/d)        | 21.479 ± 18.5197 | 24.003 ± 20.368   | 17.760 ± 15.8117  | 22.894 ± 18.722   | 0.038 | 0.947 |

**Macronutrients and energy**

| Energy intake (kcal/d) | 2633.280 ± 809.432 | 2916.675 ± 654.474 | 2267.608 ± 712.433 | 2713.37 ± 904.867 | 0.001 | - |

| SFA (mg/d)             | 28.409 ± 11.545    | 30.861 ± 11.417    | 24.761 ± 10.291    | 29.587 ± 12.033   | 0.001 | 0.628 |
| MUFA (mg/d)            | 32.008 ± 12.917    | 35.155 ± 13.593    | 27.591 ± 10.563    | 33.253 ± 13.241   | 0.001 | 0.817 |
| PUFA (mg/d)            | 20.082 ± 9.568     | 22.589 ± 10.515    | 17.403 ± 8.316     | 20.235 ± 9.087    | 0.001 | 0.717 |
| Trans fat (g/d)        | 0.0007 ± 0.0003    | 0.001 ± 0.0003     | 0.0086 ± 0.0001    | 0.0005 ± 0.001    | 0.097 | 0.120 |
| Total fiber (g/d)      | 47.344 ± 21.3600   | 57.263 ± 21.377    | 40.359 ± 19.203    | 44.333 ± 19.795   | 0.078 | 0.001 |

pro, protein; Cho, carbohydrate; SFA, saturated fatty acid; MUFA, monounsaturated fatty acid; PUFA, polyunsaturated fatty acid. Values are represented as means (SD).

ANOVA (P-value*) was performed to adjust potential confounding factors (energy intake).

A P-value under 0.05 is considered significant.
TABLE 3  CVD risk factors consist of anthropometric measurements and body composition, biochemical variables, and inflammatory factors among tertiles of NOVA score in obese and overweight women (n = 391).

| Variables              | UPF consumption tertiles | P-value |
|------------------------|--------------------------|---------|
|                        | T1 <383.681 | T2 383.681–467.713 | T3 >467.713 |
| **Body Composition**   |             |                     |             |
| FFM (Kg)               |             |                     |             |
| Crude                  | 47.019 ± 5.938 | 46.217 ± 5.444   | 46.263 ± 5.616 | 0.440 |
| Model 1                | 46.402 ± 0.982 | 47.858 ± 1.037   | 46.017 ± 1.332 | 0.513 |
| Model 2                | 46.286 ± 1.014 | 47.917 ± 1.058   | 46.121 ± 1.347 | 0.499 |
| FMI                    |             |                     |             |
| Crude                  | 18.977 ± 1.618 | 17.977 ± 1.443   | 17.672 ± 1.450 | 0.266 |
| Model 1                | 17.801 ± 0.246 | 18.153 ± 0.260   | 17.838 ± 0.334 | 0.625 |
| Model 2                | 17.729 ± 0.252 | 18.202 ± 0.263   | 17.882 ± 0.33 | 0.479 |
| FMI                    |             |                     |             |
| Crude                  | 13.422 ± 3.163 | 13.318 ± 3.235   | 13.610 ± 3.799 | 0.784 |
| Model 1                | 12.214 ± 0.590 | 12.903 ± 0.623   | 12.217 ± 0.800 | 0.716 |
| Model 2                | 12.168 ± 0.612 | 12.929 ± 0.638   | 12.255 ± 0.813 | 0.700 |
| BF (%)                 |             |                     |             |
| Crude                  | 42.238 ± 5.016 | 41.890 ± 5.255   | 42.550 ± 6.196 | 0.629 |
| Model 1                | 40.208 ± 1.026 | 41.033 ± 1.084   | 39.571 ± 1.392 | 0.725 |
| Model 2                | 40.174 ± 1.066 | 41.058 ± 1.112   | 39.588 ± 1.416 | 0.726 |
| BFM (Kg)               |             |                     |             |
| Crude                  | 34.936 ± 8.395 | 33.830 ± 7.801   | 35.421 ± 9.887 | 0.325 |
| Model 1                | 31.494 ± 1.421 | 33.926 ± 1.501   | 31.150 ± 1.927 | 0.450 |
| Model 2                | 31.387 ± 1.471 | 33.978 ± 1.535   | 31.251 ± 1.955 | 0.450 |
| TF (kg)                |             |                     |             |
| Crude                  | 16.965 ± 3.489 | 16.5070 ± 3.411  | 17.103 ± 4.086 | 0.393 |
| Model 1                | 15.609 ± 0.624 | 16.608 ± 0.660   | 15.450 ± 0.847 | 0.493 |
| Model 2                | 15.571 ± 0.648 | 16.630 ± 0.676   | 15.479 ± 0.861 | 0.492 |
| TF (%)                 |             |                     |             |
| Crude                  | 298.070 ± 12.616 | 312.018 ± 13.326 | 297.691 ± 17.107 | 0.736 |
| Model 1                | 297.023 ± 13.092 | 312.746 ± 13.660 | 298.300 ± 17.394 | 0.712 |
| **Anthropometric measurements** |             |                     |             |
| WC (cm)                |             |                     |             |
| Crude                  | 97.281 ± 16.058 | 97.138 ± 12.693  | 97.951 ± 17.058 | 0.933 |
| Model 1                | 92.021 ± 3.239 | 98.703 ± 3.421   | 89.857 ± 3.491 | 0.259 |
| Model 2                | 91.161 ± 3.329 | 99.287 ± 3.473   | 90.382 ± 4.423 | 0.207 |
| WHR                    |             |                     |             |
| Crude                  | 0.939 ± 0.054 | 1.637 ± 0.818    | 0.936 ± 0.051 | 0.372 |
| Model 1                | 0.931 ± 0.009 | 0.940 ± 0.010    | 0.911 ± 0.013 | 0.236 |
| Model 2                | 0.931 ± 0.010 | 0.939 ± 0.010    | 0.911 ± 0.013 | 0.233 |
| VFA (CM²)              |             |                     |             |
| Crude                  | 168.858 ± 36.720 | 176.087 ± 150.293 | 168.733 ± 42.799 | 0.764 |
| Model 1                | 154.422 ± 6.889 | 161.912 ± 7.276  | 147.917 ± 9.341 | 0.526 |
| Model 2                | 154.298 ± 7.155 | 161.986 ± 7.465  | 148.012 ± 9.506 | 0.536 |
| VFL                    |             |                     |             |
| Crude                  | 17.122 ± 12.037 | 15.612 ± 3.307   | 17.514 ± 17.260 | 0.423 |
| Model 1                | 14.815 ± 0.605 | 15.404 ± 0.639   | 14.262 ± 0.820 | 0.576 |
| Model 2                | 14.826 ± 0.628 | 15.397 ± 0.656   | 14.252 ± 0.835 | 0.589 |
| NC (cm)                |             |                     |             |
| Crude                  | 38.338 ± 12.042 | 36.958 ± 2.702   | 37.430 ± 3.942 | 0.537 |
| Model 1                | 36.130 ± 0.421 | 37.791 ± 0.445   | 36.420 ± 0.571 | 0.036 |
| Model 2                | 36.233 ± 0.433 | 37.723 ± 0.452   | 36.354 ± 0.575 | 0.068 |
| **Biochemical variables** |             |                     |             |
| SBP (mmHg)             |             |                     |             |
| Crude                  | 113.000 ± 15.0006 | 112.227 ± 12.386 | 108.333 ± 17.190 | 0.083 |
| Model 1                | 113.074 ± 1.661 | 111.479 ± 1.691  | 108.975 ± 1.734 | 0.231 |
| Model 2                | 113.374 ± 1.4497 | 110.824 ± 1.504  | 119.552 ± 1.164 | 0.222 |
| DBP (mmHg)             |             |                     |             |
| Crude                  | 77.969 ± 9.586 | 77.930 ± 9.454   | 76.547 ± 12.418 | 0.590 |
| Model 1                | 77.745 ± 1.194 | 77.736 ± 1.216   | 77.931 ± 1.247 | 0.992 |
| Model 2                | 78.237 ± 1.064 | 76.992 ± 1.069   | 78.117 ± 1.172 | 0.677 |

(Continued)
| Variables            | Crude (Mean ± SD) | Model 1 (Mean ± SD) | Model 2  (Mean ± SD) | P-value |
|----------------------|-------------------|---------------------|----------------------|---------|
| HOMA-IR              | 3.240 ± 1.346     | 3.585 ± 1.388       | 3.142 ± 1.007        | 0.073   |
| Insulin (mIU/ml)     | 8.569 ± 9.927     | 8.912 ± 10.343      | 8.536 ± 7.919        | 0.089   |
| FBG (mg/dL)          | 182.38 ± 37.483   | 189.39 ± 33.851     | 183.000 ± 37.733     | 0.371   |
| Urea (mg/dL)         | 177.71 ± 9.420    | 179.29 ± 6.765      | 184.293 ± 4.666      | 0.569   |
| TG (mg/dL)           | 112.18 ± 55.944   | 120.02 ± 59.970     | 116.144 ± 64.776     | 0.922   |
| HDL (mg/dL)          | 47.267 ± 10.965   | 47.340 ± 11.662     | 45.536 ± 9.567       | 0.518   |
| GOT (mg/dL)          | 95.244 ± 23.856   | 97.109 ± 24.795     | 92.029 ± 23.850      | 0.420   |
| GPT (mg/dL)          | 17.720 ± 7.441    | 18.604 ± 8.179      | 16.927 ± 5.976       | 0.358   |
| AIP                  | 0.366 ± 0.236     | 0.362 ± 0.240       | 0.361 ± 0.272        | 0.990   |
| CR1-I                | 4.029 ± 1.206     | 4.194 ± 1.209       | 4.294 ± 2.100        | 0.542   |
| AC                   | 3.029 ± 1.206     | 3.194 ± 1.209       | 3.294 ± 2.100        | 0.542   |
| CHOL Index           | 47.976 ± 21.460   | 49.769 ± 23.040     | 46.492 ± 23.306      | 0.657   |

(Continued)
processed meat (fast food) \( (P = 0.001) \), oil (sauce group) \( (P = 0.005) \), sweet (\( P = 0.001 \)) were statistically different among UPF tertiles, with it being higher in the third tertile. With increasing UPF consumption, non-dairy beverages, cookies (cakes), dairy beverages, potato chips (salty), processed meat (fast food), oil, sauce, and sweet have increased in the crude and adjusted model.

CVD risk factors among the UPF tertiles

The association of CVD risk factors among UPF consumption tertiles is shown in Table 3. UPF consumption was associated with the HOMA–IR index \( (P = 0.024) \), hs-CRP \( (P = 0.001) \), and TYG–WC \( (P = 0.026) \). On the contrary, it was marginally associated with the markers TGF \( (P = 0.077) \), AC \( (P = 0.072) \), CRI–1 \( (P = 0.062) \), and NC \( (P = 0.068) \).


dietary measurements, body composition, biochemical variables, and inflammatory factors.

Association between UPF consumption and CVD risk factors, anthropometric measurements, body composition, biochemical variables, and inflammatory factors.
TABLE 4 Association between NOVA score and CVD risk factors, anthropometric measurements, body composition, biochemical variables, and inflammatory factors in obese and overweight women (n = 391).

| Variables          | NOVA score | P-value | P-value* |
|--------------------|------------|---------|----------|
|                    | β (SE)     | CI (95%)|          |
| Body composition   |            |         |          |
| FFM (Kg)           | Crude      | −0.001 (0.002) | 0.005, 0.003 | 0.682 | - |
|                    | Model 1    | −0.004 (0.004) | 0.011, 0.003 | - | 0.278 |
|                    | Model 2    | −0.004 (0.004) | 0.001, 0.001 | - | 0.056 |
| FFM (Kg)           | Model 1    | 0.001 (0.002) | 0.005, 0.004 | - | 0.878 |
|                    | Model 2    | −5.286 (0.002) | 0.004, 0.004 | - | 0.981 |
| FFM (Kg)           | Crude      | −0.004 (0.004) | 0.014, 0.006 | 0.427 | - |
|                    | Model 1    | 0.001 (0.002) | 0.005, 0.004 | - | 0.201 |
|                    | Model 2    | −0.001 (0.001) | 0.003, 0.001 | - | 0.376 |
| FFMI               | Crude      | 0.001 (0.004) | 0.006, 0.008 | - | 0.056 |
|                    | Model 1    | 0.001 (0.004) | 0.006, 0.008 | - | 0.768 |
|                    | Model 2    | 0.001 (0.004) | 0.006, 0.008 | - | 0.768 |
| FMI                | Crude      | 0.003 (0.002) | 0.001, 0.007 | 0.115 | - |
|                    | Model 1    | 0.001 (0.004) | 0.006, 0.008 | - | 0.878 |
|                    | Model 2    | −0.001 (0.001) | 0.003, 0.001 | - | 0.878 |
| BF (%)             | Crude      | −0.004 (0.004) | 0.014, 0.006 | 0.427 | - |
|                    | Model 1    | 0.001 (0.002) | 0.005, 0.004 | - | 0.201 |
|                    | Model 2    | −5.286 (0.002) | 0.004, 0.004 | - | 0.981 |
| BF (%)             | Crude      | −0.004 (0.004) | 0.014, 0.006 | 0.427 | - |
|                    | Model 1    | 0.001 (0.002) | 0.006, 0.008 | - | 0.768 |
|                    | Model 2    | 0.001 (0.004) | 0.006, 0.008 | - | 0.768 |
| BFMI (Kg)          | Crude      | 0.006 (0.003) | 0.001, 0.013 | 0.084 | - |
|                    | Model 1    | −0.002 (0.006) | 0.013, 0.009 | - | 0.719 |
|                    | Model 2    | −0.002 (0.006) | 0.014, 0.009 | 0.658 | - |
| TF (kg)            | Crude      | 0.002 (0.001) | 0.001, 0.005 | 0.097 | - |
|                    | Model 1    | −0.001 (0.002) | 0.005, 0.004 | - | 0.812 |
|                    | Model 2    | −0.001 (0.002) | 0.006, 0.004 | - | 0.709 |
| TF (%)             | Crude      | 0.035 (0.028) | 0.020, 0.089 | 0.213 | - |
|                    | Model 1    | 0.001 (0.044) | 0.086, 0.088 | - | 0.988 |
|                    | Model 2    | −0.005 (0.045) | 0.094, 0.083 | - | 0.904 |
| VFA (cm²)          | Crude      | 0.028 (0.037) | 0.044, 0.100 | 0.442 | - |
|                    | Model 1    | −0.005 (0.082) | −0.168, 0.157 | - | 0.951 |
|                    | Model 2    | −0.007 (0.085) | −0.174, 0.159 | - | 0.930 |
| VFL                | Crude      | 0.002 (0.005) | 0.007, 0.012 | 0.647 | - |
|                    | Model 1    | 0.005 (0.011) | 0.017, 0.028 | - | 0.651 |
|                    | Model 2    | 0.006 (0.012) | 0.017, 0.029 | - | 0.076 |
| Biochemical variables |          |         |          |
| Insulin (mIU/ml)   | Crude      | −6.160 (0.001) | 0.001, 0.001 | 0.617 | - |
|                    | Model 1    | 0.001 (0.001) | 0.001, 0.000 | - | 0.230 |
|                    | Model 2    | 0.001 (0.001) | 0.001, 0.001 | - | 0.273 |
| HOMA_IR            | Crude      | 0.001 (0.001) | 0.002, 0.001 | 0.671 | - |
|                    | Model 1    | −2.996 (0.001) | 0.002, 0.002 | - | 0.981 |
|                    | Model 2    | 0.001 (0.001) | 0.001, 0.033 | - | 0.055 |
| QUICKI (mg/lit)    | Crude      | −1.731 (0.001) | 0.001, 0.001 | 0.205 | - |
|                    | Model 1    | −4.306 (0.001) | 0.001, 0.001 | - | 0.720 |
|                    | Model 2    | −3.775 (0.001) | 0.001, 0.001 | - | 0.042 |
| hs-CRP (mg/l)      | Crude      | 0.001 (0.003) | 0.005, 0.005 | 0.962 | - |
|                    | Model 1    | 0.001 (0.003) | 0.006, 0.007 | - | 0.875 |
|                    | Model 2    | 0.001 (0.003) | 0.006, 0.007 | - | 0.875 |
| FBG (mg/dL)        | Crude      | −0.004 (0.005) | 0.014, 0.006 | 0.273 | - |
|                    | Model 1    | −0.004 (0.006) | 0.017, 0.009 | - | 0.506 |
|                    | Model 2    | −0.006 (0.007) | 0.020, 0.007 | - | 0.335 |
| SBP (mmHg)         | Crude      | −0.012 (0.007) | 0.027, 0.002 | 0.102 | - |

(Continued)
TABLE 4 Continued

| Variables        | NOVA score | P-value | P-value* |
|------------------|------------|---------|----------|
|                  | β (SE)     | CI (95%)|          |
| Model 1          |            |         |          |
| Model 2          |            |         |          |
| DBP (mmHg)       |            |         |          |
| Crude            | −0.008 (0.005) | −0.018, 0.002 | 0.134 | - |
| Model 1          | −0.004 (0.086) | −0.016, 0.008 | - | 0.503 |
| Model 2          | −0.007 (0.006) | −0.019, 0.005 | - | 0.236 |
| TC (mg/dL)       |            |         |          |
| Crude            | 0.003 (0.019) | −0.036, 0.041 | 0.893 | - |
| Model 1          | 0.012 (0.023) | −0.032, 0.055 | - | 0.598 |
| Model 2          | 0.020 (0.022) | −0.024, 0.064 | - | **0.073** |
| TG (mg/dL)       |            |         |          |
| Crude            | 0.003 (0.032) | −0.060, 0.067 | 0.916 | - |
| Model 1          | 0.031 (0.042) | −0.052, 0.115 | - | 0.456 |
| Model 2          | 0.041 (0.043) | −0.044, 0.126 | - | 0.344 |
| HDL (mg/dL)      |            |         |          |
| Crude            | −0.005 (0.006) | −0.016, 0.006 | 0.391 | - |
| Model 1          | −0.004 (0.007) | −0.017, 0.010 | - | 0.588 |
| Model 2          | −0.002 (0.007) | −0.016, 0.011 | - | 0.720 |
| LDL (mg/dL)      |            |         |          |
| Crude            | −0.010 (0.013) | −0.036, 0.015 | 0.433 | - |
| Model 1          | −0.043 (0.015) | −0.030, 0.030 | - | 0.997 |
| Model 2          | 0.007 (0.016) | −0.024, 0.038 | - | 0.662 |
| GOT (mg/dL)      |            |         |          |
| Crude            | −0.004 (0.004) | −0.012, 0.0003 | 0.274 | - |
| Model 1          | −0.007 (0.005) | −0.017, 0.003 | - | 0.167 |
| Model 2          | −0.006 (0.005) | −0.017, 0.004 | - | 0.245 |
| GPT (mg/dL)      |            |         |          |
| Crude            | −0.006 (0.007) | −0.020, 0.008 | 0.391 | - |
| Model 1          | −0.016 (0.009) | −0.034, 0.003 | - | 0.097 |
| Model 2          | −0.015 (0.010) | −0.034, 0.004 | - | 0.117 |
| PAI-1 (mg/dL)    |            |         |          |
| Crude            | −0.019 (0.022) | −0.063, 0.025 | 0.401 | - |
| Model 1          | −0.012 (0.033) | −0.077, 0.053 | - | 0.705 |
| Model 2          | −0.005 (0.033) | −0.071, 0.061 | - | 0.883 |
| MCP1 (mg/dL)     |            |         |          |
| Crude            | −0.047 (0.052) | −0.15, 0.055 | 0.363 | - |
| Model 1          | −0.041 (0.072) | −0.184, 0.102 | - | 0.570 |
| Model 2          | −0.039 (0.073) | −0.184, 0.107 | - |          |
| TGF (mg/dL)      |            |         |          |
| Crude            | 0.034 (0.036) | −0.038, 0.106 | 0.106 |          |
| Model 1          | 0.092 (0.038) | 0.016, 0.167 | - | **0.018** |
| Model 2          | 0.101 (0.040) | 0.023, 0.180 | - | **0.012** |
| IL-1β (mg/dL)    |            |         |          |
| Crude            | 0.001 (0.001) | −0.001, 0.003 | 0.250 | - |
| Model 1          | 0.001 (0.001) | −0.002, 0.003 | - | 0.596 |
| Model2           | 0.001 (0.001) | −0.001, 0.003 | - | **0.060** |
| AIP (mg/dL)      |            |         |          |
| Crude            | 2.472 (0.001) | 0.001, 0.01 | 0.853 | - |
| Model 1          | 0.001 (0.001) | 0.001, 0.001 | - | 0.482 |
| Model2           | 0.001 (0.001) | −0.001, 0.011 | - | 0.072 |
| CRI-I            |            |         |          |
| Crude            | 0.001 (0.001) | −0.001, 0.002 | 0.476 | - |
| Model 1          | 0.001 (0.001) | −0.001, 0.002 | - | 0.277 |
| Model2           | 0.001 (0.001) | −0.001, 0.002 | - | **0.064** |
| CRI-II           |            |         |          |
| Crude            | −3.679 (0.001) | −0.001, 0.001 | 0.907 | - |
| Model 1          | 0.001 (0.001) | −0.001, 0.001 | - | 0.574 |
| Model2           | 0.001 (0.001) | 0.001, 0.001 | - | 0.431 |
| AC               |            |         |          |
| Crude            | 0.001 (0.001) | −0.001, 0.002 | 0.476 | - |

(Continued)
biochemical variables, and inflammatory factors in crude and adjusted models present with β-value and a 95% CI is shown in Table 4. In the model 1, there was a significant association between UPF consumption and TGF (β: 0.101, 95% CI: 0.023, 0.180, p = 0.012). Also, there was a significant association between UPF consumption and AC (β: 0.011, 95% CI: 0.001, 0.032, p = 0.034), VLF (β: 0.006, 95% CI: −0.017, 0.029, p = 0.076), and ISQIUKI (β: −3.775, 95% CI: 0.001, 0.001, P = 0.042). With increasing one gram of UPF intake, AC increases to 0.011, VLF increases by 0.006, and QUICKI is significantly reduced by −3.775 mg/lit. The other variables in Table 3 had no significant association.

Discussion

To the best of our knowledge, this is the first study investigating the relationship between UPF intake and cardiometabolic risk in overweight and obese Iranian women.

In the current study, we found an inverse association between the NOVA score and FFM. In addition, we observed a positive association between the NOVA score and VFL, AC, the HOMA-IR-index, QUICKI, TC, TGF, IL-1B, and the CRI-I. The positive association observed between UPFs and mentioned markers might be partly explained by their poorer nutritional quality compared with the NOVA scores’ lower tertiles. In fact, UPFs tend to be higher in saturated fats, sugar, and energy, and poorer in dietary fiber (5, 9, 21, 33). The positive association between consumption of UPF and inflammatory markers that have been seen among women may be explained by the greater accumulation of body fat in women (34). In line with our study, in 2021, a systematic review and meta-analysis of 7 cohort studies (207,291 adults) showed a significant positive association between UPF consumption and the risk of CVDs among adults with a BMI of more than 25 kg/m² (35). Moreover, a recent narrative review study by Matos et al. (36) concluded that the consumption of UPFs is positively associated with the prevalence of chronic complications, including obesity, hypertension, CVDs, type 2 diabetes, and consequently the risk of all-cause mortality (36). The mechanism by which UPF is associated with CVD is summarized in Figure 1.

In our study, individuals at higher tertiles of NOVA (compared to tertile 1) had higher NC, AC, TyG-WC, HOMA-IR-INDEX, CRI-I, TGF, and hs-CRP levels. Beslay et al., in a large observational prospective study of 110,260 adults, indicated that higher consumption of UPF was associated with a gain in BMI and higher risks of overweight and obesity (37). Also, a prospective cohort of healthy subjects in Italy showed that adults in the highest quartile of UPF consumption
UPF consumption has been linked to obesity, which can stimulate the chronic inflammation cascade and increase the risk of CVD and all-cause mortality. 

had a higher risk of CVD (38). It is well known that adipose tissue produces cytokines that induce inflammatory markers production (39). Thus, the association between the consumption of UPFs and the inflammatory response is expected to be mostly dependent on adiposity. A cross-sectional study displayed that there might be a direct association between consumption of ultra-processed foods and CRP levels, under the assumption that the high-glycemic index of these food products could stimulate the whole chronic inflammation cascade, along with an indirect association mediated by obesity. They suggest that decreased consumption of UPFs can reduce chronic low-grade inflammation, perhaps by reducing obesity (40).

In the present study, participants with higher NOVA scores had higher consumption of cakes and sweets, processed meats, and fast foods. Bonaccio et al., in 2021, indicated that a high proportion of UPF in the diet was associated with an increased risk of CVD and all-cause mortality, probably because of its high dietary content of sugar (38). Rising evidence suggests that the consumption of UPF products determined by the low-nutritional quality and high-calorie content adversely contribute to an unhealthy dietary pattern, which enhances the risk of all-cause mortality as a substantial risk factor (36). In addition, additives in such foods containing noncaloric artificial sweeteners, emulsifiers, and thickening agents cause numerous chronic disorders such as metabolic dysfunction, systemic inflammation, endothelial dysfunction, and disrupted immune response (41–43). More than that, synthetic compounds used in the packaging of UPFs, such as bisphenol A, can act as...
xenohormones. Particularly, bisphenol A has been indicated to impair reproductive function and augment the risk of cancer-cause mortality (44, 45). Recently, a study conducted in the US displayed that UPF consumption was related to increased exposure to phthalates (44), which has suggested associations with obesity (46). Some food additives specific to UPFs might be involved in obesity etiology. For instance, saccharin, an artificial sweetener, could potentiate glucose-stimulated insulin release from isolated pancreatic β-cells (47), leading to insulin resistance and possibly weight gain. Several emulsifiers (such as carboxymethyl cellulose and polysorbate-80) induced metabolic perturbations, alterations to the gut microbiota, and low-grade inflammation in mice (48). Carrageenan, in the top 20 used additives, might augment insulin resistance and inhibit insulin signaling in mouse liver and human HepG2 cells (49, 50), which might, in turn, induce weight gain (51). Trans fatty acids found in UPFs containing hydrogenated oils have been associated with cardiovascular disease (52) and obesity (53), apparently by altering nutrient handling in the liver, the adipose tissues, and the skeletal muscle (54). Acrylamide, a neo-formed compound created during thermal processing of food as a result of the Maillard reaction, was shown to induce adipocyte differentiation and obesity in mice (55).

The present study possesses some strengths and limitations. At first, to the best of our knowledge, this is the first study to have evaluated the association between processed food intake and CVD risk in overweight and obese Iranian women. Second, dietary intake was assessed using a validated questionnaire. Third, in the current study, we assessed several inflammatory markers, other biochemical parameters, and body composition as risk factors for CVD.

Nevertheless, despite these strengths, we must acknowledge some limitations in the present study. First, the cross-sectional nature of this study limited the ability to suggest a causal relationship between UPF intake and the risk of cardiovascular diseases. Second, some errors may be present in the dietary assessment, mostly due to recall bias and misclassification errors; to overcome such errors, we evaluated biomarkers such as vitamin C to better capture individuals’ variability in intakes. Third, our result may not be generalizable to normal-weight women. At final, although we considered known potential confounders, residual confounding cannot be ruled out.

Conclusion

In conclusion, an increase of one gram of UPFs consumption is associated with an increase in TGF, AC, and VFL but with a decrease in QUICKI. Higher consumption of UPF is significantly associated with an enhanced risk of adult inflammation and cardiometabolic risk factors. Further large studies involving participants of different ages and genders are highly warranted, in addition to experimental studies, to draw a more definite conclusion and disentangle the mechanisms by which UPFs may affect health.

Data availability statement

Participants of this study disagreed on their data being shared publicly, so supporting data is not available. Further inquiries can be directed to the corresponding author KM, mirzaei_kh@tums.ac.ir; mirzaei_kh@sina.tums.ac.ir.

Ethics statement

The studies involving human participants were reviewed and approved by Tehran University of Medical Sciences, Tehran, Iran. The patients/participants provided their written informed consent to participate in this study.

Author contributions

DH and SN wrote the paper. FS and FM-E performed the statistical analyses. SJ, MD, AS, and JB critically reviewed and revised the manuscript. KM had full access to all of the data in the study and took responsibility for the integrity and accuracy of the data. All authors read and approved the final manuscript.

Funding

This study is funded by grant from the Tehran University of Medical Sciences (TUMS) (Grant ID: 97-03-161-41017).

Acknowledgments

We are grateful to all the participants for their contribution to this research.

Conflict of interest

The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

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References

1. World Health Organization (WHO). Cardiovascular Diseases (2021). Available online at: https://www.who.int/news-room/fact-sheets/detail/cardiovascular-diseases-(cvs)

2. Mozaffarian D. Dietary and policy priorities for cardiovascular disease, diabetes, and obesity: a comprehensive review. Circulation. (2016) 133:187-225. doi: 10.1161/CIRCULATIONAHA.115.018855

3. Sarrafzadegan N, Mohammadifar N. Cardiovascular disease in Iran in the last 40 years: Prevalence, mortality, morbidity, challenges and strategies for cardiovascular prevention. Arch Iran Med. (2019) 22:204–10.

4. Luiten CM, Steenhuis IH, Eyles H, Ni Mhurchu C, Waterlander WE. Ultra-processed foods have the worst nutrient profile, yet they are the most available packaged products in a sample of New Zealand Supermarkets. Public Health Nutr. (2016) 19:539–50. doi: 10.1017/S1368946416002177

5. Adams J, White M. Characterisation of UK diets according to degree of food processing and associations with socio-demographics and obesity: cross-sectional analysis of UK national diet and nutrition survey (2008-12). Int J Behav Nutr Phys Act. (2015) 12:160. doi: 10.1186/s12966-015-0317-y

6. Cedeño G, Reyes M, da Costa Louzada ML, Martínez Steele E, Monteiro CA, Corvalán C, et al. Ultra-Processed Foods and Added Sugars in the Chilean Diet (2010). Public Health Nutr. (2018) 21:125–33. doi: 10.1017/S1368946417001161

7. Costa Louzada ML, Martins AP, Canella DS, Baraldi LG, Levy RB, Claro RM, et al. Ultra-processed foods and the nutritional dietary profile in Brazil. Rev Saude Publica. (2015) 49:538. doi: 10.1590/0034-8910.201549006132

8. Martínez Steele E, Baraldi ML, LG, Louzada, Moubcarak JC, Mozaffarian D, Monteiro CA. Ultra-processed foods and added sugars in the US diet: evidence from a nationally representative cross-sectional study. BMJ Open. (2016) 6:e009892. doi: 10.1136/bmjopen-2015-009892

9. Moubcarak JC, Batal M, Louzada ML, Martínez Steele E, Monteiro CA. Consumption of ultra-processed foods predicts diet quality in Canada. Appetite. (2017) 108:512–20. doi: 10.1016/j.appet.2016.11.006

10. Moubcarak JC, Martins AP, Claro RM, Levy RB, Cannon G, Monteiro CA. Consumption of ultra-processed foods and likely impact on human health. Evid Can Public Health Nutr. (2013) 16:2240–4. doi: 10.1891/ech.2013.16.12.2240

11. Poti JM, Mendez MA, Ng SW, Popkin BM. Is the degree of food processing and convenience linked with the nutritional quality of foods purchased by us households? Am J Clin Nutr. (2015) 101:1251–62. doi: 10.3945/ajcn.114.109925

12. Slimani N, Dehavern G, Sougatnde DA, Biessey C, Chaix V, van Bakel MM, et al. Contribution of highly industrially processed foods to the nutrient intakes and its role in metabolic disease. Nutrients. (2018) 10.3655. doi: 10.3989/nut.0103365

13. Leroy J, Conklin DJ, Riggs DW, Myers JA, O'Toole TE, Hamzei J, et al. Acrolein exposure is associated with increased cardiovascular disease risk. J Am Heart Assoc. (2014) 3:e000934. doi: 10.1161/JAHA.114.000934

14. Chrysohoou C, Lewis B, Fallah R, Montazeri A, Norat T, de Vivo I, et al. Ultra-processed food consumption and risk of type 2 diabetes: a systematic review and pooled analysis of 10 cohort studies. Public Health Nutr. (2015) 18:75–83. doi: 10.1017/S1368946414002817

15. Azadbakht L, Fallah R, Norat T, de Vivo I, de Ferranti S, Trichopoulos D, et al. Ultra-processed food consumption and risk of type 2 diabetes: a systematic review and dose-response meta-analysis of 207,291 participants. J Transl Med. (2021) 19:62. doi: 10.1186/s12967-016-1020-5

16. Hosseiniabsab et al. Frontiers in Nutrition (2022). 14 frontiersin.org
cross-sectional results from the Elsa-Brasil study. *São Paulo Med J*. (2019) 137:169–76. doi: 10.1590/1516-3180.2018.036070219

41. Martino JV, Van Limbergen I, Cahill LE. The role of carrageenan and carboxymethylcellulose in the development of intestinal inflammation. *Front Pediatr*. (2017) 5:96. doi: 10.3389/fped.2017.00096

42. Suez J, Korem T, Zilberman-Schapira G, Segal E, Elinav E. Non-caloric artificial sweeteners and the microbiome: findings and challenges. *Gut Microbes*. (2015) 6:149–55. doi: 10.1080/19490976.2015.1017700

43. Chassaing B, Koren O, Goodrich JK, Poole AC, Sirivasan S, Ley RE, et al. Dietary emulsifiers impact the mouse gut microbiota promoting colitis and metabolic syndrome. *Nature*. (2015) 519:92–6. doi: 10.1038/nature14232

44. Buckley JP, Kim H, Wong E, Rehbolz CM. Ultra-processed food consumption and exposure to phthalates and bisphenols in the US National Health and Nutrition Examination Survey, 2013-2014. *Environ Int*. (2019) 131:105057. doi: 10.1016/j.envint.2019.105057

45. Cimmino I, Fiory F, Perruolo G, Miele C, Beguinot F, Formisano P, et al. Potential Mechanisms of Bisphenol a (Bpa) contributing to human disease. *Int J Mol Sci*. (2020) 21:5761. doi: 10.3390/ijms21165761

46. Vafeiadi M, Myridakis A, Roumeliotaki T, Margetaki K, Chalkiadaki G, Dermitzaki E, et al. Association of early life exposure to phthalates with obesity and cardiometabolic traits in childhood: sex specific associations. *Front Public Health*. (2018) 6:327. doi: 10.3389/fpubh.2018.00327

47. Kyriazis GA, Soundaranpandian MM, Tryberg B. Sweet taste receptor signaling in beta cells mediates fructose-induced potentiation of glucose-stimulated insulin secretion. *Proc Natl Acad Sci U S A*. (2012) 109:E524–32. doi: 10.1073/pnas.1115183109

48. Roca-Saavedra P, Mender-Vilabril V, Miranda JM, Nebot C, Cardelle-Cobas A, Franco CM, et al. Food additives, contaminants and other minor components effects on human gut microbiota-a review. *J Physiol Biochem*. (2018) 74:69–83. doi: 10.1007/s13185-017-0564-2

49. Bhattacharyya S, O-Sullivan I, Katyal S, Unterman T, Tobacman JK. Exposure to the common food additive carrageenan leads to glucose intolerance, insulin resistance and inhibition of insulin signalling in HepG2 cells and C57Bl/6j Mice. *Diabetologia*. (2012) 55:194–203. doi: 10.1007/s00125-011-2333-z

50. Bhattacharyya S, Feferman L, Tobacman JK. Carrageenan Inhibits Insulin Signaling through Grb10-Mediated Decrease in Tyr(P)-Irs1 and through Inflammation-Induced Increase in Ser(P)307-Irs1. *J Biol Chem*. (2015) 290:10764–74. doi: 10.1074/jbc.M114.630853

51. Kahn SE, Hull RL, Utschneider KM. Mechanisms Linking Obesity to Insulin Resistance and Type 2 Diabetes. *Nature*. (2006) 444:840–6. doi: 10.1038/nature05482

52. Mozaffarian D, Katan MB, Ascherio A, Stampfer MJ, Willett WC. Trans fatty acids and cardiovascular disease. *N Engl J Med*. (2006) 354:1601–13. doi: 10.1056/NEJMra054035

53. Thompson AK, Minihane AM, Williams CM. Trans fatty acids and weight gain. *Int J Obes (Lond).* (2011) 35:315–24. doi: 10.1038/ijo.2010.141

54. Dorfman SE, Laurent D, Gounaris JS, Li X, Mullarkey TL, Rocheford EC, et al. Metabolic Implications of Dietary Trans-Fatty Acids. *Obesity (Silver Spring)*. (2009) 17:1200–7. doi: 10.1038/oby.2008.662

55. Lee HW, Pyo S. Acrylamide induces adipocyte differentiation and obesity in mice. *Chem Biol Interact*. (2019) 298:24–34. doi: 10.1016/j.cbi.2018.10.021