



Effect of two types of time-restricted eating on glycemic, lipid indices, and weight in women with polycystic ovary syndrome: a randomized controlled trial

Maryam Aminian^{1,2} · Masoumeh Hajshafiha³ · Mohammad Heidari⁴ · Sevana Daneghian^{1,2}

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Abstract

Purpose Polycystic ovary syndrome (PCOS) is a prevalent endocrine and metabolic disorder among women of reproductive age with significant metabolic impairments. Time-restricted eating (TRE) has emerged as a promising dietary strategy for improving metabolic health. Although both early time-restricted eating (eTRE) and mid-day time-restricted eating (mTRE) have shown beneficial metabolic effects, their comparative efficacy in women with PCOS remains unclear. This study aimed to directly compare the effects of eTRE and mTRE on glycemic control, lipid profiles, and anthropometric outcomes in women with PCOS.

Methods In this 6-week randomized controlled trial, 75 women with PCOS were allocated to one of three groups: eTRE (8:00 AM–6:00 PM), mTRE (11:00 AM–9:00 PM), or a control group with ad libitum eating. The primary outcome was fasting insulin level. Secondary outcomes included FBS, insulin resistance indices, lipid profile (total cholesterol (TC), LDL-C, HDL-C, and TG), body weight, BMI, waist circumference (WC), and dietary intake. Metabolic and anthropometric variables were assessed at baseline and post-intervention, while dietary intake was evaluated at baseline, mid-intervention, and study completion.

Results Both eTRE and mTRE significantly reduced FBS, fasting insulin, Homeostasis Model Assessment of Insulin Resistance (HOMA-IR), body weight, and WC compared with the control group ($P < 0.05$). Additionally, eTRE significantly improved TC ($P < 0.001$) and LDL-C levels ($P = 0.01$), whereas similar changes were not observed in the mTRE group.

Conclusion TRE, particularly eTRE, appears to be an effective dietary intervention for women with PCOS, offering significant benefits for glycemic control, metabolic health, and weight management.

Trial registration IRCT20221122056575N1.

Keywords Polycystic ovary syndrome · Fasting · Metabolic syndrome · Time restricted eating

Introduction

Polycystic ovary syndrome is one of the most common endocrine and metabolic disorders in women of reproductive age [1]. Its prevalence ranges from 5.5% to 11.5% worldwide, depending on the diagnostic criteria [2]. In Iran, the prevalence is estimated at 19.4%, based on the Rotterdam criteria [3]. PCOS is characterized by reproductive abnormalities, including menstrual disorders, infertility, and hyperandrogenism. Also, metabolic complications such as insulin resistance (IR), abdominal obesity, and hyperinsulinemia are often seen in women with PCOS [4].

The etiology of PCOS is multifactorial and not yet fully understood, although genetic factors are believed to play a

✉ Sevana Daneghian
daneghian.s@gmail.com

¹ Food and Beverages Safety Research Center, Urmia University of Medical Sciences, Urmia, Iran

² Department of Nutrition, School of Medicine, Urmia University of Medical Sciences, Urmia, Iran

³ Department of Obstetrics and Gynecology, School of Medicine, Urmia University of Medical Sciences, Urmia, Iran

⁴ Department of Epidemiology and Biostatistics, School of Medicine, Urmia University of Medical Sciences, Urmia, Iran

significant role [5]. Insulin resistance, which is often associated with hyperandrogenism, is thought to contribute substantially to the development of both reproductive and metabolic dysfunctions associated with the condition [6, 7]. Insulin resistance affects approximately 75% of lean women and 95% of obese women with PCOS [8]. Contributing to an increased risk of metabolic disorders such as type 2 diabetes mellitus (T2DM), obesity, and cardiovascular disease. Around 60–70% of women with PCOS are overweight or obese, which exacerbates the risk of developing these conditions [9].

Lifestyle modifications, such as changes in diet, exercise, and behavior, are the first recommended treatment for PCOS [10]. Recently, dietary approaches have gained popularity due to their potential to aid weight loss and improve insulin sensitivity [11]. Various diets, such as low glycemic index, dietary approaches to stop hypertension diet (DASH), Mediterranean, low-carbohydrate, ketogenic, pulse-based, low-starch/low-dairy, and vegetarian diets, have been proposed to manage PCOS by addressing its metabolic and hormonal imbalances [12–19]. However, despite these general recommendations, many women with PCOS experience challenges in adhering to dietary guidelines, including caloric restriction [20], and exercise routines [21].

Time restricted eating is type of intermittent fasting [22]. TRE has gained popularity in recent years for its focus on limiting the timing of food intake rather than caloric restriction [23]. Typically, TRE involves eating within a 6 to 10-hour window, followed by fasting for the remaining hours of the day, allowing for ad libitum food intake during the eating window [20]. The goal of time-restricted eating is to align eating patterns with the body's circadian rhythm, optimizing nutrient intake when the body is most receptive [24]. Research indicates that TRE can improve weight loss, glycemic control, and cardiometabolic health [25, 26]. In women with PCOS, studies have shown that eight-hour time-restricted eating (8 h TRE) significantly improves metabolic and endocrine profiles [27–29]. While some studies have suggested that the effects of TRE may depend on the timing of the eating window, the exact time periods used have not been consistently defined [30, 31]. Meta-analyses have indicated that eTRE leads to more pronounced improvements in metabolic outcomes compared to later time-restricted eating (lTRE) [32].

Furthermore, to date, no human studies have compared the effects of 10-hour TRE protocols at different times of day in women with PCOS. Therefore, the present study aims to investigate the effects of two distinct time-restricted eating on glycemic indices, lipid profiles, and weight in women with PCOS.

Method

Participants and recruitment

The study included 75 adult women diagnosed with polycystic ovary syndrome according to the Rotterdam criteria, confirmed by a gynecologist. Conducted at the infertility clinic of Kosar University Hospital in Urmia, Iran, from December 2022 to January 2023, participants were recruited through clinic referrals if they were aged 18–40 years and had a BMI between 25 and 34.9 kg/m². Written informed consent was obtained from all participants. Exclusion criteria included night-shift work, fasting for more than 14 h, alcohol or smoking history, pregnancy or breastfeeding, gastrointestinal issues, eating disorders, systemic diseases, and certain medications (e.g., corticosteroids, β -receptor blockers), those diagnosed with hypertension, diabetes, or other metabolic diseases. Additionally, participants with insomnia, special diets, night eating syndrome, or those who were professional athletes were excluded. The study was approved by the Ethics Committee of Urmia University of Medical Sciences (Approval number: [IR.UMSU.REC.1401/318]) and was conducted in compliance with the principles of the Declaration of Helsinki. The study is registered at the Iranian Registry of Clinical Trials (<https://irct.bhdasht.gov.ir/trial/66984>; IRCT20221122056575N1).

Sample size

The sample size was determined based on the trial by Li et al. [27], which assessed changes in fasting insulin levels before and after the intervention. The means and standard deviations for these changes were 15.600 ± 5.100 and 12.300 ± 4.900 , respectively. A sample size calculation was performed using a paired t-test with 95% confidence and 80% power, resulting in an estimated requirement of 21 participants per group. To account for a 20% dropout rate, 25 participants were included in each group. The calculation was performed using STATA version 18 (Supplementary file).

Study design

This study was a parallel randomized controlled trial aimed at investigating the effects of two types of time-restricted eating over a 6-week period on glycemic indices, lipid profiles, and weight in women with PCOS. Participants were randomly assigned in a 1:1:1 ratio to the eTRE group (eating ad libitum during a 10-hour window from 08:00 to 18:00 and fasting for the remainder of the day), mTRE group (eating ad libitum during a 10-hour window from 11:00 to 21:00 and fasting for the remainder of the day), and

a control group (eating ad libitum with no time restriction), using block randomization with block sizes of 3 and 6. The randomization sequence was generated prior to participant enrollment using the Sealed Envelope online randomization list generator (Sealed Envelope Ltd., London, UK; <https://www.sealedenvelope.com/simple-randomiser/v1/lists>). Eligible participants were enrolled and assigned sequentially according to the computer-generated allocation list. Participants in the eTRE and mTRE groups were instructed to consume only water and unsweetened tea (up to two cups) during the fasting period. At the beginning of the trial, all participants provided written informed consent and agreed to supply accurate data regarding their food intake.

The primary outcome was fasting insulin level. Secondary outcomes included glycemic variables (FBS, HOMA-IR, Quantitative Insulin-Sensitivity Check Index (QUICKI)), lipid profile (TC, TG, LDL, HDL), and anthropometric measurements (body weight, BMI, WC) measured at the beginning and end of the intervention. Also changes in energy intake and macronutrient consumption. Weight was measured weekly.

Participants were asked to maintain their usual diet, physical activity levels, and medication use throughout the study period. Dietary intake and daily energy consumption were assessed using three-day 24-hour food recalls (including two weekdays and one weekend day), along with a physical activity questionnaire based on metabolic equivalent values collected at baseline, middle, and the end of the intervention. Adherence to the intervention was monitored through weekly review of meal-timing logs and regular telephone follow-up. Participants were provided with notebooks to record the timing of their first and last daily meals throughout the intervention period, and these records were collected weekly to monitor compliance with the assigned eating windows. In addition, participants received weekly phone calls were conducted to reinforce adherence and monitor any intervention-related adverse events or difficulties. Due to the behavioral nature of the dietary intervention, participant blinding was not feasible. Investigators were also aware of group allocation.

Biochemical measurements

At the start and end of the study, after an overnight fast, 5 mL of venous blood was drawn from participants for biochemical assessments. The blood samples were centrifuged at 4000 rpm for 10 min, and the resulting serum was stored at -80°C until analysis. Serum fasting insulin levels were measured using ELISA kits (Pars Azmoon Co, Iran). The lipid profile (TC, TG, LDL, and HDL) and FBS levels were analyzed using a BT1500 autoanalyzer (Biotechnica Instruments SpA). Homeostatic Model Assessment for Insulin

Resistance and the QUICKI index were calculated using the respective formulas.

Anthropometric measurements

Height and weight were measured weekly using a digital scale and stadiometer with a precision of 0.1 cm and 100 g, respectively, with participants wearing minimal clothing and no footwear. BMI was calculated using the formula: $\text{weight (kg)} / \text{height}^2 (\text{m}^2)$. Waist circumference was measured after exhalation, with a flexible tape placed between the hip bones and the lowest rib, ensuring the tape was horizontal and not compressing the skin. For reliability, measurements were taken in triplicate, and the mean of the three readings was used. These measurements were taken at the same time each week.

Statistical analysis

Statistical analyses were performed using STATA software version 18. A P-value of <0.05 was considered statistically significant. Prior to analysis, homogeneity between individuals before and after the study was assessed. Consequently, all analyses were conducted according to the per-protocol principle. The general characteristics of participants in the control and intervention groups before the intervention were compared using one-way ANOVA for continuous variables and chi-square (χ^2) test for categorical variables, with results presented as mean $\pm$ standard deviation (SD) for continuous variables and frequency (%) for categorical variables.

For within-group comparisons, we employed paired samples t-tests and Wilcoxon signed-rank tests based on the normality of the data, which was evaluated using the Shapiro-Wilk test. Energy and macronutrients intakes were calculated using the adapted version of NUTRITIONIST IV for Iranians (version 7.0; N-Squared Computing, Salem, OR, United States). To analyze changes in dietary intake and the metabolic equivalent of task (MET) at baseline, 3 weeks, and 6 weeks, repeated measures ANOVA was employed. For between-group comparisons, one-way analysis of variance (ANOVA) was used, followed by Bonferroni post-hoc tests for pairwise comparisons. In cases where the assumptions of normality were violated, the non-parametric equivalent tests were applied. To assess the effects of TRE on serum lipid profile, glycemic index, and anthropometric measurements, linear regression models were utilized to adjust for potential confounders, including WC, insulin levels, and the QUICKI index.

Results

A total of 90 participants who met the eligibility criteria were enrolled in the trial and randomized into the eTRE, mTRE, and control groups. After randomization, 15 participants were excluded from the study: 5 due to Poor compliance with eating window, 5 due to Taking medication, 3 due to pregnancy, and 2 due to Alcohol consumption and Work-related travel. Thus, the study was completed with 75 participants: 25 in the eTRE group, 25 in the mTRE group, and 25 in the control group (Fig. 1). General and baseline characteristics of the groups are presented in Table 1 and supplementary Tables. Significant differences were observed in baseline WC, insulin levels, and QUICKI values among the groups, indicating potential confounding factors. No adverse events related to the intervention were reported by any of the participants.

Energy intake and body weight

ANOVA results indicated significant differences in the changes in weight, BMI, and WC among the three groups ($P<0.001$). Pairwise comparisons revealed significant reductions in all three parameters in both the eTRE ($P<0.001$) and mTRE ($P<0.001$) groups compared to the control group. However, no significant difference was observed in the changes in waist circumference between the eTRE and mTRE groups ($P=0.22$, Fig. 2a and c).

Energy intake was assessed using three 24-hour dietary recalls collected during the intervention. A significant difference in energy intake changes was observed among the eTRE, mTRE, and control groups ($p<0.05$). Both the eTRE ($\Delta = -186.42 \pm 127.67$ kcal/day) and mTRE ($\Delta = -67.38 \pm 85.94$ kcal/day) groups experienced a reduction in energy intake, while the control group showed an increase ($\Delta = 45.06 \pm 84.38$ kcal/day; $p<0.001$ and $p<0.05$, respectively). Additionally, the two TRE groups differed significantly in their changes in energy intake ($p<0.001$, Fig. 2d). A significant difference in carbohydrate intake changes was

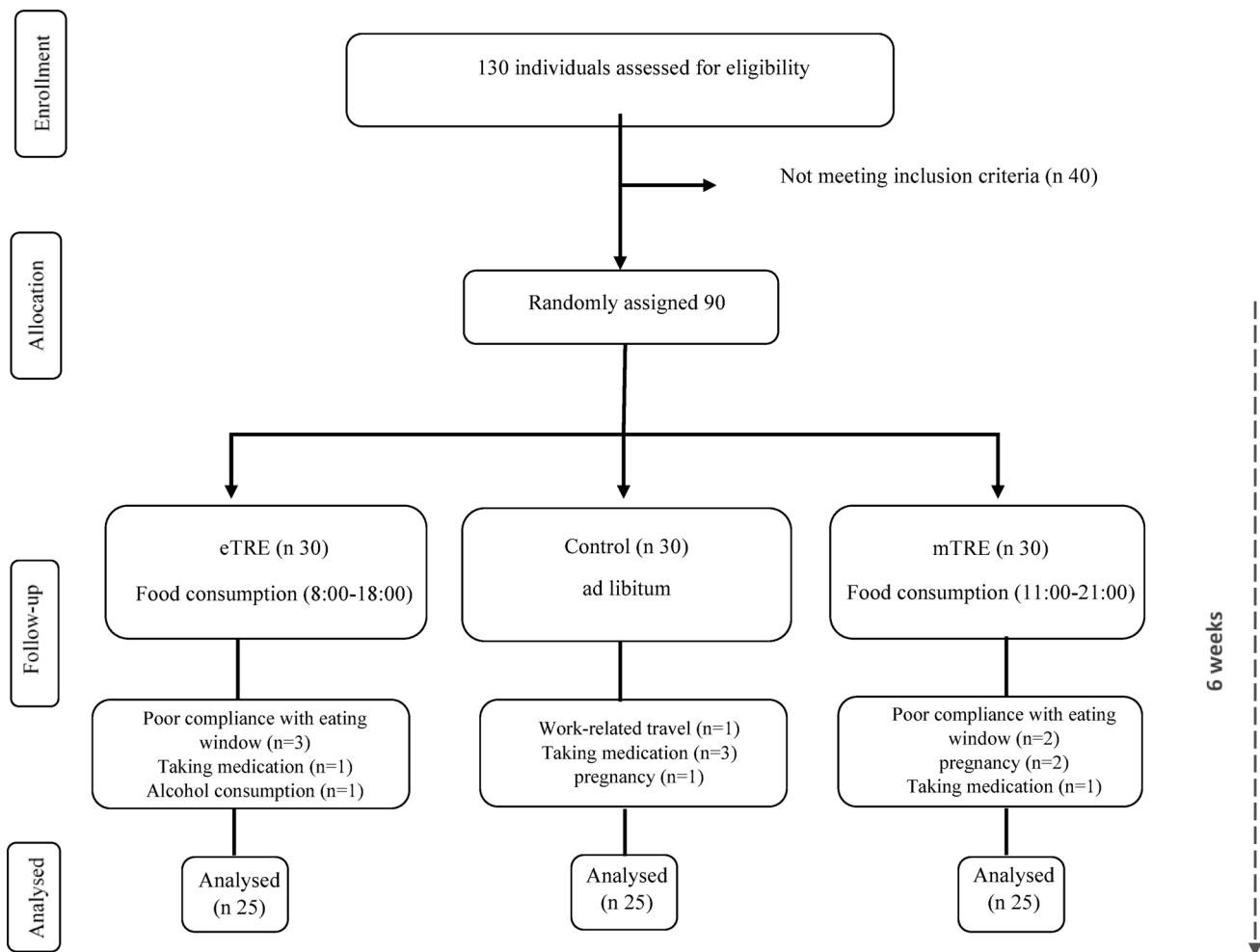


Fig. 1 The flow chart of study participants

Table 1 Baseline characteristics of participants in the intervention and control groups

	Group				<i>P</i> value
	Control (<i>N</i> =25) mean (SD)	eTRE (<i>N</i> =25) mean (SD)	mTRE (<i>N</i> =25) mean (SD)	Total (<i>N</i> =25) mean (SD)	
Age	27.56 (4.13)	28.36 (3.69)	27.04 (3.6)	27.65 (3.8)	0.47
Height (cm)	1.61 (0.05)	1.59 (0.05)	1.62 (0.06)	1.612 (0.06)	0.13
Weight (kg)	78.66 (6.25)	79.04 (9.004)	81.08 (10.87)	79.593 (8.85)	0.58
WC (cm)	96.28 (7.66)	102.96 (8.3)	100.62 (9.28)	99.957 (8.78)	0.02
BMI (Kg/m ²)	30.31 (2.53)	31.03 (2.67)	30.48 (2.68)	30.611 (2.61)	0.6
FBS (mg/dl)	100.64 (13.2)	100.04 (11.3)	94 (8.57)	98.227 (11.44)	0.07
Insulin (μU/ml)	14.19 (4.72)	18.24 (7.24)	14.31 (6.64)	15.584 (6.49)	0.04
HOMA-IR	3.62 (1.6)	4.55 (1.96)	3.37 (1.73)	3.850 (1.82)	0.05
QUICKI index	0.13 (0.008)	0.13 (0.008)	0.14 (0.01)	0.139 (0.009)	0.03
TC (mg/dl)	172.6 (42.23)	177.52 (27.95)	175.84 (32.65)	175.32 (34.383)	0.87
TG (mg/dl)	159.4 (43.73)	158.44 (65.53)	174.4 (80.89)	164.08 (64.728)	0.62
HDL-C (mg/dl)	36.04 (5.93)	38.64 (10.5)	38.35 (7.78)	37.68 (8.260)	0.48
LDL-C (mg/dl)	116.08 (25.91)	107.28 (20.07)	104.92 (22.22)	109.42 (23.06)	0.19
Energy intake (kcal/day)	1879.86 (125.88)	1915.42 (241.04)	1952.34 (248.05)	1915.87 (211.72)	0.48
Carbohydrate (gr)	261.38 (17.63)	268.64 (36.89)	278.7 (35.59)	269.57 (31.69)	0.15
Protein (gr)	79.66 (8.3)	79.94 (12.19)	81.36 (12.97)	80.32 (11.21)	0.85
Fat (gr)	57.3 (6.32)	57.9 (7.92)	56.90 (8.23)	57.36 (7.45)	0.89

Quantitative variables are reported as mean ± standard deviation

p values were computed by the one-way ANOVA.

p value < 0.05 was considered statistically significant.

observed between the eTRE and mTRE groups ($p < 0.01$). Both the eTRE ($\Delta = -36.54 \pm 22.83$ g/day) and mTRE ($\Delta = -18.48 \pm 14.84$ g/day) groups showed a reduction in carbohydrate intake, while the control group exhibited no significant change ($\Delta = 6.4 \pm 19.46$ g/day). In the between-group analysis, significant differences were found across the groups, with pairwise comparisons revealing significant differences between all groups ($p < 0.001$, Fig. 2e). A significant difference in protein intake changes was noted among the eTRE group ($p = 0.02$). The eTRE group showed a reduction ($\Delta = -3.54 \pm 7.24$ g/day), while the mTRE ($\Delta = 0.96 \pm 5.17$ g/day) and control groups ($\Delta = 1.94 \pm 4.72$ g/day; $p < 0.001$ and $p = 1$, respectively) experienced an increase in intake (Fig. 2f). For fat intake, a significant increase was observed in the control group ($\Delta = 1.3 \pm 2.98$ g/day; $p < 0.05$), while a significant decrease was seen in the eTRE group ($\Delta = -2.9 \pm 5.08$ g/day; $p < 0.05$). Differences in fat intake changes were also significant among the groups, particularly between the control and eTRE groups ($p < 0.01$, Fig. 2g).

Glycemic indices

Significant changes in FBS, insulin levels, HOMA-IR, and QUICKI index were observed among the three groups ($P < 0.01$, Fig. 2h and k). The eTRE group showed a greater reduction in FBS ($\Delta = -4.84 \pm 3.68$ mmol/L) compared to the mTRE group ($\Delta = -2.12 \pm 4.86$ mmol/L; $p < 0.05$) and the control group ($\Delta = 0.24 \pm 2.91$ mmol/L; $p < 0.001$). Insulin levels significantly decreased in both the eTRE ($\Delta =$

-2.28 ± 2.80 mmol/L) and mTRE ($\Delta = -1.23 \pm 2.91$ mmol/L) groups, compared with the control group ($\Delta = 0.10 \pm 0.27$ mmol/L; $p < 0.001$ and $p = 0.002$, respectively). HOMA-IR levels showed significant reductions in both the eTRE ($\Delta = -0.66 \pm 0.56$) and mTRE ($\Delta = -0.33 \pm 0.59$) groups, compared with the control group ($\Delta = 0.03 \pm 0.11$; $p < 0.001$ and $p = 0.001$, respectively). The QUICKI scores increased significantly in both the eTRE ($\Delta = 0.002 \pm 0.001$) and mTRE ($\Delta = 0.001 \pm 0.002$) groups, compared with the control group ($\Delta = 0.001 \pm 0.002$; $p = 0.001$ and $p = 0.01$, respectively).

Lipid profile

Significant changes in TC levels were observed among the groups (ANOVA $P < 0.05$, Fig. 2l). The eTRE group experienced a greater reduction in TC levels ($\Delta = -5.48 \pm 4.61$ mmol/L) compared to the mTRE group ($\Delta = -0.38 \pm 4.91$ mmol/L; $p < 0.05$) and the control group ($\Delta = -0 \pm 3.74$ mmol/L; $p < 0.001$). Significant differences in LDL levels were observed among the groups (ANOVA $P < 0.05$, Fig. 2o). The eTRE group showed a larger reduction in LDL levels ($\Delta = -3.96 \pm 6.01$ mmol/L) compared to the mTRE group ($\Delta = -0.84 \pm 9.54$ mmol/L; $p < 0.05$) and the control group ($\Delta = -0.48 \pm 2.12$ mmol/L; $p < 0.001$). No significant differences were observed in HDL and TG levels among the groups. Furthermore, no significant differences were found in HDL and TG levels in any of the pairwise comparisons (Fig. 2m, n).

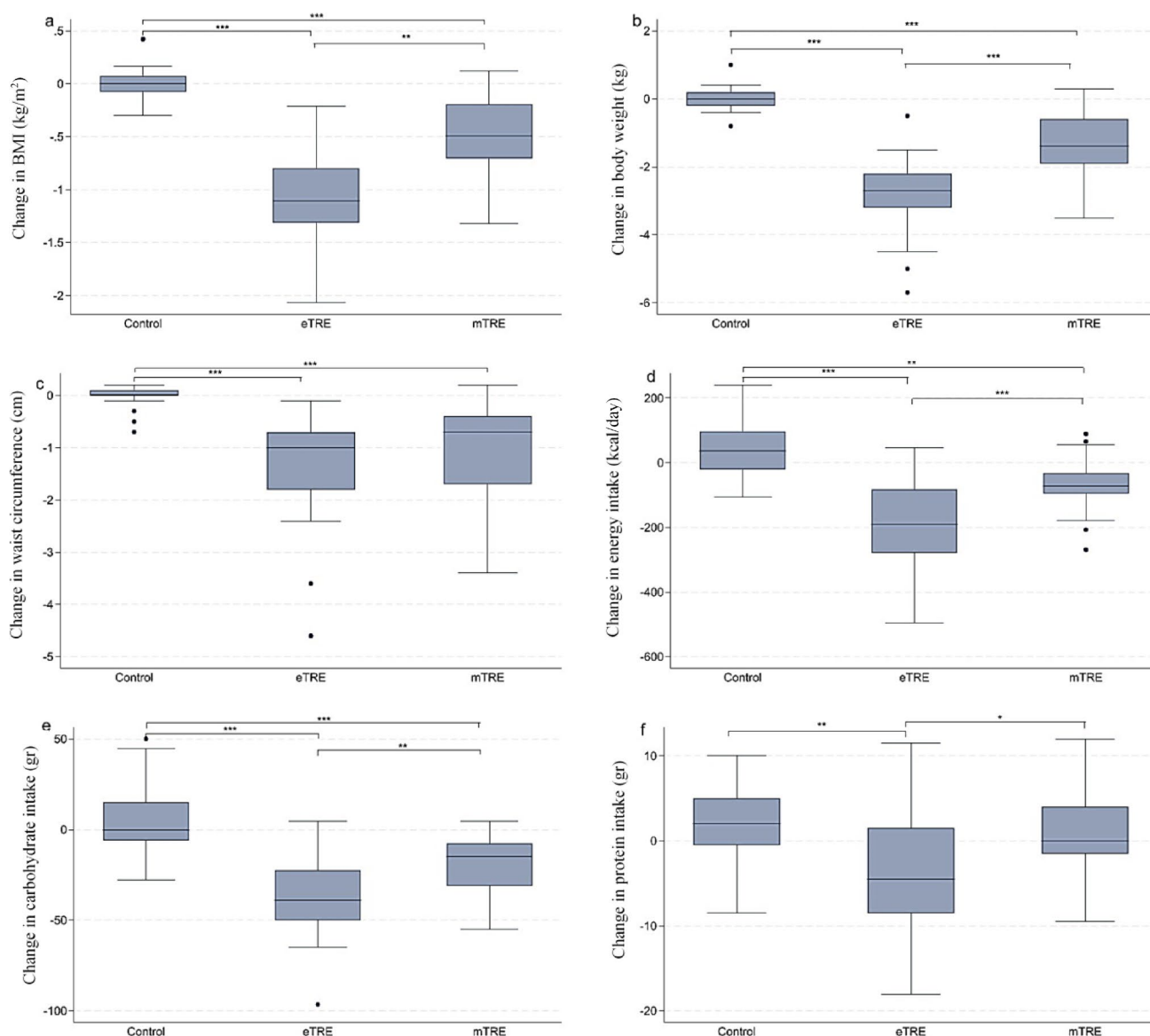


Fig. 2 Energy intake and metabolic health-related parameters. **a** Change in BMI after 6 weeks of intervention, *** $p < 0.001$, ** $p = 0.001$. **b** Change in body weight after 6 weeks of intervention, *** $p < 0.001$. **c** Change in waist circumference after 6 weeks of intervention, *** $p < 0.001$; **d** Change in energy intake after 6 weeks of intervention, *** $p < 0.001$, ** $p = 0.001$. **e** Change in carbohydrate intake after 6 weeks of intervention, *** $p < 0.001$, ** $p = 0.004$. **f** Change in protein intake after 6 weeks of intervention, ** $p = 0.004$, * $p = 0.02$. Energy intake and metabolic health-related parameters. **g** Change in fat intake after 6 weeks of intervention, ** $p = 0.003$, * $p = 0.03$. **h** Change in FBS

after 6 weeks of intervention, *** $p < 0.001$, * $p = 0.04$. **i** Change in insulin after 6 weeks of intervention, *** $p < 0.001$, ** $p < 0.05$; **j** Change in insulin resistance index (measured with HOMA-IR) after 6 weeks of intervention, *** $p < 0.001$, ** $p = 0.001$, * $p = 0.01$. **k** Change in QUICKI index after 6 weeks of intervention, ** $p = 0.001$, * $p = 0.01$. **l** Change in TC after 6 weeks of intervention, *** $p < 0.001$. **m** Change in TG after 6 weeks of intervention. **n** Change in HDL after 6 weeks of intervention. **o** Change in LDL after 6 weeks of intervention, ** $p = 0.006$

Additional detailed statistical results, including comparisons of changes in metabolic health parameters and pre- and post-intervention data, are presented in Supplementary Tables 1 and 2."

Discussion

The present study found that six weeks of both time-restricted eating interventions were associated with reductions in body weight, improvements in insulin sensitivity, and decreases in fasting blood glucose. These changes were more pronounced in the early time-restricted eating group.

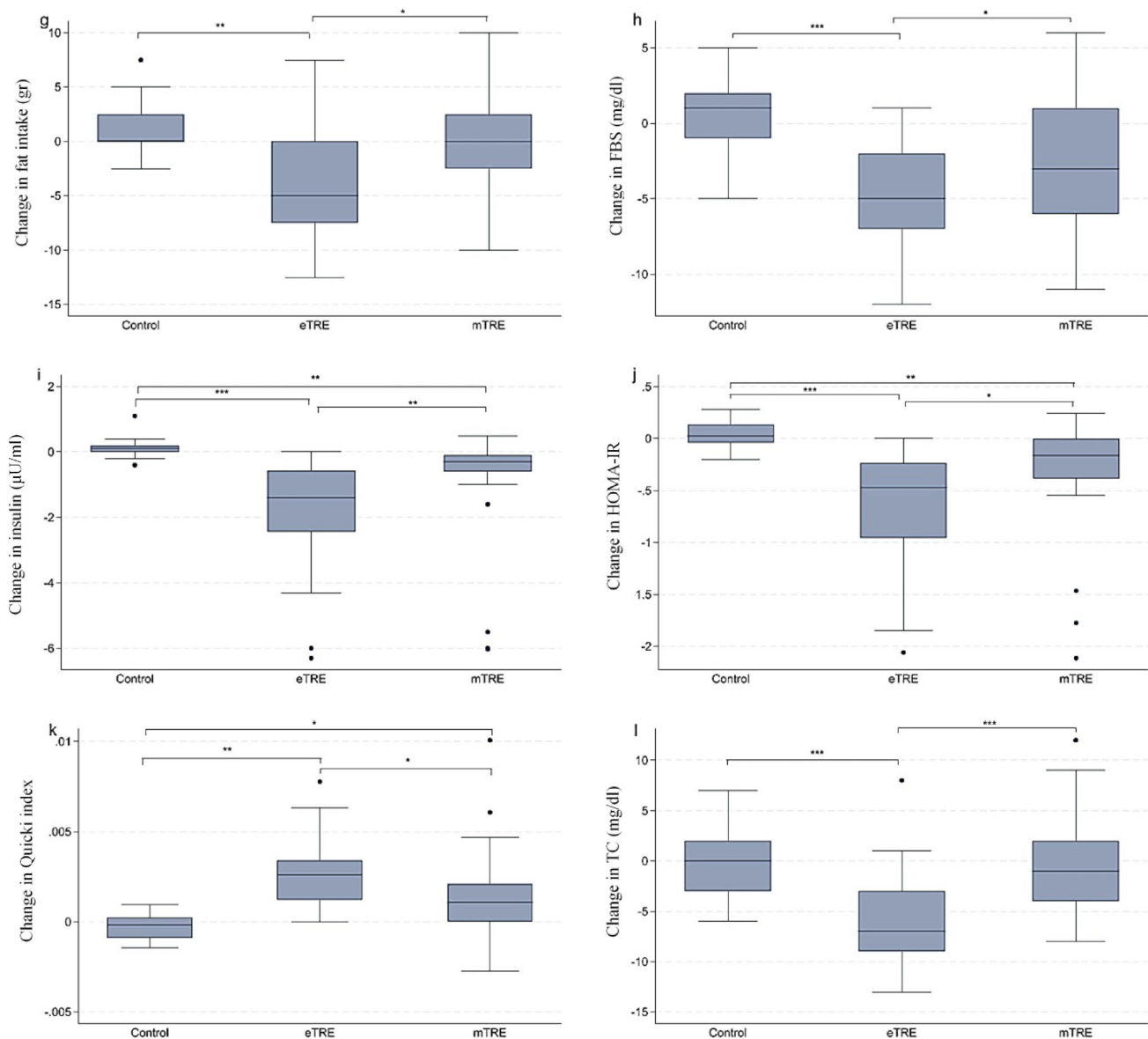


Fig. 2 (continued)

Regarding lipid profiles, the eTRE group, but not the mTRE group, demonstrated significant reductions in total cholesterol and LDL levels compared with both the mTRE and control groups, while no significant changes were observed in HDL or triglyceride levels among the groups. No adverse events were reported during the trial.

Both time-restricted eating groups demonstrated reductions in energy intake despite the absence of prescribed caloric restriction. The extent of this reduction differed between the two intervention groups. One possible explanation for the greater reduction in energy intake in the eTRE group is the omission of dinner, which is traditionally among the largest and most energy-dense meals in the Iranian eating pattern. This difference may have partly influenced

the variation in metabolic outcomes observed between the eTRE and mTRE groups.

Consistent with the observed reductions in energy intake, both eTRE and mTRE resulted in significant decreases in body weight, BMI, and waist circumference compared with the control group. These findings align with previous studies in women with PCOS demonstrating improvements in anthropometric indices following time-restricted eating interventions. For example, Li et al. [27] and Feyzioglu et al. [28] reported significant reductions in weight and BMI after 8-hour time-restricted eating protocols, although changes in body fat distribution were not consistently observed. Evidence from meta-analyses suggests that both early and later time-restricted eating can lead to weight loss,

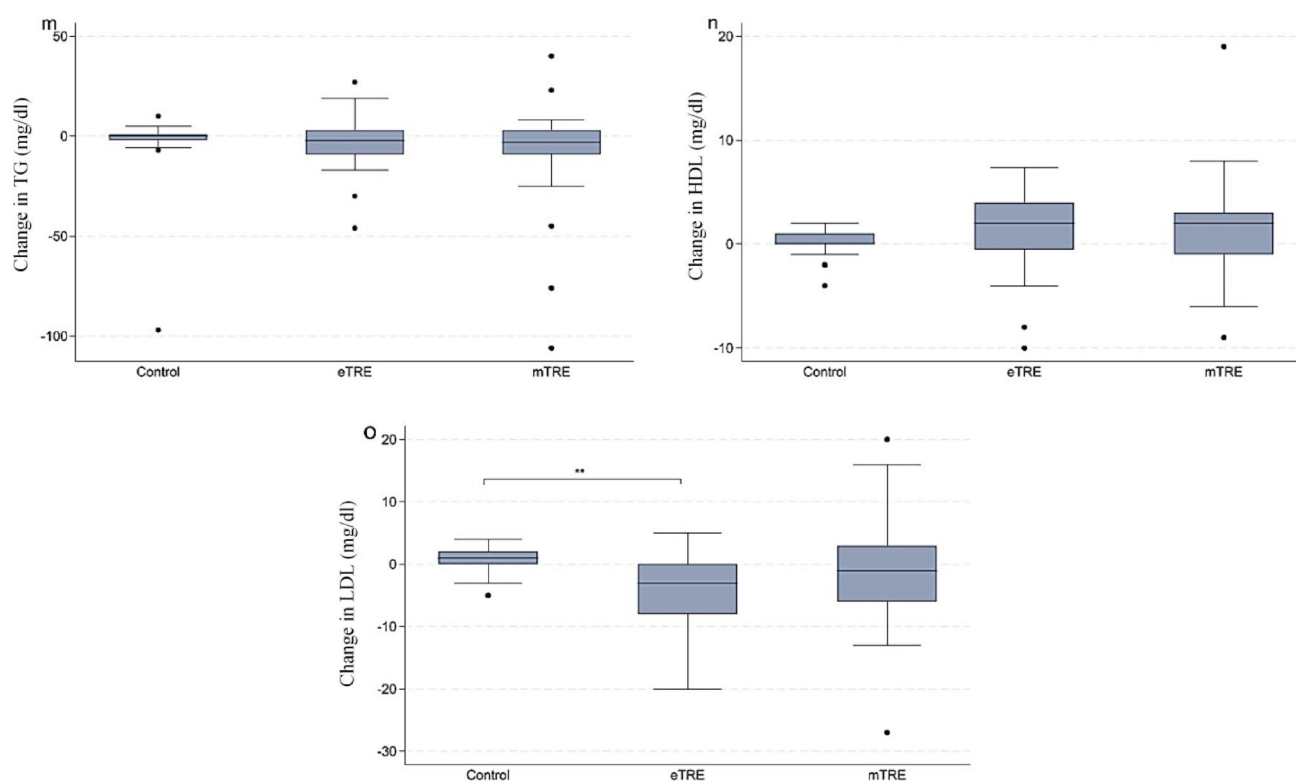


Fig. 2 (continued)

although eating earlier in the day may be associated with slightly greater effects. In contrast to some pooled analyses reporting no significant difference between early and later time-restricted eating, our study observed a greater reduction in anthropometric measures in the early time-restricted eating group [32]. This difference may be explained by variations in study populations and intervention designs [33], as our study focused specifically on women with PCOS and applied clearly defined 10-hour eating windows. The reductions in anthropometric measures observed in this study may be partly related to spontaneous decreases in energy intake with time-restricted eating, as reported in previous studies [32–34]. In addition, aligning food intake earlier in the day with circadian rhythms may improve metabolic efficiency and increase thermogenesis, which could further support weight-related outcomes [35–37]. However, the present study was not designed to separate the individual effects of reduced energy intake and meal timing on changes in anthropometric measures.

Hyperinsulinemia caused by insulin resistance leads to increased androgen production through both direct and indirect pathways and contributes to the reproductive consequences of PCOS [38, 39]. Previous studies suggest that TRE can improve glucose regulation and insulin sensitivity [40–43]. A meta-analysis conducted by Liu et al. [32] showed that eTRE significantly improved fasting glucose

and HOMA-IR compared with non-TRE, whereas ITRE had a weaker effect on HOMA-IR and did not significantly affect, in contrast FBS to our findings. Moreover, eTRE provided greater improvements in HOMA-IR than later eating windows. Two studies assessing TRE in women with PCOS reported significant reductions in glycemic parameters, including fasting insulin, HOMA-IR, and HbA1c; however, findings for FBS were inconsistent, with Feyzioglu et al. [28] reporting a significant decrease and Li et al. [27] observing no significant change. Similarly, our ad libitum study observed early TRE can significantly improve insulin sensitivity levels compared with mTRE.

The effects of TRE on lipid profiles have been inconsistent across studies, with some reporting improvements in specific lipid markers and others showing minimal or no significant effects [43–45]. In the present study, the lipid response was largely driven by improvements in TC and LDL-C with eTRE, whereas other lipid fractions showed no significant changes. These findings suggest that while TRE, particularly eTRE, may have beneficial effects on certain lipid parameters, its overall impact on lipid profiles remains variable. Previous evidence supports this variability. A meta-analysis reported no significant effects of either early or later TRE on lipid profiles in populations with normal baseline lipid levels, indicating that baseline metabolic status may influence responsiveness [32]. Additionally, longer

fasting durations commonly applied in eTRE protocols may differentially affect lipid metabolism without inducing uniform changes across all lipid fractions [46]. The more pronounced cholesterol-lowering effects observed with eTRE may also relate to improved alignment with circadian rhythms, which have been shown to regulate hepatic lipid synthesis and clearance. Collectively, these findings suggest that while eTRE may benefit specific lipid parameters, particularly cholesterol-related markers, its overall impact on lipid profiles remains context-dependent and influenced by individual and methodological factors.

Taken together, the observed differences between eTRE and mTRE may be partly explained by circadian regulation of metabolism [47]. Aligning food intake with circadian rhythms has been shown to optimize glucose handling, insulin sensitivity, and the thermic effect of food, with greater metabolic efficiency in the morning compared with later hours of the day [36, 48]. This temporal alignment may account for the more pronounced metabolic benefits observed with eTRE. Moreover, studies have shown that eating patterns misaligned with circadian rhythms, such as during Ramadan, where food is restricted to nighttime, can lead to variable or even adverse metabolic effects [31, 49]. In addition the early TRE group demonstrated elevated mRNA expression of BMAL1 (Brain and Muscle Arnt-Like 1), a critical activator in regulating circadian rhythms [41].

The present study has several limitations. First, investigators were not blinded during the intervention and data analysis phases. Second, the relatively small sample size may limit the generalizability of the findings. Third, adherence-related factors and potential barriers to TRE were not formally assessed. In addition, although participants followed a 10-hour eating window, variability in meal timing within each group may have contributed to outcome variability. Fourth, the absence of post-intervention follow-up limits conclusions regarding the long-term sustainability and safety of the observed effects. Finally, because reductions in energy intake and body weight occurred spontaneously, the independent effects of meal timing could not be fully disentangled from those of caloric reduction, which may have influenced the observed metabolic outcomes. Therefore, additional well-designed randomized controlled trials (RCTs) are recommended to use larger sample sizes and iso-caloric (calorie-matched) designs to specifically examine the independent effect of meal timing on metabolic health.

In conclusion, TRE, particularly eTRE, may be associated with improvements in body weight, insulin resistance, and specific lipid parameters (TC and LDL-C) in women with PCOS. These findings indicate that TRE may serve as a practical dietary approach to improve metabolic health in this population. Further well-designed studies are needed to

confirm these findings and to better define the role of meal timing in metabolic regulation among women with PCOS.

Supplementary Information The online version contains supplementary material available at <https://doi.org/10.1007/s00394-026-04034-3>.

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Author contributions The authors' responsibilities were as follows: Daneghian and Aminian conceived and designed the study and analysed the data with Heidari. Hajshafiha provided material and technical support. Aminian enrolled participants, collected all data and wrote the manuscript. Daneghian critically revised the manuscript for important intellectual content and had primary responsibility. All authors read and approved the final manuscript.

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Data availability The datasets generated and/or analyzed during the current study are available from the corresponding author on reasonable request.

Declarations

Conflict of interest There are no conflicts of interest to declare.

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