Association of chrono-nutrition components with cardiometabolic health in a sample of Iranian adults: a cross-sectional study

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Abstract

Chrono-nutrition is an emerging field that examines how the frequency and timing of meals impact health. Previous research shows inconsistency in the relationship between chrono-nutritional components and cardiometabolic health. We investigated cross-sectional associations between these components and cardiometabolic health in 825 Iranian adults aged 20-59 years. Dietary data, including the number of eating occasions (EOs), meal timing, and meal irregularity of energy intake, were collected using three 24-hour dietary recalls. Anthropometric measurements, blood pressure, and laboratory tests (fasting plasma glucose, lipid profile, insulin, uric acid, and c-reactive protein) were conducted. Insulin resistance and sensitivity (HOMA-IR, HOMA-IS), the triglyceride-glucose, the lipid accommodation product and body mass index (BMI) were calculated. The demographic and morning-evening questionnaire (MEQ) was completed. General linear regression was used to assess associations between chrono-nutritional components and outcomes. Interactions with age and BMI were examined in all associations. Chrono-nutrition components were not significantly related to cardiometabolic risk factors in the total population. However, a lower number of EOs was associated with an increased LDL/HDL-C ratio (β (95% CI): 0.26 (0.06–0.48)) among overweight and obese participants. Additionally, less irregularity in breakfast energy intake was associated with a lower total cholesterol/HDL-C ratio (-0.37 (-0.95 to -0.18)) and a lower LDL-C/HDL-C ratio (-0.32 (-0.79 to -0.13)) among participants with a normal BMI (all $p < 0.05$). The study concluded that more frequent meals, and regular energy intake might enhance cardiometabolic health cross-sectionally, highlighting the need for prospective studies to further investigate these associations and the mediating role of BMI.

Abbreviations

BP = blood pressure; BMI = body mass index; CRP = c-reactive protein; CVD = cardiovascular disease; EOs = eating occasions; FPG = fasting plasma glucose; FDR = false discovery rate; GLP-1 = glucagon-like peptide-1; HDL-C = high-density lipoprotein cholesterol; HOMA-IR = homeostatic model assessment for insulin resistance; HOMA-IS = homeostatic model assessment for insulin sensitivity; IPAQ = international physical activity questionnaire; LDL-C = low-density lipoprotein cholesterol; LAP index = lipid Accommodation Product Index; MEQ = morning evening questionnaire; TG = triglycerides; TC = total cholesterol; TyG index = triglyceride-glucose index; WC = waist circumference.

Introduction

Chrono-nutrition is an exciting and rapidly growing field in nutritional epidemiology that examines the interplay of meal frequency, timing, and regularity. This innovative area underscores how "when to eat" can significantly impact health[1]. The timing of food intake could influence various physiological processes and metabolism. Additionally, irregular eating patterns can disrupt the biological clock, causing misalignment in wake/sleep, fasting/feeding, and light/dark cycles, potentially leading to metabolic dysregulation[2, 3].

Meal timing patterns are known to be factors associated with the development of chronic diseases, e.g., atherosclerosis and metabolic abnormalities[4-6]. Irregularity in meal timing can disrupt the circadian rhythm, which can cause abnormal metabolic regulation and increased cardiometabolic risks[7]. Current evidence also shows that nutrient composition[8-10], frequency, time[11, 12], and regularity of meals[11, 13] can affect cardiometabolic risk factors, including insulin resistance, dyslipidemia, and obesity. Eating in circadian misalignment worsens several cardiometabolic factors, particularly glucose tolerance[14-16], and impairs insulin sensitivity and secretion[17, 18]. A study of Korean adults showed that eating two meals a day increased the risk of metabolic syndrome compared to eating three meals a day[19]. Furthermore, studies have shown an increased incidence of obesity among shift workers, revealing the role of circadian rhythms[20-22]. Prior research has focused on one dimension of chrono-nutrition. In this study, we will examine all three dimensions of chrono-nutrition.

Despite our ever-growing knowledge of circadian rhythms, we still have little insight into meal timing patterns in the context of mixed meals and their impact on cardiometabolic health. Therefore, this study aimed to identify the relationships between chrono-nutritional components and cardiometabolic health in the Iranian adult population.

Methods

Study design

A cross-sectional study was conducted among apparently healthy men and women (who did not report any previous diagnosis of chronic diseases such as diabetes, cardiovascular diseases, and chronic kidney, lung, and liver diseases) from Iran who attended the healthcare centers of Tehran (February 2019 to August 2019). A sample size of 546 individuals was calculated using the formula $n = (z^2p(1-p))/d^2$ [23], based on the prevalence of obesity (68.5%) in Tehran[24], an error

coefficient of d = 0.04 and an α level of 0.05. Considering the effect design of 1.3 and the exclusion of participants with under- and overreporting (20%), the final sample size was estimated to be 850 participants. We recruited using two-stage cluster sampling from five geographic areas of Tehran, selecting participants from 25 healthcare centers using a proportion-to-size sampling method. The inclusion criteria required participants to be 20-59 years old, have a body mass index (BMI) between 18.5 and 39.9 kg/m², and, crucially, not be diagnosed with any acute diseases. Exclusion criteria included pregnancy, lactation, and individuals with under- or overreporting of total energy intake.

Ethical Approval

The sample was collected by coordinating with the health care centers of Tehran. This study was conducted according to the guidelines of the Declaration of Helsinki, and all procedures were ethically approved by the Ethics Committee of Tehran University of Medical Sciences (ethics number: IR.TUMS.VCR.REC.1399.295). Participants were fully informed of the study's purpose, and all provided written informed consent before participation. The researcher and illiterate participants had a simple language conversation to give them information, and informed consent was then stamped or fingerprinted as a form of agreement.

Dietary intake assessment, eating occasion, and meal timing

Dietary data were obtained according to three 24-hour dietary recalls on non-consecutive days within the week, one weekend, and two weekdays. We conducted all recalls by trained dietitians during a private interview. The first 24-hour dietary recall was recorded during the first visit to the health care center. The following data were collected via telephone on random days. Eating occasions (EOs) were defined as events that provided at least 50 kilocalories, with a separation in time from a preceding or following eating event of at least 15 minutes[25]. Subjects reported the following types of EOs in which food was consumed: breakfast, lunch, dinner, and snacks. The definition of the main mealtime of food intake was explained in a prior article[26]. The fasting window or nightly fasting duration was defined by calculating the hours between the last EOs reported in the 24-hour dietary recall for the previous day and the first EOs obtained from a question regarding the current day. This method allowed us to accurately assess the fasting duration based on participants' responses.

Daily and main meal intake of all food items, derived from three 24-hour dietary recalls, were converted into grams per day by using household measures and standard portions[27]. The intake

of food groups was adjusted for energy intake using the residual method[28]. We used Nutritionist IV software (First Databank, San Bruno, CA, USA), modified for Iranian foods, to obtain the values of energy and nutrient intake per day. Based on the predefined dietary energy cut-off values, men and women were excluded if their reported average dietary energy intake levels were below < 800 kcal/d or above > 4000 kcal/d and < 500 kcal/d or above > 3500 kcal/d, respectively[29]. We excluded participants who underreported or overreported their total energy intake from the analysis to evaluate the potential impact on the results. Out of the 850 participants, we excluded 25 participants—two individuals due to underreporting and the other 23 participants due to overreporting their energy intake. Ultimately, 825 participants were included. (Figure S1)

Energy intake irregularity at the main meal level

The irregularity score of meal energy intake was calculated. The variance in energy intake per meal was used as a proxy. The absolute difference of the individual energy intake from the 3-day mean energy intake was divided by the 3-day mean energy intake, multiplied by 100, and then the average over the three days. A low score indicated more regular energy intake patterns, while a higher score reflected more irregular energy intake patterns[30].

Data collection

The data were collected from each participant through a face-to-face interview. Sociodemographic information was gathered using prespecified data extraction forms and included age, sex, smoking status (not smoking, ex-smoking, current smoking), education level (illiterate, under diploma and diploma, educated), occupation status (employed, unemployed, retired), night sleep duration on weekdays/weekend, and supplement intake (yes or no).

Physical activity

Physical activity was measured by the short form of the validated International Physical Activity Questionnaire (IPAQ) [31]. Participants reported the time spent walking or performing moderate- and/or vigorous-intensity activities within the previous seven days. The overall physical activity level was measured in the form of metabolic equivalent minutes per week (MET-minutes/week). MET scores were then categorized into three levels: a point score < 600 MET-min/week indicated low physical activity, a point score 600 - 3000 MET-min/week indicated moderate physical activity and a point score >3000 MET-min/week indicated high physical activity[32].

Morning Evening Questionnaire (MEQ)

The MEQ was a 19-item scale with several different options developed by Horn and Steberg in which the subject was asked to specify the rhythm and habits of life and the hours of sleep and wakefulness at night[33]. The questions had different options and specific scoring methods. The participants were asked about their hours of sleep and wakefulness and their preferences for physical and mental tasks to determine their daily mood. The questionnaire options did not have equal values , and based on the initial analysis of its creators, the possibilities of some questions being given different values than other questions. The score range varied from 16 to 86; higher scores indicated a preference for morningness, while lower scores suggested eveningness, based on the Persian Validation Questionnaire[34].

Assessment of blood pressure

Blood pressure (BP) was measured by a digital barometer (BC 08, Beurer, Germany) after at least 10 -15 minutes of rest and sitting. BP was measured twice for each person, and the average BP was reported for each person.

Anthropometric measurements

Weight was measured using a Seca weighing scale (Seca and Co. KG; 22 089 Hamburg, Germany; Model: 874 1321009; designed in Germany; made in China) with light clothing (without shoes, coat, or raincoat). A wall stadiometer board with a sensitivity of 0.1 cm was used to measure standing height without shoes. BMI was calculated as weight (in kilograms) divided by height (in meters squared). Waist circumference (WC) was measured using a nonstretchable fiberglass measuring tape at the midpoint between the lower border of the rib cage and the iliac crest, according to the guiding protocol of the WHO[35].

Laboratory investigations

Participants donated 10 ml of blood from 7:00 -10:00 a.m. after fasting for 12 hours. Blood samples were subsequently collected in acid-washed test tubes without anticoagulants. After being stored at room temperature for 30 minutes and after clot formation, blood samples were centrifuged at 1500 × g for 20 minutes. The serum samples were stored at –80 °C until future testing. Fasting plasma glucose (FPG) was assayed by the enzymatic (glucose oxidase) colorimetric method using a commercial kit (Pars Azmun, Tehran, Iran). Serum total cholesterol (TC) and high-density lipoprotein cholesterol (HDL-C) were measured using the cholesterol oxidase phenol aminoantipyrine method, and serum triglyceride (TG) was measured using the

glycerol-3 phosphate oxidase phenol aminoantipyrine enzymatic method. Serum low-density lipoprotein cholesterol (LDL-C) was calculated using the Friedewald formula[36]. The serum insulin concentration was measured using commercial kits (Insulin AccuBind ELISA, USA, Monobind, Inc.) and enzyme-linked immunosorbent assays (ELISAs). Serum uric acid was measured by calorimetry using commercial kits (Bionic, Iran, Bionic, Inc.) and biolysis 24. Serum C-reactive protein (CRP) was measured by a commercial kit (CRPLX, Germany, Roche, Inc.) via the immunoturbidimetric method.

Definition of cardiometabolic outcomes

Hypercholesterolemia was a vital cardiovascular disease (CVD) risk factor among the population. Both increased serum TC and decreased HDL-C were related to CVD risk. The TC/HDL-C ratio was an independent lipoprotein predictor of the development of CVD[37]. The LDL-C/HDL-C ratio was defined as an index of CVD and served as the main target for therapy[38, 39].

Serum uric acid was the end product of purine metabolism in the body. Hyperuricemia was related to an increased future risk of type 2 diabetes(40) and appeared to be a consequence of insulin resistance[41].

The lipid accommodation product (LAP) index, a marker of CVD, was a simple indicator of high lipid accumulation in adults[42] and had greater sensitivity and specificity than waist circumference measurements for detecting insulin resistance[43]. Based on the values of WC and fasting TG, the LAP score was calculated using the sex difference formula: in men = (WC (Cm) - 65) * TG (mmol/L) and in women = (WC (Cm) -58)* TG (mmol/L).

Homeostatic model assessment (HOMA) was a measure of insulin resistance (HOMA-IR) and β-cell function among diabetic and nondiabetic people[44]. The HOMA of beta cell function or insulin sensitivity (HOMA-IS) was thought to be a good measure of beta cell function. High HOMA-IR and low HOMA-IS values were associated with glucose intolerance and subsequent risk of type 2 diabetes(45, 46). HOMA-IR = fasting insulin ((μIU/mL)*FPG (mg/dl))/405, and HOMA-IS =(20 * fasting insulin (μIU/mL))/(FPG (mg/dl) -3.5).

The triglyceride-glucose (TyG) index was a marker of insulin resistance[47] and predicts the development of metabolic disorders and CVD[48]. The TyG index was calculated based on the following formula: In (fasting triglyceride (TG) [mg/dl]* fasting plasma glucose (FPG) [mg/dl]) / 2.

Statistical analysis

The statistical analysis was conducted with SPSS version 26 (IBM). Descriptive statistics were primarily reported as the means ± SDs and/or percentages for the total population and stratified with BMI (BMI < 25 VS. BMI ≥ 25). The $\chi 2$ test and one-way ANOVA were used for categorical and continuous variables to show the differences between general characteristics and dietary habits according to chrono-nutrition components, number of EOs, meal timing, and irregularity of the main meal scores in overall population. Additionally, one-way ANOVA was employed to compare the number of EOs and meal timing between weekends and weekdays.

To address the possibility of false positive results from conducting multiple statistical tests, we controlled for multiple comparisons by applying the False Discovery Rate (FDR) method, setting the FDR threshold at 5%. This approach ensures that no more than 5% of the statistically significant results are expected to be false positives, maintaining the integrity of the findings[(49)].

Independent variables, including the number of EOs, meal timing, and irregularity in the energy intake of meals, were divided into two groups based on the median number of EOs (less than 6.33 n/day vs. more than 6.33 n/day), early-B (early-Breakfast), 5:00 – 8:00 a.m. vs. late-B, 8:00–11:00 a.m., early-L (early-Lunch) 11:00 a.m. - 1:30 p.m. vs. late-L 1:30 – 4:00 p.m., early-D (early-Dinner), 6:00 – 8:45 p.m. vs. late-D 8:45 – 11:00 p.m., and less irregularity-B ≤ 31.77 vs. more irregularity-B > 31.77, less irregularity-L ≤ 30.19 vs. more irregularity-L >30.19 and less irregularity-D ≤ 34.02 vs. more irregularity-D > 34.02, respectively. We used logistic regression to investigate the associations between chrono-nutritional components and cardiometabolic risk factors while controlling for confounders, including age, sex, education, energy intake, physical activity, income, supplement intake, menopausal status, smoking status, MEQ score, fasting window, sleep duration, and BMI. Additionally, the interaction effect of BMI on all associations was assessed in a sensitivity analysis, where the model was adjusted for all confounders except BMI. Similarly, the interaction effect of age (< 41 years old vs. ≥ 41 years old) on all associations was assessed in a sensitivity analysis, where the model was adjusted for all confounders except age.

Results

In this cross-sectional study, 825 participants—140 males (16.96%) and 685 females (83.03%)—with ages ranging from 20 – 59 years and a mean ± SD age of 42.17 ± 10.5 years—were analyzed. Participants had moderate to low levels of physical activity, with most participants reporting not smoking. The mean ± SD energy intake was 1681.63 ± 374.12 kcal/day, with three main meals (breakfast, lunch, and dinner) comprising roughly equal calorie intake. The mean ± SD average number of EOs was 6.35 ± 0.93, with a range of 1-11 n/day, and only 1.17% and 4.51% of the population had ≤ 4 and ≥ 8 EOs, respectively. In addition, the daily irregularity energy score was 22.30 ± 19.01, ranging from 3.71 - 92.12, and the MEQ score was 58.65 ± 5.73, ranging from 36 – 78. All the variable data were available for 825 participants. Participants with a BMI ≥ 25 exhibited significantly lower physical activity levels, with 64.38% categorized as having low activity, compared to just 33.53% in the BMI < 25 group. Furthermore, non-smokers were notably more prevalent among those with a BMI ≥ 25 (96.98%) than in the BMI < 25 group (91.46%). This group was also older on average, at 43.79 years, compared to 38.98 years for the BMI < 25 participants, highlighting a distinct age disparity between the two groups. The general and characteristics, eating habits, and serum biomarkers of the study participants were presented in **Table 1,** both for the total population and stratified by BMI.

The difference between number of EOs and meal timing based on weekend and weekday data were presented in Table S1, with no significant differences observed.

Table 2 indicates the differences in general characteristics and dietary habits based on the number of eating occasions (EOs): those with less EOs (≤ 6.33) compared to those with more EOs (> 6.33). The group with more EOs tended to have greater morningness ($p < 0.001$) after adjusting for sex and age. Additionally, they consumed more total energy ($p = 0.002$), particularly at breakfast ($p = 0.02$) and dinner ($p = 0.03$), than the group with fewer EOs. Individuals with more EOs had a shorter fasting window ($p < 0.001$) and shorter sleep duration ($p < 0.001$), but exhibited more regular breakfast consumption ($p = 0.002$) along with earlier breakfast ($p < 0.001$) and dinner ($p = 0.01$) intake habits.

The differences between lifestyle and eating behavior according to the time of the main meal were indicated in Table 3. Earlier B participants (before 8:00 a.m.) were more likely to be more morningness ($p < 0.001$) and a greater number of EOs ($p < 0.001$) but a shorter fasting window

($p < 0.001$) and shorter sleep duration ($p < 0.001$) than later B participants (after 8:00 a.m.). In addition, earlier lunch ($p = 0.009$) and dinner ($p = 0.01$) were also observed in this group. According to the lunch time analysis, the individuals in the earlier-L group (before 1:30 p.m.) had a lower BMI than those in the later-L group (after 1:30 p.m.), $p = 0.03$. The time of breakfast ($p < 0.001$) and dinner intake ($p = 0.002$) for earlier-L participants were earlier than those for later-L participants. Later-D participants (before 8:45 p.m.) had a shorter fasting window ($p = 0.03$), a lower frequency of intake ($p = 0.01$), and later breakfast ($p = 0.007$) and lunch ($p < 0.001$) consumption in comparison to earlier-D participants (after 8:45 p.m.).

Table 4 illustrated differences between the two groups based on the irregularity energy score of the main meal, labelled "less irregular" and "more irregular". The less irregular-B group, ≤ 31.77, consumed more energy at breakfast ($p = 0.009$) but had lower irregular energy scores at lunch and dinner than did the more irregular-B group (> 31.77), $p < 0.001$, and $p < 0.001$. Furthermore, less irregular-L participants, ≤ 30.19, had fewer energy intake during lunch and dinner and less irregular-B scores than did more irregular-L participants, > 30.19 ($p < 0.001$), in all associations. The more irregular-D group, >34.02, consumed more daily and lunch energy but less breakfast energy than did the other group, $p < 0.001$, $p < 0.001$, and $p = 0.002$, respectively. Additionally, the more irregular D group had greater irregularity scores at breakfast and lunch than did the other groups, $p < 0.001$ for both. However, they slept less and had a shorter fasting duration in comparison to less irregular-D participants ($p = 0.003$ and $p = 0.02$, respectively).

Chrono-nutrition components showed no significant associations with cardiometabolic risk factors across the entire population. Also, there was no interaction by age observed in any of the associations. Due to a significant interaction by BMI, the data was stratified based on BMI categories. (Table S2, S3, and S4).

In the BMI-stratified analysis, having fewer number of EOs was associated with a higher LDL-C/HDL-C ratio (β (95% CI), 0.26 (0.06 – 0.48), $P_{FDR} = 0.04$)) among overweight and obese individuals. However, no significant association was found between the number of EOs and other cardiometabolic risk factors, as shown in Table 5.

In Table 6, meal timing was not associated with cardiometabolic risk when stratified by BMI.

Only, for participants with a normal BMI, less irregularity of breakfast energy intake was associated with lower TC/HDL-C (-0.37 (-0.95 – -0.18), P_{FDR} = 0.01) and LDL-C/HDL-C ratio (-0.32 (-0.79 - -0.13), P_{FDR} = 0.01). (Table 7)

Discussion

Chrono-nutrition components were not significantly associated with cardiometabolic risk factors in the overall population. However, when stratified by BMI, a lower number of EOs was linked to a higher LDL/HDL-C ratio among overweight and obese individuals. Additionally, more consistent breakfast energy intake was associated with improved lipid profiles, specifically lower TC/HDL-C and LDL-C/HDL-C ratios, in participants with a normal BMI.

In our study, the negative association between the LDL/HDL-C ratio and the number of EOs aligns with findings by Tąpolska et al., who reported that participants consuming four or more meals daily had lower TG levels and higher HDL-C levels compared to those who consumed three or fewer meals [50]. Consistent with our findings, other studies also demonstrated that a greater number of EOs was associated with lower cholesterol concentrations[51, 52]. Increased meal frequency (nibbling) might also decrease the insulin concentration[53, 54]. However, Arciero *et al* did not observe a significant association between the frequency of eating and cholesterol concentration[55]. Additionally, similar to our nonsignificant associations, in previous research, the number of EOs was not significantly associated with TG [52] or BP[56].

We did not find any associations between meal timing and cardiometabolic health in contrast to Garaulet *et al*. who reported that early lunch eaters (before 3:00 p.m.) experienced more weight loss and lower insulin resistance during weight loss treatment than late lunch eaters (after 3:00 p.m.) among 420 obese Spanish adults despite the similarities in appetite hormones, energy expenditure, and intake of macronutrients. Late eating patterns also decrease insulin sensitivity [57], change metabolism[58] and result in weight gain and obesity. Moreover, compared with a delayed eating schedule from 12:00 – 23:00, a daytime eating schedule from 8:00 – 19:00 for eight weeks (the intake of three main meals and two snacks by similar macronutrient contributions) promoted weight loss and improvements in energy metabolism and insulin[59].

Another finding of this study was that greater irregularity in energy intake at breakfast was associated with elevated TC/HDL-C and LDL-C/HDL-C ratio, as a potential increase in cardiometabolic risk. Plot *et al*. reported that higher irregular energy intake at breakfast and

lunch led to a greater risk of metabolic syndrome and a greater BMI[30]. Moreover, eating meals regularly was inversely associated with metabolic syndrome, insulin resistance[13], lipid profiles[60], which was similar to our findings. However, irregularity in energy intake at breakfast and between meals was related to increased metabolic syndrome risk factors among British adults[30].

Several mechanisms linking the frequency of meals, meal timing, regularity and health status were known. A previous study showed that a greater number of EOs decreased cholesterol due to decreased insulin secretion and promoted appetite control[61]. This reduction was associated with cholesterol synthesis, as insulin activated the key enzyme in biosynthesis, hydroxy methyl glutaryl-CoA (HMG-CoA) reductase[51]. An increase in blood glucose and consequent insulin resulted in increased endogenous cholesterol synthesis [52]. Regular intake can result in more stable plasma levels of intestinal satiety hormones, such as glucagon-like peptide-1 (GLP-1), cholecystokinin and peptide YY[57]. Additionally, delayed meal timing may result in decreased melatonin and cortisol concentrations, which play key roles in energy hemostasis by affecting the peripheral circadian rhythm in humans[62]. In addition, several factors, such as age and sex, are known to be linked to skipping meals or irregularity in meals[63, 64]. Young adults skipped their meals more often, men were more likely to skip their breakfast, and women were more likely to skip their lunch and dinner. Additionally, behavioural factors such as smoking status, alcoholic drinks, and physiological and biomedical factors are related to irregular meal intake [63]. However, we did not observe any age-related interactions in our associations.

Meal frequency, meal timing and meal skipping are interrelated factors that influence energy distribution throughout the day. Both the content and timing of meals may crucial for health. These findings highlight the importance of chrono-nutrition in cardiometabolic health and provide valuable insights into lifestyle and eating behavior differences. Future research should aim to establish causal links, investigate long-term impacts, and delve deeper into the mechanisms at play.

Limitations

This was a cross-sectional study, and it was impossible to derive causal relationships from the data. Therefore, this study could only provide associations between chrono-nutritional components and cardiometabolic health [65]. Additionally, the study relied on self-reported data

for the assessment of chrono-nutrition components, such as the frequency of meals and snacks, meal timing, and regularity. This method might be subject to recall and social desirability biases, which could lead to inaccurate measurements and potentially weaken the observed associations[66]. Moreover, The three dietary reports included only one weekend and two weekdays, limiting the capture of differences between weekdays and weekends. No formal interaction with sex could be assessed, although some differences were observed between men and women. A limitation was the inability to assess sex-specific analysis.

To the best of our knowledge, this is the first study to explore the associations between all chrono-nutrition components and cardiometabolic health in Iranian adults. Furthermore, chronotype, which influences the timing of food intake and eating patterns, was assessed and controlled as a confounder in all associations.

Conclusion

Our findings provided evidence that a lower number of EOs, and more irregular energy intake scores at breakfast might be associated with worse cardiometabolic health. More regular intake of more meals seem to improve cardiometabolic health, highlighting the importance of chrono-nutrition in managing cardiometabolic health. However, prospective studies must confirm these associations and clarify their long-term effects.

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Conflict of interest

The authors report no conflicts of interest.

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Authorship

A.L, Z.A, and S.Sb contributed to the conception/design of the research; A.L., and S.Sb contributed to the acquisition, analysis, or interpretation of the data; A.L, S.Z, and M.M drafted the manuscript; S.Sb, and K.Dj critically revised the manuscript; and S.Sb agreed to be fully accountable for ensuring the integrity and accuracy of the work. All the authors have read and approved the final manuscript.

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Table 1. Baseline lifestyle, sociodemographic, and dietary characteristics of the total population sample and stratified by BMI (n=825).

Characteristics	**Total population***	**BMI < 25**	**BMI ≥ 25**
Number (%) (n (%))	825 (100)	328 (39.75)	497 (60.25)
Age$_{(\text{Yr})}$	42.21 ± 10.62	38.98 ± 11.47	43.79 ± 9.63
Sex (women)	685 (83.03)	269 (82.01)	416 (83.71)
Physical activity level $_{(\text{MET.Minutes.WK})}$			
Low (n (%))	430 (52.13)	110 (33.53)	320 (64.38)
Moderate (n (%))	315 (36.94)	187 (57.01)	128 (25.75)
High (n (%))	80 (9.69)	31 (9.46)	49 (9.86)
Education			
Illiterate (n (%))	56 (6.74)	19 (5.79)	37 (6.82)
Under diploma and diploma (n (%))	472 (57.15)	162 (49.32)	310 (62.37)
Educated	297 (36.05)	145 (44.22)	152 (30.58)
Smoking Status			
Not smoking (n (%))	782 (94.83)	300 (91.46)	482 (96.98)
Ex-smoking (n (%))	14 (1.71)	12 (3.66)	2 (0.40)
Smoking (n (%))	29 (3.53)	16 (4.88)	13 (2.62)
Sleep duration (h:m)	6:49 ± 1:09	6:47 ± 1:12	6:51 ± 1:06
Supplement intake (Yes) (n (%))	201 (24.33)	76 (23.17)	135 (27.16)
Energy Intake (Kcal/day**)**			
Daily	1681.63 ± 374.15	1662.85± 374.23	1685.98 ± 381.45
Breakfast	418.32 ± 151.54	419.41± 148.26	417.67± 158.66
Lunch	535.85 ± 179.34	537.43 ± 183.38	534.43 ± 176.99
Dinner	508.17 ± 196.30	507.08 ± 196.64	510.99 ± 196.07
Breakfast (% of TEI)	25.09 ± 7.73	24.93 ± 7.72	27.07 ± 7.74
Lunch (% of TEI)	32.16 ± 8.91	31.95 ± 8.89	32.25 ± 8.94
Dinner (% of TEI)	30.29 ± 9.48	30.40 ± 9.49	30.18 ± 9.46
Eating occasions (EOs) (n/day**)**	6.35 ± 0.93	6.34 ± 0.95	6.36 ± 0.91
Frequency main meals (n/day**)**	2.92 ± 0.16	2.90 ± 0.15	2.95 ± 0.18

Frequency snacks (n/day**)**	3.43 ± 0.83	3.40 ± 0.81	3.46 ± 0.85
Breakfast irregularity score	34.16 ± 20.03	34.12 ± 19.71	34.19 ± 20.39
Lunch irregularity score	37.41 ± 13.71	38.18 ± 14.02	36.63 ± 13.48
Dinner irregularity score	36.13 ± 26.14	35.86 ± 23.82	36.61 ± 28.96
Daily irregularity score	22.30 ± 19.01	23.12 ± 18.76	23.12 ± 19.34
Breakfast time (h:m, a.m.**)**	8:05 ± 0:44	8:07 ± 0:42	8:01 ± 0:46
Lunch time (h:m, p.m.**)**	1:58 ± 0:33	1:54 ± 0:35	2:08 ± 0:31
Dinner time (h:m, p.m.**)**	8:42 ± 0:34	8:45 ± 0:33	8:39 ± 0:35
Morning Evening Questionnaire (MEQ)	58.65 ± 5.73	58.13 ± 5.70	59.49 ± 5.77
SBP (mmHg)	118.22 ± 14.36	113.61 ± 14.22	121.54 ± 14.51
DBP (mmHg)	78.35 ± 9.32	76.59 ± 8.62	79.98 ± 9.74
WC (cm)	89.09 ± 11.63	78.80 ± 6.46	92.32 ± 9.87
BMI (Kg.m2)	27.34 ± 3.01	22.71 ± 1.72	29.07 ± 3.05
LAP Index (cm.mmol/I)	49.25 ± 33.93	39.24 ± 29.27	59.17 ± 35.19
FPG (mg.dl)	105.13 ± 19.02	102.83 ± 17.88	105.23 ± 19.97
TG (mg.dl)	144.53 ± 72.11	135.15 ± 78.39	154.58 ± 65.31
$\frac{\mathbf{LDL-C}}{\mathbf{HDL-C}}$	2.41 ± 0.80	2.30 ± 0.75	2.47 ± 0.75
$\frac{\mathbf{TC}}{\mathbf{HDL-C}}$	4.03 ± 1.06	3.83 ± 0.92	4.13 ± 1.14
Uric Acid (mg/dl)	4.63 ± 1.30	4.45 ± 1.26	4.72 ± 1.33
Insulin Serum (µU/ml)	13.58 ± 12.50	13.09 ± 11.90	14.37 ± 12.70
HOMA-IR	3.66 ± 2.94	3.36 ± 2.91	3.84 ± 3.08
HOMA-IS	2.56 ± 1.98	2.45 ± 1.90	2.74 ± 2.14
CRP (µg/dl)	0.23 ± 0.21	0.19 ± 0.16	0.24 ± 0.23
TyG- index (cm.mgdl)	4.82 ± 2.82	4.13 ± 2.38	5.25 ± 3.09

Abbreviations:

H:m, hour:minute; EOs, eating occasions; TEI, total energy intake; BMI, Body Mass Index; SBP, systolic blood pressure; DBP, diastolic blood pressure; FPG, fasting plasma glucose; TG, triglyceride; $\frac{\boldsymbol{LDL-C}}{\boldsymbol{HDL-C}}$, $\frac{\text{low-density lipoprotein}}{\text{high-density lipoprotein}}$; $\frac{TC}{HDL-C}$, $\frac{\text{total cholesterol}}{\text{high-density lipoprotein}}$; LAP, lipid accumulation product; HOMA-IR, Homeostatic Model Assessment for Insulin Resistance; HOMA-IS, Homeostatic Model Assessment for Insulin sensitivity; CRP, C- Reactive protein; TyG, triglyceride-glucose.

*Values are mean ± SD otherwise it is indicated.

Table 2: The difference between general characteristics and dietary habits according to the number of eating occasion (EOs) in Iranian adults (n=825).

variables	Number of Eating Occasion (EOs) (n/day)		
	Less EOs (≤ 6.33) (n = 465)	**More EOs (> 6.33)** (n = 360)	**P value**
Sex, women n (%)	385 (82.79)	318 (88.33)	0.32
Age (yr)	41.92 ± 10.37	42.47 ± 10.39	0.45
Morning evening questionnaire score (MEQ)*	57.44 ± 7.30	59.27 ± 5.75	**<0.001**
Body mass index (BMI)*	26.94 ±4.01	27.30 ±4.41	0.29
Total daily energy intake (kcal/day)*	1639.71 ± 379.10	1721.68 ± 375.60	**0.002**
Breakfast energy intake (kcal/day)*	405.72 ± 159.12	433.28 ± 148.46	**0.01**
Lunch energy intake (kcal/day)*	540.96 ± 182.19	530.71 ± 171.87	0.42
Dinner energy intake (kcal/day)*	489.92 ± 204.02	529.01 ± 181.65	**0.03**
Supplement intake (yes/no) Yes n (%)	100 (21.50)	101 (28.05)	0.93
Breakfast time (h:m, a.m.)*	8 : 09 ± 0 : 47	7 :54 ± 0 :41	**<0.001**
Lunch time (h:m, p.m.)*	1 :54 ± 0 : 35	1 :52 ± 0 : 31	0.62
Dinner time (h:m, p.m.)*	8 :49 ± 0 : 38	8 : 40 ± 0 : 30	**0.01**
Fasting window (h:m)*	9 : 56 ± 1 : 19	9 :06 ± 1:09	**<0.001**
Sleep duration (h:m)*	8 :53 ± 1 : 23	8 :36 ± 1 :41	**<0.001**
Breakfast irregularity score*	36.02 ± 20.04	31.79 ± 18.89	**0.002**
Lunch irregularity score*	37.66 ± 13.01	38.21 ± 14.51	0.13
Dinner irregularity score*	35.94 ± 23.88	34.20 ± 22.05	0.29

Abbreviations:

EOs, eating occasions; n, number; h:m, hour:minute; BMI, body mass index; MEQ, morning evening questionnaire.

Values are mean ± SD otherwise it is indicated.

Calculated by χ 2 and one-way ANOVA for qualitative and quantitative variables, respectively.

*Adjusted for sex and age.

Significant pvalue ($P < 0.05$) is presented in bold

Table 3: The difference between general characteristics and dietary habits according to main meal timing in Iranian adults (n=825).

Variables	Breakfast time (h:m)			Lunch time (h:m)			Dinner time (h:m)		
	Earlier-B (Before 8:00 a.m.) (n =422)	**Later-B (After 8:00 a.m,)** (n = 402)	**P value**	**Earlier-L (Before 1:30 p.m.)** (n = 414)	**Later-L (After 1:30 p.m.)** (n = 411)	**P value**	**Earlier-D (Before 8:45 p.m.)** (n = 411)	**Later-D (After 8:45 p.m.)** (n = 414)	**P value**
Sex, women (%)	359 (85.07)	344 (85.57)	0.14	351 (84.78)	352 (85.46)	0.11	364 (88.56)	339 (81.88)	0.17
Age (yr)	42.33 ±10.61	41.99 ±10.46	0.46	42.29 ±10.56	42.04 ± 10.56	0.72	42.45 ± 10.58	41.87 ± 10.50	0.42
Morning evening questionnaire score (MEQ)*	59.05 ± 6.38	57.38 ± 7.05	**<0.001**	58.48 ± 6.78	58.03 ± 6.65	0.32	58.63 ± 6.55	57.01 ± 6.95	0.09
Body mass index (BMI)*	26.68 ± 4.50	27.26 ± 4.02	0.09	26.81 ± 4.44	27.42 ± 4.19	**0.03**	26.92 ± 4.16	27.32 ± 4.49	0.17
Total daily energy intake (kcal/day)*	1643.08 ± 305.96	1709.24 ± 430.89	0.82	1655.58 ± 356.37	1695.71 ± 398.47	0.12	1690.59 ± 361.00	1661.1 ± 397.52	0.26
Breakfast	423.28	412.85	0.35	413.19	422.52	0.38	424.92	410.8	0.18

energy intake (kcal/day)*	± 146.98	± 163.33		± 150.36	± 159.30		± 142.54	3 ± 166.70	
Lunch energy intake (kcal/day)*	532.27 ± 175.54	540.51 ± 180.02	0.49	527.36 ± 176.88	544.63 ± 178.15	0.15	540.13 ± 168.18	532.21 ± 186.99	0.51
Dinner energy intake (kcal/day)*	507.43 ± 194.10	508.27 ± 196.88	0.95	509.27 ± 191.31	504.27 ± 196.98	0.66	509.20 ± 200.31	506.27 ± 190.59	0.83
Supplement intake (yes/no) Yes n (%)	101 (23.93)	100 (24.87)	0.51	99 (23.91)	102 (24.81)	0.85	94 (22.87)	107 (25.87)	0.21
Number EOs (n/day)	6.48 ± 0.84	6.16 ± 0.88	**<0.001**	6.32 ± 0.90	6.33 ± 0.87	0.86	6.42 ± 0.89	6.25 ± 0.87	**0.01**
Breakfast time (h:m, a.m.)*	-	-	-	7:56 ± 0 :42	8:09 ± 0 :47	**<0.001**	7:58 ± 0 :47	8:07 ± 0 :45	**0.007**
Lunch time (h:m, p.m.)*	1 :50 ± 0 : 33	1 :56 ± 0 : 34	**0.009**	-	-	-	1 :46 ± 0 : 32	1 :57 ± 0 : 34	**<0.001**
Dinner time (h:m, p.m.)*	8 : 42 ± 0 : 32	8 : 48 ± 0 : 37	**0.01**	8 : 41 ± 0 : 35	8 : 49 ± 0 : 34	**0.002**	-	-	-
Fasting window (h:m)*	9:06 ± 1 : 13	10:01 ± 1 : 14	**<0.001**	9:27 ± 1 : 17	9:37 ± 1 : 18	0.07	9:38 ± 1 : 16	9:26 ± 1 : 17	**0.03**

Sleep duration (h:m)*	8:12 ± 1 : 24	9:03 ± 1 : 39	**<0.001**	8:30 ± 1 : 26	8:42 ± 1 : 41	0.05	8:41 ± 1 : 26	8:31 ± 1:14	0.12
Breakfast irregularity score*	33.49 ± 19.15	41.85 ± 13.51	0.32	33.43 ± 19.26	34.71 ± 20.26	0.74	32.47 ± 19.52	35.85 ± 20.14	**0.01**
Lunch irregularity score*	37.13 ± 13.51	37.87 ± 13.92	0.46	37.91 ± 13.51	37.71 ± 13.69	0.06	36.61 ± 13.96	37.37 ± 13.72	**0.04**
Dinner irregularity score*	34.45 ± 22.59	36.00 ± 23.96	0.35	34.47 ± 23.11	35.47 ± 23.14	0.37	34.47 ± 22.96	35.87 ± 23.14	0.42

Abbreviations:

B, breakfast; L, lunch; D, dinner; n, number; h:m, hour:minute; BMI, body mass index; MEQ, morning evening questionnaire; EOs, eating occasions.

Values are mean ± SD otherwise it is indicated.

Calculated by χ 2 and one-way ANOVA for qualitative and quantitative variables, respectively.

*Adjusted for sex and age.

Significant pvalue ($P < 0.05$) is presented in bold

Table 4: The difference between general characteristics and dietary habits according to main meal irregularity energy intake score in Iranian adults (n=825).

Variables	**Breakfast irregularity score** (Range : 0.6– 133.4, median : 31.77)			**Lunch irregularity score** (Range : 1.5 – 102.4, median: 30.19)			**Dinner irregularity score** (Range :1.4 – 133.5, median : 34.02)		
	Less irregular-B ≤ 31.77 (n =412)	**More irregular--B >31.77 (n=413)**	**P value**	**Less irregular-L ≤ 30.19 (n =410)**	**more irregular--L >30.19 (n =415)**	**P value**	**Less irregular-D ≤ 34.02 (n = 411)**	**More irregular-D >34.02 (n = 414)**	**P value**
Sex, women n (%)	356 (86.40)	347 (90.55)	0.71	341 (83.17)	362 (87.22)	0.06	346 (84.18)	357 (86.23)	0.31
Age (yr)	41.31 ± 10.43	42.01 ± 10.69	0.92	42.46 ±10.58	41.86 ±10.49	0.41	41.77 ±10.48	42.56 ± 10.56	0.27
Morning evening questionnaire score (MEQ)*	57.44 ± 7.30	59.27 ± 5.75	0.09	58.50 ± 6.91	58.00 ± 6.60	0,27	58.51 ± 6.64	58.01 ± 6.87	0.29
Body mass index (BMI)*	26.92 ± 4.25	27.31 ± 4.39	0.30	26.79 ±4.50	27.43 ±4.02	0.10	26.92 ± 4.37	27.02 ± 4.29	0.51
Total daily energy intake (kcal/day)*	1691.07 ± 318.10	16391.68 ± 421.00	0.18	1643.08 ± 438.89	1709.35 ± 305.26	**0.02**	1623.08 ± 406.70	1729.35 ± 342.43	**<0.001**

Breakfast energy intake (kcal/day)*	437.73 ± 125.88	393.23 ± 177.40	**0.009**	420.28 ± 128.22	415.16 ± 177.89	0.59	434.09 ± 150.76	402.88 ± 159.66	**0.002**
Lunch energy intake (kcal/day)*	526.96 ± 164.12	546.71 ± 181.13	0.37	488.99 ± 179.74	581.51 ± 162.49	**<0.001**	514.15 ± 181.99	558.63 ± 178.15	**<0.001**
Dinner energy intake (kcal/day)*	505.92 ± 204.16	510.01 ± 186.13	0.78	484.70 ± 171.62	530.96 ± 124.16	**<0.001**	508.19 ± 154.63	507.83 ± 229.12	0.92
Supplement intake Yes n (%)	100 (24.27)	101 (24.45)	0.91	93 (22.68)	108 (26.02)	0.51	97 (23.60)	104 (25.12)	0.57
Number of EOs (n/day)	6.36 ± 0.86	6.28 ± 0.92	0.18	6.37 ± 0.83	6.28 ± 0.94	0.14	6.39 ± 0.84	6.26 ± 0.91	0.03
Breakfast time (h:m, a.m.)*	8 : 09 ± 0 : 47	7 :54 ± 0 :41	0.91	8 : 01 ± 0 : 44	8 : 04 ± 0 : 45	0.28	8 : 03 ± 0 : 45	8:03 ± 0 :45	0.96
Lunch time (h:m, p.m.)*	1 :54 ± 0 : 35	1 :52 ± 0 : 31	0.51	1 :52 ± 0 : 31	1 :53 ± 0 : 36	0.62	1 :52 ± 0 : 33	1 :53 ± 0 : 34	0.70
Dinner time (h:m, p.m.)*	8 :43 ± 0 : 30	8 : 48 ± 0 : 38	0.06	8 : 44 ± 0 : 33	8 : 46 ± 0 : 36	0.41	8 : 45 ± 0 : 37	8 : 46 ± 0 : 35	0.67
Fasting window (h:m)*	9 : 30 ± 1 : 23	9 : 35 ± 1:16	0.22	9 : 29 ± 1 : 15	9 : 35 ± 1 : 21	0.31	9 : 26 ± 1 : 12	9 : 38 ± 1 : 24	**0.02**
Sleep duration (h:m)*	8 : 41 ± 1 : 30	8 : 31 ± 1 : 38	0.32	8 : 42 ± 1 : 34	8 : 33 ± 1 : 35	0.09	8 : 46 ± 1 : 38	8 : 26 ± 1 : 29	**0.003**

Breakfast irregularity score*	-	-	-	28.23 ± 17.95	40.06 ± 20.01	**<0.001**	29.84 ± 18.57	38.44 ± 20.25	**<0.001**
Lunch irregularity score*	32.26 ± 7.01	34.27 ± 16.56	**<0.001**	-	-	-	32.26 ± 8.53	42.71 ± 15.76	**<0.001**
Dinner irregularity score*	29.96 ± 20.68	40.20 ± 24.32	**<0.001**	26.68 ± 20.01	43.70 ± 22.91	**0.01**	-	-	-

Abbreviations:

B, breakfast; L, lunch; D, dinner; n, number; H:m, hour:minute; BMI, body mass index; MEQ, morning evening questionnaire; EOs, eating occasions.

Values are mean ± SD otherwise it is indicated.

Calculated by χ 2 and one-way ANOVA or qualitative and quantitative variables, respectively.

*Adjusted for sex and age.

Significant pvalue ($P < 0.05$) is presented in bold

Table 5: Associations between number of eating occasions (EOs) and cardiometabolic risk factors stratified by body mass index (BMI)**, BMI < 25 vs. BMI ≥ 25, in 825 Iranian adults (Beta and 95% confidence interval).

Outcomes	BMI category	Number of Eating Occasion (EOs) (n/day) (Rang, 1-11; median, 6.33)		
		Less EOs ≤ 6.33 (n = 465)	More EOs > 6.33 (n = 360)	P_{FDR*}
SBP	BMI < 25 (n = 328)	-3.21 (-7.12 – 0.39)	References	0.11
	BMI ≥ 25 (n = 497)	0.88 (-1.73 – 3.41)	References	0.55
DBP	BMI < 25 (n = 328)	-6.96 (-12.98 – 0.65)	References	0.23
	BMI ≥ 25 (n = 497)	1.43 (-0.31 – 3.21)	References	0.15
LAP Index	BMI < 25 (n = 328)	-13.01 (-27.32 – 0.28)	References	0.12
	BMI ≥ 25 (n = 497)	-1.71 (-3.29 – 0.23)	References	0.15
$\frac{TC}{HDL-C}$	BMI < 25 (n = 328)	0.08 (-045 – 0.32)	References	0.54
	BMI ≥ 25 (n = 497)	0.26 (0.06 – 0.48)	References	**0.04**
$\frac{LDL-C}{HDL-C}$	BMI < 25 (n = 328)	0.23 (0.005 – 0.45)	References	0.13
	BMI ≥ 25 (n = 497)	0.18 (0.04 – 0.37)	References	0.09
Uric Acid	BMI < 25 (n = 328)	-0.03 (-0.64 – 0.03)	References	0.16
	BMI ≥ 25 (n = 497)	-0.02 (-0.25 – 0.21)	References	0.91
HOMA-IR	BMI < 25 (n = 328)	-0.83 (-1.61 – 0.08)	References	0.16
	BMI ≥ 25 (n = 497)	-0.16 (-0.73 – 0.41)	References	0.73
HOMA-IS	BMI < 25 (n = 328)	0.44 (-0.19 – 0.86)	References	0.87

	BMI ≥ 25 (n = 497)	0.003 (-0.43 – 0.44)	References	0.90
CRP (µg.dl)	BMI < 25 (n = 328)	0.04 (-0.03 – 0.09)	References	0.16
	BMI ≥ 25 (n = 497)	0.03 (-0.06 – 0.01)	References	0.27
TyG-index	BMI < 25 (n = 328)	-0.23 (-0.54 - 0.01)	References	0.12
	BMI ≥ 25 (n = 497)	-0.03 (-0.05 - -008)	References	0.09

Abbreviations:

B, breakfast; L, lunch; D, dinner; SBP, systolic blood pressure; DBP, diastolic blood pressure; LAP, lipid accumulation product; $\frac{TC}{HDL-C}$, $\frac{\text{total cholesterol}}{\text{high-density lipoprotein}}$; $\frac{LDL-C}{HDL-C}$, $\frac{\text{low-density lipoprotein}}{\text{high-density lipoprotein}}$; HOMA-IR, Homeostatic Model Assessment for Insulin Resistance; HOMA-IS, Homeostatic Model Assessment for Insulin sensitivity; CRP, C- Reactive protein; TyG- index , triglyceride-glucose index.

¤General linear regression was used and model was adjusted for age, sex, education, energy intake, physical activity, sleep duration, supplement intake, menopausal status, smoking, fasting window, and MEQ, values are Beta (95% confidence interval) of outcomes.

* P(FDR) refers to P values obtained in linear regression models, Multiple testing adjustments were performed using the false discovery rate at 5%.

**The cutoff of 25 was used to categorize BMI (Body Mass Index) into two main groups: BMI < 25 as normal weight and BMI ≥ 25 as overweight/obese.

Significant pvalue (P < 0.05) is presented in bold

Table 6: Associations between meal timing and cardiometabolic risk factors stratified by body mass index (BMI)**, BMI < 25 vs. BMI ≥ 25, in 825 Iranian adults (Beta and 95% confidence interval).

Outcomes	BMI category	Breakfast time (Median = 8:00 (h:m))			Lunch time (Median = 1:30 p.m.)			Dinner time (Median = 8:45 p.m.)		
		Earlier-B (Before 8:00 a.m.) (n =422)	**Later-B** (After 8:00 a.m.) (n = 402)	**P_{FDR*}**	**Earlier-L** (Before - 13:30 p.m.) (n = 414)	**Later-L** (After 1:30 p.m.) (n = 411)	**P_{FDR*}**	**Earlier-D** (Before 8:45 p.m.) (n = 411)	**Later-D** (After 8:45 p.m.) (n = 414)	**P_{FDR*}**
SBP	BMI < 25 (n = 328)	-0.30 (-3.57 – 3.08)	Reference s	0.85	-1.23 (-4.47 – 1.99)	Reference s	0.67	-0.03 (-2.31 – 2.23)	Reference s	0.86
	BMI ≥ 25 (n = 497)	-1.03 (-3.59 – 1.57)	Reference s	0.66	-1.42 (-4.51 – 1.12)	Reference s	0.68	-0.81 (-2.44 -1.31)	Reference s	0.90
DBP	BMI < 25 (n = 328)	1.70 (-0.46 – 3.71)	Reference s	0.80	-1.53 (-3.63 – 0.55)	Reference s	0.75	1.21 (-0.51 – 3.34)	Reference s	0.90
	BMI ≥ 25 (n = 497)	-0.94 (-2.19 – 0.17)	Reference s	0.73	-1.04 (-2.07 – 0.87)	Reference s	0.66	-0.76 (-2.91 – 1.01)	Reference s	0.82

LAP Index	BMI < 25 (n = 328)	-0.21 (-2.43 – 2.13)	Reference	0.92	0.01 (-2.19 – 2.123)	Reference	0.87	-0.48 (-2.85 – 1.88)	Reference	0.84
	BMI ≥ 25 (n = 497)	0.04 (-5.32 – 4.82)	Reference	0.89	-0.79 (-7.13 – 5.01)	Reference	0.79	-1.63 (-5.34 – 0.89)	Reference	0.98
$\frac{TC}{HDL-C}$	BMI < 25 (n = 328)	0.03 (-0.19 – 0.26)	Reference	0.93	-0.09 (-0.31 – 0.13)	Reference	0.70	-0.11 (-0.33 – 0.11)	Reference	0.83
	BMI ≥ 25 (n = 497)	0.03 (-0.16 – 0.22)	Reference	0.89	0.14 (-0.05 – 0.33)	Reference	0.93	0.09 (-0.09 – 0.19)	Reference	0.91
$\frac{LDL-C}{HDL-C}$	BMI < 25 (n = 328)	-0.04 (-0.23 – 0.14)	Reference	0.91	-0.04 (-0.22 – 0.15)	Reference	0.78	-0.10 (-0.23 – 0.08)	Reference	0.98
	BMI ≥ 25 (n = 497)	0.05 (-0.09 – 0.15)	Reference	0.73	0.16 (0.01 – 0.33)	Reference	0.40	0.06 (-0.08 – 0.21)	Reference	0.91
Uric Acid	BMI < 25 (n = 328)	-0.006 (-0.32 – 0.31)	Reference	0.91	-0.13 (-0.43 – 0.17)	Reference	0.75	-0.33 (-0.64 – 0.02)	Reference	0.40
	BMI ≥	-0.15 (-	Referenc	0.63	-0.18 (-	Reference	0.93	0.04 (-0.21	Referenc	0.86

	25 (n = 497)	0.38 – 0.02)	es	0.48 – 0.02)	s	– 0.22)	es
HOMA-IR	BMI < 25 (n = 328)	0.52 (-0.05 – 1.14)	Referenc es	0.59	-0.29 (- 1.38 – 0.83)	Reference s	0.40	-0.15 (- 0.98 – 69)	Referenc es	0.80
	BMI ≥ 25 (n = 497)	-0.69 (- 1.28 – - 0.11)	Referenc es	0.18	-0.24 (- 3.02 – - 2.25)	Reference s	0.31	-0.14 (- 0.76 – 0.12)	Referenc es	0.82
HOMA-IS	BMI < 25 (n = 328)	0.31 (-0.20 -	Referenc es	0.66	0.09 (- 0.22- 0.40)	Reference s	0.75	0.11 (-0.31 – 0.54)	Referenc es	0.84
	BMI ≥ 25 (n = 497)	0.45 (0.04 – 0.98)	Referenc es	0.23	0.18 (-0.07 – 0.45)	Reference s	0.64	-0.007 (- 0.04 – 0.02)	Referenc es	0.81
CRP (µg.dl)	BMI < 25 (n = 328)	-0.02 (- 0.06 – 0.02)	Referenc es	0.66	-0.02 (- 0.06 – 002)	Reference s	0.78	-0.11 (- 0.05 – 0.03)	Referenc es	0.98
	BMI ≥ 25 (n = 497)	0.1 (-0.2 - 0.05)	Referenc es	0.66	0.01 (-0.02 – 0.04)	Reference s	0.74	-0.02 (- 0.04 – 0.02)	Referenc es	0.82
TyG-index	BMI < 25	-0.03(-0.01 – 0.05)	Referenc es	0.69	0.04 (-0.02 – 0.03)	Reference s	0.83	0.006 (-0.03 – 0.03)	Refer ences	0.81

	(n = 328)							
	BMI ≥ 25 (n = 497)	-0.01 (-0.03 – 0.01)	Reference	0.71	-0.009 (-0.01 – 0.62)	Reference	0.67	-0.01 (-0.03 – 0.009)	Reference	0.99

Abbreviations:

B, breakfast; L, lunch; D, dinner; SBP, systolic blood pressure; DBP, diastolic blood pressure; LAP, lipid accumulation product; $\frac{\square\square}{\square\square\square-\square}, \frac{\text{total cholesterol}}{\text{high-density lipoprotein}}; \frac{\square\square\square-\square}{\square\square\square-\square}, \frac{\text{low-density lipoprotein}}{\text{high-density lipoprotein}}$; HOMA-IR, Homeostatic Model Assessment for Insulin Resistance; HOMA-IS, Homeostatic Model Assessment for Insulin sensitivity; CRP, C- Reactive protein; TyG- index, triglyceride-glucose index.

¤General linear regression was used and model was adjusted for age, sex, education, energy intake, physical activity, sleep duration, supplement intake, menopausal status, smoking, fasting window, and MEQ, values are Beta (95% confidence interval) of outcomes.

* P(FDR) refers to P values obtained in linear regression models, Multiple testing adjustments were performed using the false discovery rate at 5%.

**The cutoff of 25 was used to categorize BMI (Body Mass Index) into two main groups: BMI < 25 as normal weight and BMI ≥ 25 as overweight/obese.

Significant p-value ($P < 0.05$) is presented in bold

Table 7: Associations between meal irregularity energy intake and cardiometabolic risk factors stratified by body mass index (BMI)**, BMI < 25 vs. BMI ≥ 25, in 825 Iranian adults (Beta and 95% confidence interval).

Outcomes		Breakfast irregularity score (Range, 0.6– 133.4, median , 31.77)			Lunch irregularity score (Range, 1.5 – 102.4, median, 30.19)			Dinner irregularity score (Range,1.4– 133.5, median 34.02)		
		Less irregular-B ≤ 31.77 (n = 412)	More irregular-B >31.77 (n = 413)	P_{FDR*}	Less irregular-L ≤ 30.19 (n =410)	More irregular-L ≤ 30.19 (n = 415)	P_{FDR*}	Less irregular-D ≤34.02 (n = 411)	More irregular-D >34.02 (n = 414)	P_{FDR*}
SBP	BMI < 25 (n = 328)	-0.92 (-4.53 – 2,15)	References	0.78	1.29 (-2.26 – 4.39)	References	0.88	-1.20 (-4.5 – 2.16)	References	0.86
	BMI ≥ 25 (n = 497)	0.76 (-1.79 – 3.32)	References	0.71	0.075 (-1.91 – 3,21)	References	0.88	0.75 (-1.87 – 1.90)	References	0.79
DBP	BMI < 25 (n = 328)	0.54 (1.62 – 2.66)	References	0.66	0.32 (-1.87 – 2.51)	References	0.87	0.46 (-1.65 – 2.51)	References	0.78
	BMI ≥ 25 (n = 497)	-0.82 (-1.76 – 1.21)	References	0.64	-0.25 (-2.34 – 1.51)	References	0.93	-067 (-2.76 – 1.05)	References	0.98

LAP Index	BMI < 25 (n = 328)	-0.56 (-2.93 – 1.76)	Refere nces	0.53	-12.87 (-28.34 – 1.89)	Referenc es	0.61	-0.72 (-1.59 – 0.98)	Referen ces	0.79
	BMI ≥ 25 (n = 497)	-0.68 (-2.59 – 2.56)	Refere nces	0.67	-14.30 (-29.61 – 2.96)	Referenc es	0.40	-2.18 (-8.17 – 4.11)	Referen ces	0.99
□□ □□□ – □	BMI < 25 (n = 328)	-0.37 (-0.95 – -0.18)	Refere nces	**0.01**	0.13 (-0.08 – 35)	Referenc es	0.88	-0.17 (-0.39 – 0.04)	Referen ces	0.98
	BMI ≥ 25 (n = 497)	0.03 (-0.16 – 0.22)	Refere nces	0.67	0.05 (-0.19 – 0.21)	Referenc es	0.93	-0.003 (-0.20 – 0.19)	Referen ces	0.81
□□□ – □ □□□ – □	BMI < 25 (n = 328)	-0.32 (-0.79 -- 0.13)	Refere nces	**0.01**	0.11 (-0.06 – 0.65)	Referenc es	0.96	-0.13 (-0.31 – 0.04)	Referen ces	0.97
	BMI ≥ 25 (n = 497)	0.01 (-0.13 – 0.15)	Refere nces	0.43	-0.13 (-0.22 – 0.18)	Referenc es	0.82	0.05 (-0.09 – 0.19)	Referen ces	0.72
Uric Acid	BMI < 25 (n = 328)	0.12 (-0.18 – 0.44)	Refere nces	0.82	0.02 (-0.28 – 0.34)	Referenc es	0.83	-0.09 (-0.40 – 0.21)	Referen ces	0.79
	BMI ≥	-0.06 (-	Refere	0.63	-0.06 (-	Referenc	0.85	-0.05 (-	Referen	0.79

	25 (n = 497)	0.28 (-0.11 – 0.65) References	0.26 (-0.15 – 0.67) References	0.27 (-0.15 – 0.69) References
HOMA-IR	BMI < 25 (n = 328)	0.41 (-0.41 – 1.23) References	0.83	-0.29 (-0.68 – 0.05) References	0.88	-0.05 (-0.87 – 0.77) References	0.76
	BMI ≥ 25 (n = 497)	0.12 (-0.42 – 0.68) References	0.65	-0.35 (-0.89 – 0.62) References	0.99	-0.09 (-0.65 – 0.63) References	0.94
HOMA-IS	BMI < 25 (n = 328)	0.39 (-0.08 – 0.88) References	0.47	0.04 (-0.47 – 0.49) References	0.87	-0.26 (-0.76 – 0.22) References	0.97
	BMI ≥ 25 (n = 497)	0.22 (-0.17 – 0.63) References	0.87	0.10 (-0.06 – 0.21) References	0.85	0.27 (-0.12 – 0.68) References	0.90
CRP (µg.dl)	BMI < 25 (n = 328)	0.16 (-0.28 – 0.61) References	0.77	-0.01 (-0.04 – 0.04) References	0.96	-0.01 (-0.05 – 0.03) References	0.89
	BMI ≥ 25 (n = 497)	-0.002 (-0.004 - 0.03) References	0.75	-0.02 (-0.06 – 0.01) References	0.98	-0.03 (-0.08 – 0.02) References	0.99
TyG-index	BMI < 25	-0.005 (-0.03 – 0.03) References	0.66	-0.009 (-0.04 - 0.95) References	0.95	-0.37 (-0.95 – 0.84) References	0.84

	(n = 328)	0.02)	0.02)	0.21)
	BMI ≥ 25 (n = 497)	-0.03 (-0.16 – 0.15) References 0.78	-0.39 (-1.21 – 0.34) References 0.48	-0.15 (-0.96 – 0.38) References 0.89

Abbreviations:

B, breakfast; L, lunch; D, dinner; SBP, systolic blood pressure; DBP, diastolic blood pressure; LAP, lipid accumulation product; $\frac{\square\square}{\square\square\square-\square}, \frac{\text{total cholesterol}}{\text{high-density lipoprotein}}; \frac{\square\square\square-\square}{\square\square\square-\square}, \frac{\text{low-density lipoprotein}}{\text{high-density lipoprotein}}$; HOMA-IR, Homeostatic Model Assessment for Insulin Resistance; HOMA-IS, Homeostatic Model Assessment for Insulin sensitivity; CRP, C- Reactive protein; TyG- index, triglyceride-glucose index.

¤General linear regression was used and model was adjusted for age, sex, education, energy intake, physical activity, sleep duration, supplement intake, menopausal status, smoking, fasting window, and MEQ, values are Beta (95% confidence interval) of outcomes.

* P(FDR) refers to P values obtained in linear regression models, Multiple testing adjustments were performed using the false discovery rate at 5%.

**The cutoff of 25 was used to categorize BMI (Body Mass Index) into two main groups: BMI < 25 as normal weight and BMI ≥ 25 as overweight/obese.

Supplementary File (tables and figures)

Table S1: The difference between chrono-nutrition component according to the weekend and weekdays in Iranian adults (n=825).

Variables	**Weekdays ∞**	**weekends©**	**Pvalue ***
Number of EOs** (n/day)	6.38 ± 1.86	6.29 ± 1.81	0.75
Breakfast time (h:m, a.m.)**	8:01 ± 1:08	8:11 ± 1:23	0.53
Lunch time (h:m, p.m.)**	1:51 ± 0:50	2:08 ± 1:03	0.42
Dinner time (h:m, p.m.)**	8:38 ± 1:39	8:48 ± 1:45	0.41

Abbreviations:

EOs, eating occasions; n, number; h:m, hour:minute.

Calculated by one-way ANOVA, values are mean ± SD.

*Pvalue < 0·05 indicates significant level.

**Adjusted for sex and age.

∞ Average of two 24-hour dietary recalls.

© One 24-hour dietary recall.

Table S2: The association between number of eating occasions (EOs) and cardiometabolic risk factors in 825 Iranian adults (Beta (95% confidence interval), and interaction analysis by BMI and age).

		Number of Eating Occasion (EOs) (n/day) (Rang, 1-11; median, 6.33)				
Outcomes	**Model¤**	**Less EOs ≤ 6.33 (n = 465)**	**More EOs > 6.33 (n = 360)**	**P_{FDR*}**	**$P_{interaction}$ BMI ****	**$P_{interaction}$ Age *****
SBP	**Adjusted β (95% CI)**	-9.26 (-18.54 – 1.78)	References	0.32	0.03	0.36
DBP	**Adjusted β (95% CI)**	-5.93 (-13.65 – 2.71)	References	0.30	0.04	0.24
LAP Index	**Adjusted β (95% CI)**	-7.42 (-32.03 - 17.65)	References	0.28	0.54	0.58
□□ / □□□ – □	**Adjusted β (95% CI)**	0.81 (0.02 -1.76)	References	0.50	0.21	0.52
□□□ – □ / □□□ – □	**Adjusted β (95% CI)**	0.93 (0.09 -1.92)	References	0.20	0.42	0.71
Uric Acid (mg.dl)	**Adjusted β (95% CI)**	-0.22 (-1.34 – 0.87)	References	0.30	0.78	0.64

HOMA-IR	**Adjusted β (95% CI)**	-0.25	(-2.84 – 2.42)	References	0.59	0.92	0.42
HOMA-IS	**Adjusted β (95% CI)**	-0.35	(-2.76 – 1.46)	References	0.85	0.67	0.83
CRP (µg.dl)	**Adjusted β (95% CI)**	0.12	(-0.04 – 0.28)	References	0.78	0.06	0.69
TyG-index	**Adjusted β (95% CI)**	-0.07	(-0.18 – 0.03)	References	0.26	0.34	0.15

Abbreviations:

EOs, eating occasion; SBP, systolic blood pressure; DBP, diastolic blood pressure; LAP, lipid accumulation product; $\frac{\square\square}{\square\square\square-\square}, \frac{\text{total cholesterol}}{\text{high-density lipoprotein}}$; $\frac{\square\square\square-\square}{\square\square\square-\square}, \frac{\text{low-density lipoprotein}}{\text{high-density lipoprotein}}$; HOMA-IR, Homeostatic Model Assessment for Insulin Resistance; HOMA-IS, Homeostatic Model Assessment for Insulin sensitivity; CRP, C- Reactive protein; TyG- index, triglyceride-glucose index.

¤ General linear regression was used and the model was adjusted for age, sex, education, energy intake, physical activity, sleep duration, fasting window, supplement intake, menopausal status, smoking, MEQ, and body mass index, values are beta (95% confidence interval).

* P(FDR) refers to Pvalues obtained in linear regression models, Multiple testing adjustments were performed using the false discovery rate at 5%.

**Interaction by BMI (BMI < 25 (n = 328) vs, BMI ≥ 25 (n = 497)) was performed, with the model adjusted for all confounders except BMI.

***Interaction by age (aged < 41 years (n = 409) and ≥ 41 years (n = 416))was performed, with the model adjusted for all confounders except age

Table S3: The association between the time of main meals and cardiometabolic risk factors in 825 Iranian adults (Beta (95% confidence interval), and interaction analysis by BMI and age).

Outcomes	Model¤	Breakfast time (Median = 8:00 (h:m))					Lunch time (Median = 1:30 p.m.)					Dinner time (Median = 8:45 p.m.)				
		Earlier-B	Later-B	P_{FDR}*	$P_{interaction}$ BMI **	$P_{interaction}$ Age ***	Earlier-L	Later-L	P_{FDR}*	$P_{interaction}$ BMI **	$P_{interaction}$ Age ***	Earlier-D	Later-D	P_{FDR}*	$P_{interaction}$ BMI **	$P_{interaction}$ Age ***
		(Before 8:00 a.m.) (n =422)	(After 8:00 a.m.) (n = 402)				(Before 13:30 p.m.) (n = 414)	(After 1:30 p.m.) (n = 411)				(Before 8:45 p.m.) (n = 411)	(After 8:45 p.m.) (n = 414)			
SBP	Adjusted β (95% CI)	-0.46 (-11.48 – 10.70)	References	0.94	0.95	0.85	0.03 (-10.13 – 9.71)	References	0.63	0.75	0.68	0.21 (-11.65 – 12.05)	References	0.95	0. 96	0.85
DBP	Adjusted	0.25 (-7.62 –	References	0.85	0.99	0.91	-0.02 (-8.09	References	0.99	0.86	0.39	-0.14 (-0.49 –	References	0.39	0.33	0.76

	β (95% CI)	8.44)					– 8.06)					0.15)				
LAP Index	**Adjusted β (95% CI)**	-8.41 (-31.61 - 16.52)	References	0.61	0.55	0.63	-0.17 (-18.20 - 17.87)	References	0.68	0.52	0.43	-1.59 (-28.90 – 25.32)	References	0.79	0.76	0.37
□□ □□□ – □	**Adjusted β (95% CI)**	-0.46 (-1.27 - 0.53)	References	0.23	0.23	0.73	-0.22 (-1.01 – 0.64)	References	0.61	0.65	0.61	-0.37 (-1.26 – 0.49)	References	0.39	0.41	0.29
□□□ – □ □□□ – □	**Adjusted β (95% CI)**	-0.35 (-1.15 - 0.27)	References	0.41	0.41	0.68	--0.28 (-0.96 – 0.39)	References	0.41	0.35	0.42	-0.21 (-0.92 – 0.43)	References	0.53	0.51	0.50
Uric Acid (mg.dl)	**Adjusted β**	0.05 (-1.34 – 1.42)	References	0.31	0.24	0.35	0.19 (-0.86 -	References	0.53	0.72	0.53	-0.68 (-1.70 – 0.39)	References	0.21	0.26	0.58

	(95% CI)						1.21)									
HOMA-IR	**Adjusted β (95% CI)**	-0.31 (-2.95 – 2.11)	Reference	0.08	**0.04**	0.64	-0.26 (-2.03 – -1.46)	Reference	0.04	0.23	0.53	1.22 (-1.78 – 4.58)	Reference	0.18	0.12	0.74
HOMA-IS	**Adjusted β (95% CI)**	0,58 (-1.21 – 2.47)	Reference	0.53	0.36	0.22	1.51 (-0.06– 3.68)	Reference	0.10	**0.04**	0.65	1.06 (0.09 – 0.35)	Reference	0.07	**0.02**	0.54
CRP (µg.dl)	**Adjusted β (95% CI)**	-0.006 (-0.16 – 0.14)	Reference	0.92	0.92	0.76	-0.07 (-0.23 – 0.09)	Reference	0.37	0.46	0.49	-0.18 (-0.43 – 0.04)	Reference	0.05	**0.02**	0.42
TyG-index	**Adjusted β (95% CI)**	-0.03 (-0.19 – 0.18)	Reference	0.33	0.49	0.37	-0.09 (-0.12 - -0.09)	Reference	0.91	0.82	0.46	0.06 (-0.06 – 0.16)	Reference	0.14	0.11	0.63

Abbreviations:

B, breakfast; L, lunch; D, dinner; SBP, systolic blood pressure; DBP, diastolic blood pressure; LAP, lipid accumulation product; $\frac{\square\square}{\square\square\square-\square}$, $\frac{\text{total cholesterol}}{\text{high-density lipoprotein}}$; $\frac{\square\square\square-\square}{\square\square\square-\square}$, $\frac{\text{low-density lipoprotein}}{\text{high-density lipoprotein}}$; HOMA-IR, Homeostatic Model Assessment for Insulin Resistance; HOMA-IS, Homeostatic Model Assessment for Insulin sensitivity; CRP, C- Reactive protein; TyG- index, triglyceride-glucose index.

¤ General linear regression was used and model was adjusted for age, sex, education, energy intake, physical activity, sleep duration, supplement intake, menopausal status, smoking, MEQ, fasting window, and body mass index,values are beta (95% confidence interval).

* P(FDR) refers to P values obtained in linear regression models, Multiple testing adjustments were performed using the false discovery rate at 5%.

**Interaction by BMI (BMI < 25 (n = 328) vs, BMI ≥ 25 (n = 497)) was performed, with the model adjusted for all confounders except BMI.

***Interaction by age (aged < 41 years (n = 409) and ≥ 41 years (n = 416))was performed, with the model adjusted for all confounders except age.

Table S4: The association between main meal irregularity energy score and cardiometabolic risk factors in 825 Iranian adults (Beta (95% confidence interval), and interaction analysis by BMI and age).

Outcomes	Model¤	Breakfast irregularity score (Range, 0.6– 133.4, median , 31.77)					Lunch irregularity score (Range, 1.5 – 102.4, median 30.19)					Dinner irregularity score (Range,1.4– 133.5, median 34.02)				
		Less irregular-B	More irregular-B	P_{FD} R*	Pinteraction BMI **	$P_{interaction}$ Age ***	Less irregular-L	More irregular-L	P_{FD} R*	$P_{interaction}$ BMI **	$P_{interaction}$ Age ***	Less irregular-D	More irregular-D	P_{FD} R*	$P_{interaction}$ BMI **	$P_{interaction}$ Age ***
		≤ 31.77 (n = 412)	>31.77 (n = 413)				≤ 30.19 (n =410)	≤ 30.19 (n = 415)				≤34.02 (n = 411)	>34.02 (n = 414)			
SBP	Adjusted β (95% CI)	-1.67 (-13.17 – 10.41)	References	0.74	0.78	0.27	0.53 (-11.63 – 12.01)	References	0.98	0.82	0.67	-4.81 (-18.51 – 7.35)	References	0.96	0.53	0.40
DBP	Adjus	0.93 (-	Refere	0.8	0.53	0.43	-1.23	Refere	0.92	0.83	0.32	-0.65 (-	Refere	0.7	0.98	0.28

	ted β (95% CI)	6.82 – 8.68)	nces	3			(-9.01 – 6.54)	nces				8.79 – 7.09)	nces	9		
LAP Index	**Adjusted β (95% CI)**	-8.41 (-15.71 - 6.71)	References	0.95	0.31	0.85	-13.7 (-28.20 - - 1.07)	References	0.21	0.79	0.36	-11.29 (-31.90 – 12.4)	References	0.78	0.42	0.85
□□ □□□ – □	**Adjusted β (95% CI)**	-0.27 (-1.47 - 1.01)	References	0.76	**0.04**	0.79	0.08 (-0.91 – 0.74)	References	0.99	0.79	0.24	-0.62 (-1.72 – 0.25)	References	0.98	0.22	0.91
□□□ – □ □□□ – □	**Adjusted β (95% CI)**	-0.29 (-1.79 - 1.27)	References	0.83	0.09	0.63	0.02 (-0.76 – 0.79)	References	0.99	0.85	0.58	-0.27 (-1.02 – 0.51)	References	0.79	0.42	0.63
Uric Acid (mg.dl)	**Adjusted β**	-0.31 (-1.51 – 0.71)	References	0.95	0.56	0.73	0.53 (-0.75 - -	References	0.99	0.45	0.52	-0.28 (-1.29 – 0.67)	References	0.98	0.79	0.73

	(95% CI)					1.12)									
HOMA-IR	**Adjusted β (95% CI)**	-0.08 (-3.65 – 2.19)	Reference	0.98	0.72	0.68	-0.26 (-2.43 – 2.06)	Reference	0.23	**0.04**	0.71	1.22 (-2.29 – 3.38)	Reference	0.97	0.36	0.68
HOMA-IS	**Adjusted β (95% CI)**	0.79 (-1.21 – 2.63)	Reference	0.81	0.53	0.61	0.81 (-1.01 – 2.09)	Reference	0.83	0.28	0.64	0.52 (-1.29 – 2.34)	Reference	0.81	0.60	0.73
CRP (µg.dl)	**Adjusted β (95% CI)**	0.07 (-0.19 – 0.24)	Reference	0.76	0.61	0.38	0.006 (-0.13 – 0.16)	Reference	0.97	0.69	0.75	-0.12 (-0.29 – 0.04)	Reference	0.97	0.16	0.27
TyG-index	**Adjusted β (95% CI)**	0.02 (-0.61 – 0.97)	Reference	0.95	0.51	0.47	-0.19 (-0.45 - - 0.11)	Reference	0.21	0.07	0.63	0.07 (-0.36 – 0.12)	Reference	0.72	0.34	0.42

Abbreviations:

B, breakfast; L, lunch; D, dinner; SBP, systolic blood pressure; DBP, diastolic blood pressure; LAP, lipid accumulation product; $\frac{\square\square}{\square\square\square-\square}$, $\frac{\text{total cholesterol}}{\text{high-density lipoprotein}}$; $\frac{\square\square\square-\square}{\square\square\square-\square}$, $\frac{\text{low-density lipoprotein}}{\text{high-density lipoprotein}}$; HOMA-IR, Homeostatic Model Assessment for Insulin Resistance; HOMA-IS, Homeostatic Model Assessment for Insulin sensitivity; CRP, C- Reactive protein; TyG- index, triglyceride-glucose index.

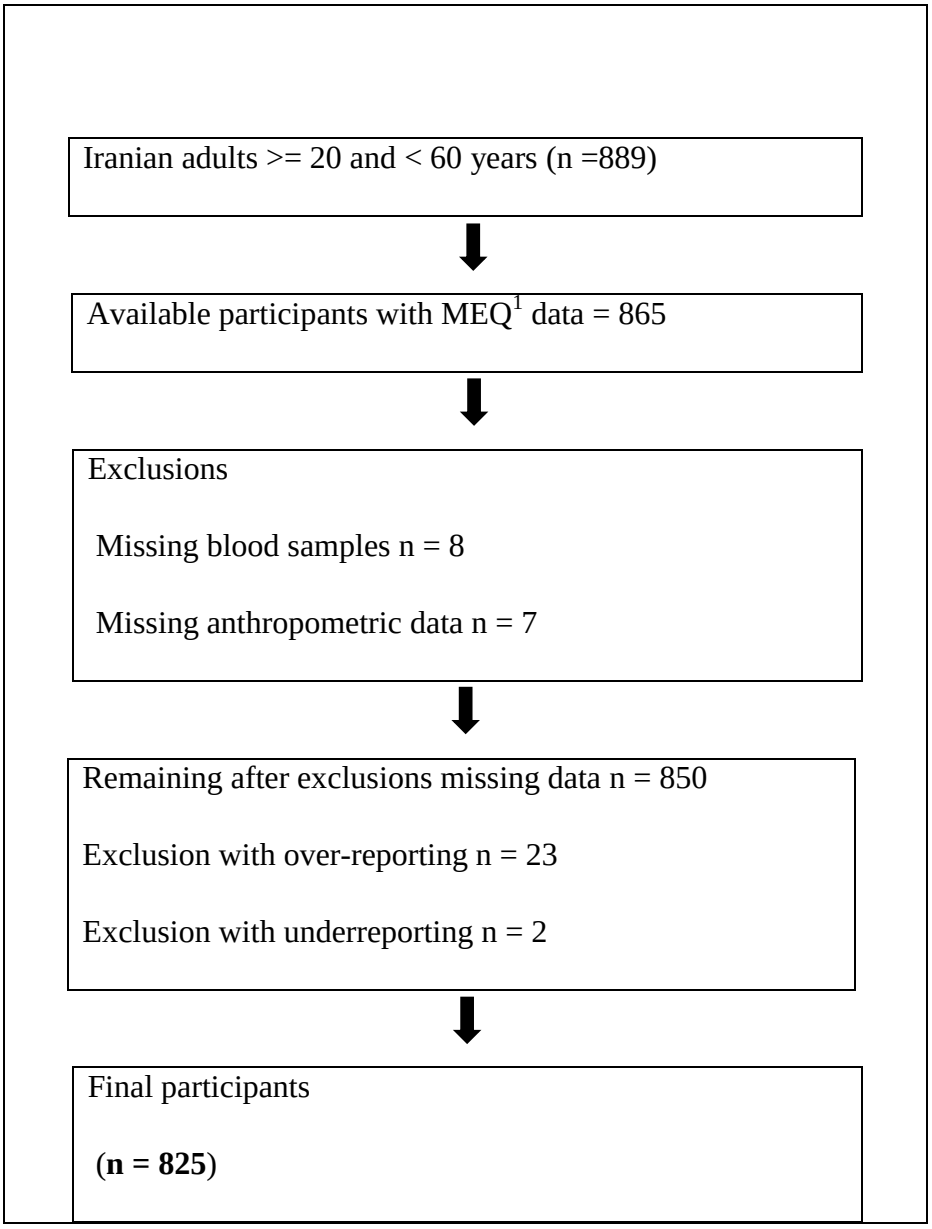
¤General linear regression was used and model was adjusted for age, sex, education, energy intake, physical activity, sleep duration, supplement intake, menopausal status, smoking, fasting window, and MEQ, values are Beta (95% confidence interval) of outcomes.

* P(FDR) refers to Pvalues obtained in linear regression models. Multiple testing adjustments were performed using the false discovery rate at 5%.

**The cutoff of 25 was used to categorize BMI (Body Mass Index) into two main groups: BMI < 25 as normal weight and BMI ≥ 25 as overweight/obese.

***Interaction by age (aged < 41 years (n = 409) and ≥ 41 years (n = 416))was performed, with the model adjusted for all confounders except age.

Figure S1: Study Flow Diagram for participant data from the Iranian adults.



[1] MEQ, morning evening questionnaire.