ORIGINAL ARTICLE

Comparative Effects of 16:8 Intermittent Fasting and Continuous Caloric Restriction on Metabolic Syndrome Components in obese Women: A Non-randomized Controlled Clinical Trial

Effets comparatifs du jeûne intermittent 16:8 et de la restriction calorique continue sur les composants du syndrome métabolique chez les femmes obèses : Un essai clinique contrôlé non randomisé

Nesrine Dhieb[1], Rym Ben Othman[1,2], Inchirah Karmous[3], Ramla Mizouri[1], Meriem Nouira[4], Amel Gamoudi[1], Awatef Kacem[1], Wafa Douiri[1], Nadia Ben Mansour[4], Henda Jamoussi[1]

1. Institut national de nutrition et de technologie alimentaire de Tunis, Tunisia.
2. University of Tunis el manar faculty of medicine of Tunis ;
3. Research Unit on Obesity UR18ES01, Faculty of Medicine, University Tunis El Manar, Tunis 1007, Tunisia
4. Hôpital Charles Nicolle, Tunisia

Abstract

Introduction: Intermittent fasting (IF) is gaining interest as an effective method to combat obesity

Objective : to compare the effects of 16:8 intermittent fasting (IF 16:8) and continuous caloric restriction (CCR) on anthropometric parameters and components of metabolic syndrome in obese women.

Methods : A non-randomized controlled clinical trial was conducted with obese women followed for three months. The patients were divided into two groups: IF (45 patients) and CCR (55 patients), each undergoing a 25% reduction in caloric intake. Anthropometric parameters, body composition and metabolic profile were evaluated.

Results : The average age was 34.10 ± 8.44 years in the IF group and 34.62 ± 8.80 years in the CCR group, with BMI values of 38.63 ± 5.15 kg/m² and 34.84 ± 6.69 kg/m², respectively. Both groups experienced significant weight loss after three months, with the IF group showing greater weight change (-7.38 ± 4.1 kg vs. -5.41 ± 3.84 kg, p=0.03). Fat mass and waist circumference reductions were more pronounced in the IF group (p=0.04 and p=0.0001, respectively). Furthermore, IF was more effective than CCR in reducing blood glucose (p=0.04) and triglyceride levels (p=0.02) and increasing HDL-cholesterol (p=0.01). The early feeding window (8h to 16h) in the IF group was associated with greater reductions in weight, fat mass, waist circumference and HOMA insulin resistance index (p=0.001 for all) compared to the 12h to 20h window.

Conclusion : The study suggests that 16:8 intermittent fasting could be a viable alternative to continuous caloric restriction for managing obesity and associated metabolic disorders.

Keywords : obesity ; intermittent fasting ; low-calorie diet ; weight

Résumé

Contexte : Le jeûne intermittent (JI) suscite un intérêt croissant en tant que méthode efficace pour lutter contre l'obésité.

Objectif : Comparer les effets du jeûne intermittent 16:8 (JI 16:8) et de la restriction calorique continue (RCC) sur les paramètres anthropométriques et les composants du syndrome métabolique chez des femmes obèses.

Méthodes : Un essai clinique contrôlé non randomisé a été mené auprès de femmes obèses suivies pendant trois mois. Les patientes ont été réparties en deux groupes : JI (45 patientes) et RCC (55 patientes), chacune ayant une réduction calorique de 25 %. Les paramètres anthropométriques, la composition corporelle et le profil métabolique ont été évalués.

Résultats : L'âge moyen était de 34,10 ± 8,44 ans dans le groupe JI et de 34,62 ± 8,80 ans dans le groupe RCC, avec des IMC respectifs de 38,63 ± 5,15 kg/m² et 34,84 ± 6,69 kg/m². Les deux groupes ont connu une perte de poids significative après trois mois, avec une perte plus importante dans le groupe JI (-7,38 ± 4,1 kg contre -5,41 ± 3,84 kg, p=0,03). La réduction de la masse grasse et du tour de taille était plus marquée dans le groupe JI (p=0,04 et p=0,0001, respectivement). De plus, le JI s'est révélé plus efficace que la RCC pour réduire la glycémie (p=0,04) et les triglycérides (p=0,02) et pour augmenter le HDL-cholestérol (p=0,01). La fenêtre alimentaire précoce (de 8h à 16h) dans le groupe JI était associée à des réductions plus importantes du poids, de la masse grasse, du tour de taille et de l'indice HOMA d'insulinorésistance (p=0,001 pour tous) par rapport à la fenêtre de 12h à 20h.

Conclusion : Cette étude suggère que le jeûne intermittent 16:8 pourrait représenter une alternative viable à la restriction calorique continue pour la prise en charge de l'obésité et des troubles métaboliques associés.

Mots-clés : obésité ; jeûne intermittent ; régime hypocalorique ; poids

Correspondance

Rym Ben Othman

Institut national de nutrition et de technologie alimentaire de Tunis, Tunisia
Email: rym.benothman@fmt.utm.tn

LA TUNISIE MEDICALE-2025; Vol 103 (08): 1116-1121 DOI: 10.62438/tunismed.v103i8.5777

Introduction

Obesity is a chronic disease that results from extremely complex mechanisms. It constitutes a major public health problem worldwide. According to the World Health Organization, the prevalence of obesity has tripled since 1975, affecting 16% of the global adult population in 2022 [1]. In Tunisia, the prevalence of obesity has almost doubled over the past twenty years, rising from 14% in 1997 to 26% in 2016 [2]. This rapidly expanding scourge, despite countless efforts to curb it, is responsible for high morbidity and mortality and a deterioration in quality of life [3]. The management of obesity is difficult. It is based primarily on hygienic-dietary measures and psychotherapy. Most weight loss diets, including continuous caloric restriction, have limited short-term effectiveness and are rather counterproductive with the yo-yo effect they generate [4]. In recent years, new diets including intermittent fasting (IF) have been described, offering a new concept of lifestyle modification to subjects with obesity. Different types of fasting (alternate day fasting, 5:2 fasting and time-restricted fasting) have been the subject of clinical trials. The results are promising in the management of obesity and metabolic diseases [5,6]. However, it is 16:8 IF that has attracted considerable interest from the scientific community. Studies comporting the 16 :8 IF to other dietary approches, following different protocols (randomization, trial duration, window schedule, sample size, etc.) are becoming more frequent and the results are controversial [7]. Some studies have de monstrated the superiority of the 16 :8 IF for weight loss and metabolic parameters, while others have concluded that it has the same impact as other diets [8].

To our knowledge, in Tunisia, no study has been interested in evaluating the impact of 16:8 IF on the anthropometric and metabolic profile of the obese subject. In this context, we conducted this study with two main objectives. The primary objective was to compare the effects of 16:8 IF and continuous caloric restriction (CCR), after a 3-month follow-up, on anthropometric parameters, body composition and components of metabolic syndrome in obese women. The secondary objective was to assess the impact of the feeding window schedule on these outcomes.

Methods

Study design

This study was a non-randomized, controlled, interventional clinical trial with two parallel groups over a three-month intervention period. It was conducted at the Obesity Research Unit of the National Institute of Nutrition and Food Technology in Tunis between October 2022 and March 2023.

Participants

The inclusion criteria encompassed women aged between 18 and 50 years, with a BMI ≥ 30 kg/m², who consented to adhere to the study protocol. Exclusion criteria included patients who were pregnant, breastfeeding or menopausal; diabetic or hypertensive; consuming medications (such as corticosteroids) or specific supplements (like probiotics) that might affect weight evolution; diagnosed with dysthyroidism (hyperthyroidism or hypothyroidism); or affected by any other conditions potentially impacting weight evolution. Additionally, patients who had undergone bariatric surgery, modified their diets within the 12 weeks preceding the study commencement or had severe eating disorders or psychiatric illnesses were not included.

Patients were excluded if they became pregnant, stopped the diet for a week, were difficult to contact, had an acute illness (viral or bacterial infection) or an intercurrent condition during follow-up, were discovered to have diabetes or hypertension requiring treatment.

Study protocol

Each participant in this study received personalized care from a multidisciplinary team, including a doctor, nutritionist and psychologist.

The protocol involved several steps. Initially, there was an initial evaluation (T0) followed by the prescription of a therapeutic diet along with educational guidance. Subsequently, each patient received regular follow-up appointments every 15 days to monitor and reinforce adherence to the prescribed diet. After a follow-up period of 3 months (T1), a re-evaluation was conducted. This re-evaluation encompassed assessments of anthropometric measurements and biological parameters.

The initial evaluation included an interview and a physical examination. The anthropometric measurements included height, weight, body composition and waist circumference. The BMI was calculated using the formula weight (kg) / height (m²) and interpreted according to the WHO classification. Abdominal obesity was defined by a waist circumference ≥80 cm in women [9]. Body composition parameters (body fat mass and body lean mass) were acquired before and after 3 months of intervention by impedance meter TANITA ® BC418M

Dietary Intervention

Each patient received personalized nutritional guidance. The dietary prescriptions for all patients included free choice of diet, allowing the women to choose between IF or CCR. The dietary prescriptions for all patients included:

- Reducing spontaneous caloric intake by 25%.
- Moderately increasing protein intake to 1 to 1.2 grams per kilogram of body weight per day.
- Limiting saturated fat intake to 7% of total energy intake (AET) and minimizing the use of cooking fat.
- Prioritizing the consumption of low or medium glycemic index (IG) carbohydrates.
- Ensuring adequate dietary fiber intake of 25-30 grams per day.
- Restricting the consumption of high energy density foods, especially those high in lipids or sugars, and

avoiding sugary drinks.
- Choosing low energy density foods such as fruits and vegetables and maintaining hydration by drinking sufficient water.
- Controlling portion sizes and encouraging slow eating during meals.
- Advising against watching TV during meals.

In addition, for patients practicing intermittent fasting, the following recommendations were provided:
- Restricting the daily eating window to 8 hours to extend the overnight fasting period to 16 hours.
- Selecting a meal schedule tailored to their lifestyle, either from 8 am to 4 pm (early IF group) or from 12 pm to 8 pm (late IF group).
- Distributing energy intake across 2 meals and a snack within the eating window.
- Prohibiting the consumption of any food or caloric beverages during the fasting period while allowing water, tea, and black coffee without sugar. Adherence to intermittent fasting was defined as respecting the food intake window for at least 5 days per week.

To ensure good adherence, participants were contacted by phone once a week and in person every two weeks. At each check, patients benefited from an evaluation of anthropometric parameters and adherence to IF and dietary advice given during the first consultation in order to correct dietary errors.
We advised all our patients to exercise moderate physical activity daily, either a walk of 30 to 60 minutes every day or a sporting activity of their choice.

Biological Assessment

An 8-hour fasting blood sample was collected to measure metabolic parameters, including fasting blood glucose and glycated hemoglobin. Glycoregulation disorders were defined using the criteria set forth by the American Diabetes Association in 2021 [10].
Insulin resistance was assessed using the HOMA-IR (Homeostasis Model Assessment) index, calculated as fasting insulin (µU/dL) multiplied by fasting blood glucose (mmol/L) divided by 22.5. Insulin resistance was identified by a HOMA-IR index equal to or greater than 2.4.
The lipid profile analysis included measurements of total cholesterol (TC), triglycerides (TG), and HDL-cholesterol (HDL-C). Hypertriglyceridemia was characterized by triglyceride levels equal to or greater than 1.7 mmol/L, while hypercholesterolemia was indicated by total cholesterol levels equal to or greater than 5.2 mmol/L. HypoHDLemia was defined as HDL-cholesterol levels less than 1.3 mmol/L for women.
The diagnosis of metabolic syndrome followed the International Diabetes Federation (IDF) definition [11], requiring the presence of at least three of the following criteria:
- Waist circumference ≥ 80 cm in women
- High triglyceride levels ≥ 1.7 mmol/L or treatment for hypertriglyceridemia
- Low HDL cholesterol levels < 1.3 mmol/L for women, or treatment for hypoHDLemia
- High blood pressure: Systolic BP ≥ 130 mmHg or diastolic BP ≥ 85 mmHg, or known hypertensive patient under treatment
- High fasting blood glucose ≥ 100 mg/dL (5.6 mmol/L)

Evolution of Anthropometric and Metabolic Parameters

After 3 Months: After 3 months of follow-up, we re-evaluated the weight, waist circumference, body composition, blood pressure and metabolic parameters assessed during the first consultation. The variation of each parameter X was calculated according to the following formula:
variation$X = X_{T0\ month} - X_{T1}$
where:
XT0=Initial X (X before the diet)
XT1=X after 3 months of follow-up
The percentage of weight loss compared to the initial weight was calculated according to the following formula:

$$\%\ \text{Weight Loss} = \left(\frac{WT0 - WT1}{WT0}\right) \times 100$$

Ethics Statement

This project received approval from the Ethics Committee of the National Institute of Nutrition and Food Technology in Tunis (02/2021). Each participant in this study was informed about the study protocol and signed an informed consent form prior to their inclusion. All procedures were carried out in accordance with relevant guidelines and regulations, ensuring the ethical conduct of the research. The trial was registred in the the Pan African Clinical Trial Registry under number PACTR202409898073796.

Statistical analysis

The data were entered and analyzed using SPSS software version 23. In the descriptive study, we calculated absolute frequencies and relative frequencies (percentages) for qualitative variables. We calculated means, medians and standard deviations and determined extreme values for quantitative variables. In the analytical study, the comparison of two groups on independent series was performed using the Student's t-test. The comparison of two means on paired series was performed using the paired Student's t-test. The non-parametric Mann-Whitney U test was used to compare two means for groups with a size less than 30. The comparison of percentages on independent series was performed by the Pearson chi-square test and in case of non-validity of this test, by the Fisher's exact bilateral test. The study of the association between two quantitative variables was studied by the Pearson correlation coefficient and in case of non-validity of this test and abnormal distribution; the Spearman rank correlation coefficient was used. The significance threshold was set at 0.05.

Results

Seventy five out of one hundred recruited obese women adhered to the study protocol. In the IF group, 23.3% are in class 1, 43.3% in class 2 and 33.3% in class 3. In the RCC group, 33.3% are in class 1, 28.9% in class 2 and 37.9%

in class 3. Figure 1 presents a flowchart illustrating the distribution of the study population.

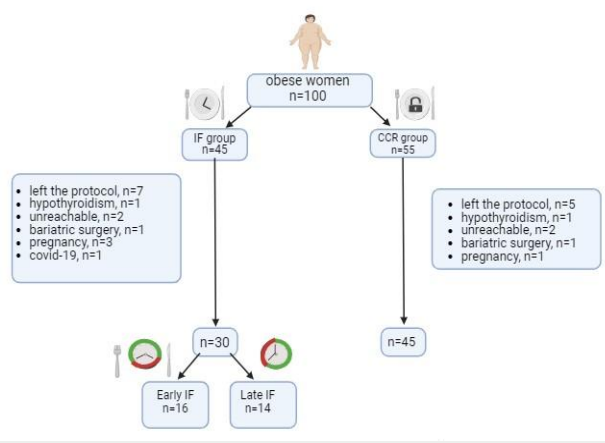

Figure 1. Flowchart of the Population (created by biorender.com)

IF=Intermittent Fasting ; **CCR**= Continous Caloric Restriction ; **Early IF**= This group follows a meal schedule from 8 am to 4 pm ; **Late IF**= This group adheres to a meal schedule from 12 pm to 8 pm.

The average age of the patients in the intermittent fasting group (IF) (34.10±8.44 years) was comparable to that of the patients in the continuous caloric restriction group (CCR) (34.62±8.80 years) (p=0.8).
Two-thirds of the patients had prediabetes before the dietary intervention (T0), 54.7% in the IF group and 57.8% in the CCR group.

Twelve patients (40%) from the IF group had an increase in their lean mass after 3 months. The frequency of patients with metabolic syndrome decreased by 45% in the IF group and by 37% in the RCC group. The difference was not statistically significant between the two groups (p=0.26). The variation of differents parameters are present in table 1.

Table 1. Comparative Analysis of Changes in Anthropometric and Metabolic Parameters between CCR and IF Groups over Time

	CCR group n=45		variation	P T0-T1	IF group n=35		variation	P T0-T1	P intergroup
	T0	T1			T0	T1			
Weight (Kg)	102.71±22.03	97.30±20.97	- 5.41± 3.84	0.0001	102.96±11.77	95.75±11.25	-7.38 ± 4.1	0.0001	0.03
Waist circumference (cm)	113.06±15.29	108.9±15.3	-4.16±3.85	0.0001	117.46±11.13	109.93±10.64	-8.56±3.5	0.0001	<0.001
Fat mass (Kg)	47.25 ±14.86	43.24±14.74	-4.01 ±2.72	0.0001	47.43±8.65	41.89±8.56	-5.54 ± 3.06	0.0001	0.04
Lean mass (Kg)	53.69±4.49	52.47±4.25	-1.25±2.45	0.06	50.44±4.98	50.81±5.86	0.38±2.53	0.06	0.09
Fasting glycemia (mmol/l)	5.48±0.58	5.11±0.56	-0.36±0.37	0.0001	5,8±0,64	5,33±0,43	-0.54±0.40	0.0001	0.049
HbA1c(%)	5.48±0.58	5.11±0.56	-0.36±0.37	0.0001	5.57±0,46	5.33±0.43	-0.37±0.29	0.0001	0.25
Insulin (µUI/ml)	22.64±8.35	11.29±4.1	-11.35±6.02	0.0001	17.58±6.81	14.83±6.87	-2.75±1.68	0.03	0.001
HOMA-IR	5.64±2.18	2.67±0.98	-2.97±1.58	0.0001	4.73±2.1	3.62±1.82	-1.1±0.59	0.004	0.0001
HDL (mmol/l)	1,16±0,22	1,16±0.27	-0.003±0,01	0.09	1.19±0.24	1.29±0.22	+0.10±0.22	0.016	0.018
Triglycerides (mmol/l)	1.24±0.64	1.18±0.53	-0.056±0.034	0.28	1.19±0.54	0.94±0.49	-0.24 ± 0.37	0.0001	0.025
Total cholesterol(mmol/l)	4.68±0.95	4.58±0.75	-0.21±0.19	0.08	4.85±0.80	4.41±0.63	-0.42±0.20	0.18	0.09

IF=Intermittent Fasting ; **CCR**= Continous Caloric Restriction, **HOMA-IR**= Homeostatic Model Assessment of Insulin Resistance ; **T0**: Baseline measurement. **T1**: Follow-up measurement at 3 months

More than half of the IF patients (53.5%) chose the feeding window from 12 PM to 8 PM (Late IF). We studied the same parameters in the IF group, which we differentiated into early and late according to the chosen window.The results are illustrated in Table 2. Results showed that early IF was more effective for weight loss and metabolic parameters but not blood pressure in our population.

Table 2. Comparison of Metabolic and Anthropometric Parameters in Early and Late Intermittent Fasting Groups

	Early IF n=16		variation	P T0-T1 †	Late IF n=14		variation	P T0-T1 †	P intergroup*
	T0	T1			T0	T1			
Weight (Kg)	104.59±11.58	94.53±10.97	-10.06±3.50	0.001	101.09±12.13	96.69±11.86	-4.32±2.1	0.0001	0.001
Waist circumference(cm)	120.10±10.81	109.18±10.57	-10.06±3.50	0.0001	114.57±11.86	108.78±11.82	-4.32±2.1	0.01	<0.001
Fat mass (Kg)	47.66±9.34	41.19±18.88	-6.47±2.76	0.0001	47.16±8.14	43.70±8.29	-3.45±1.58	0.0001	0.0001
Lean mass (Kg)	53.88±6.49	53.85 ±6.52	-0.42 ±1.38	0.3	51.82 ±5.25	51.7 ±5.05	-0.47 ±2.58	0.07	0.23
Fasting glycemia (mmol/l)	5.48±0.58	5.11±0.56	-0.36±0.37	0.0001	5.8±0.64	5.33±0.43	-0.54±0.4	0.0001	0.04
HOM-IR	5.64±2.18	2.67±0.98	-2.97±1.58	0.0001	4.73±2.1	3.62±1.82	-1.1±0.59	0.004	0.0001
HDL (mmol/l)	1.16±0.22	1.16±0.27	-0.003±0.01	0.09	1.19±0.24	1.29±0.22	+0.10±0.22	0.01	0.01
Triglycerides (mmol/l)	1.24±0.64	1.18±0.53	-0.056± 0.03	0.28	1.19±0.54	0.94±0.49	-0.24 ± 0.37	0.0001	0.02
SBP (mmHg)	120.60±12.2	116.50±8.5	- 4.1±10.2	0.01	123.5±0.86	118.8±7.1	-4.6±5.5	0.0001	0.76
DBP (mmHg)	6.81±0.91	6.56±0.72	0.25±0.44	0.3	7.17±0.72	6.85±0.53	0.32±0.54	0.2	0.4

***P**: Student's t-test for independent samples (comparison between the two groups G1 and G2)
†P: Paired Student's t-test (comparison of weight loss within the same group)
Early IF= This group follows a meal schedule from 8 am to 4 pm ; **Late IF**= This group adheres to a meal schedule from 12 pm to 8 pm; **T0**: Baseline measurement. **T1**: Follow-up measurement at 3 months ; **HbA1c**: Hemoglobin A1c ; **HDL**: High-Density Lipoprotein ; **SBP**: Systolic Blood Pressure ; **DBP** : Diastolic Blood Pressure.

Discussion

Our study showed a significantly greater weight reduction in the Intermittent Fasting Group (IF) than in the continous caloric restriction (CCR).This weight loss was associated with a significantly more marked decrease in fat mass and waist circumference in the IF group than in the CCR. Intermittent fasting was also more effective than regular caloric restriction on the decrease in blood glucose and triglyceride levels and on the increase in HDL-cholesterol. The limited feeding window between 8 a.m. and 4 p.m. was more effective on weight as well as on insulin sensitivity than the one between 12 p.m. and 8 p.m.

Our results align with several studies that have demonstrated the effectiveness of IF on weight loss in obese subjects and its superiority to CCR. Among these, the randomized study by Chow et al. [12], conducted with 20 participants with obesity divided into 2 groups: IF group 16:8 (n=11) and CCR group (n=9), showed a significantly greater weight loss in the IF group (-3.6 kg) than in the CCR group (-1.5kg) after a follow-up of 12 weeks. The difference was statistically significant. On the other hand, other studies have not demonstrated the superiority of IF over CCR. A recent meta-analysis [14], grouping several clinical studies conducted with overweight and obese patients who followed different IF protocols, concluded that IF is as effective as CCR on the reduction of body weight and that it could be proposed to obese subjects as an alternative approach to CCR. Lowe et al [15] conducted a randomized clinical trial in California with 116 obese subjects and found no significant difference between the two groups. The study by Kunduraci and Ozbek [16] also showed no superiority of IF over CCR on weight.

Weight loss observed in IF groups is explained by a multitude of adaptation mechanisms during periods of prolonged fasting [17]. Indeed, fasting for 10 to 14 hours or more leads to the depletion of liver glycogen reserves and the hydrolysis of triglycerides into free fatty acids in adipocytes. The free fatty acids released into the circulation are transported into hepatocytes where they produce ketone bodies, acetoacetate and β-hydroxybutyrate which constitute a main source of energy for many tissues, especially the brain, during fasting. These ketone bodies are actively transported into cells where they are metabolized into acetyl CoA, which enters the tricarboxylic acid cycle and generates Adenosine triphosphate. Thus, the weight loss induced by IF is explained by lipolysis and the production of ketone bodies which are satiating.

The timing of the feeding window could also have an impact on weight evolution. Several studies have shown the beneficial effect of an early feeding window on weight loss. Sutton et al. [18] conducted a controlled, randomized, crossover, and isocaloric clinical trial for 5 weeks to test intermittent fasting with an early feeding window. The study showed that feelings of satiety upon waking and a full stomach increased significantly in the early time restricted eating group. The authors concluded that early fasting could curb evening food intake and therefore, facilitate weight loss. This hypothesis is consistent with studies [19–21] conducted on rodents, which have shown that early time-restricted feeding reduce appetite hormones and consequently decrease weight. Other human studies [22–24] have also demonstrated that aligning food intake with circadian rhythms reduces the sensation of hunger and promotes weight loss.

Circadian systems are a network of biological clocks, consisting of a central clock in the suprachiasmatic nuclei of the hypothalamus and many secondary clocks in the brain and peripheral organs, which synchronize all physiological (lipogenesis, oxidation of fatty acids in the liver, etc.) and behavioral processes to the day-night alternation [25]. As a conductor, the central clock coordinates the peripheral clocks which integrate signals reporting the energy state of cells and, in return, regulate many metabolic pathways allowing to optimize the use of energy substrates. Indeed, food intake at an inappropriate circadian time, i.e., during the sleep period, leads to deregulations of peripheral clocks (present in the liver, pancreas, adipose tissue, skeletal muscle, etc.) causing metabolic and hormonal disorders that can lead to the development of obesity [26]. In the morning, ghrelin, an orexigenic hormone, is secreted in a pulsatile rhythm. It presents three secretion peaks, around 8 a.m., 1 p.m., and 6 p.m. Cortisol, a so-called stress hormone, triggers food intake by ending satiety, between 7 and 8 a.m., when it is at its maximum plasma concentration [27]. At 10 a.m., adiponectin begins to be secreted and ends at 8 p.m., with a secretion peak reached at 11 a.m. Adiponectin is a major regulator of glucose and lipid metabolism. It improves glycolysis and fatty acid oxidation via the activation of AMPK, a kinase involved in supporting energy homeostasis, and also reduces hepatic glucose production. These mechanisms increase glucose utilization and insulin sensitivity and prevent fat accumulation [28]. Insulin, secreted during food ingestion, stimulates substrate storage by activating the genes of fatty acid synthesis (such as acetyl-CoA carboxylase) and glycogenesis genes, and by inhibiting the transcription of gluconeogenesis and fatty acid oxidation genes. Its secretion gradually increases to reach a peak between 4 and 5 p.m. which allows to announce satiety and to end food intake [29]. Then, leptin secretion increases around 4 p.m. to reach a peak around 7 p.m. to return to the baseline level at 2 a.m. It suppresses food intake, increases lipolysis, and inhibits fat accumulation [36]. Thus, daytime meals at fixed times synchronize many peripheral clocks and help to rebalance the energy balance [30].

Our study was the first in Tunisia to examine the impact of Intermittent Fasting (IF) versus Continuous Caloric Restriction (CCR) over a long follow-up period of 3 months. However, it was a non-randomized clinical trial, where each participant had the freedom to choose her diet type based on her lifestyle. A significant number of participants dropped out during the course of the study. Furthermore, the study population consisted exclusively of female participants.

Conclusion

Given the weight and metabolic benefits of intermittent fasting, we recommend this type of diet in the management of obesity, if it suits their lifestyle, while respecting contraindications. It is important to consider prescribing this dietary approach with qualified health professionals, in order to establish a personalized eating rhythm that is more recommended than ever by learned societies, as part of precision medicine. At present, there is no general consensus on the ideal time to eat/fast or the optimal duration of the feeding window. Moreover, these parameters may be different from one person to another, particularly depending on genetic heritage, individual history and lifestyle.

References

1. Phelps NH, Singleton RK, Zhou B, Heap RA, Mishra A, Bennett JE, et al. Worldwide trends in underweight and obesity from 1990 to 2022: a pooled analysis of 3663 population-representative studies with 222 million children, adolescents, and adults. The Lancet 2024;403:1027–50. https://doi.org/10.1016/S0140-6736(23)02750-2.
2. Khelil M, Ben Abdelaziz A, Zanina Y, Yahia F, Ben Hassine D, Ben Rejeb N, et al. Epidemiology of obesity in Tunisia: HSHS4 study (Hammam Sousse Sahloul Heart Study). Tunis Med 2022;100:551–60.
3. Apovian CM. Obesity: definition, comorbidities, causes, and burden. Am J Manag Care 2016;22:s176-185.
4. Amigo I, Fernández C. Effects of diets and their role in weight control. Psychol Health Med 2007;12:321–7. https://doi.org/10.1080/13548500600621545.
5. Patterson RE, Sears DD. Metabolic Effects of Intermittent Fasting. Annu Rev Nutr 2017;37:371–93. https://doi.org/10.1146/annurev-nutr-071816-064634.
6. Moon S, Kang J, Kim SH, Chung HS, Kim YJ, Yu JM, et al. Beneficial Effects of Time-Restricted Eating on Metabolic Diseases: A Systemic Review and Meta-Analysis. Nutrients 2020;12:1267. https://doi.org/10.3390/nu12051267.
7. Patikorn C, Roubal K, Veettil SK, Chandran V, Pham T, Lee YY, et al. Intermittent Fasting and Obesity-Related Health Outcomes: An Umbrella Review of Meta-analyses of Randomized Clinical Trials. JAMA Netw Open 2021;4:e2139558. https://doi.org/10.1001/jamanetworkopen.2021.39558.
8. Parr EB, Devlin BL, Hawley JA. Perspective: Time-Restricted Eating—Integrating the What with the When. Adv Nutr 2022;13:699–711. https://doi.org/10.1093/advances/nmac015.
9. Alberti KGMM, Zimmet P, Shaw J. Metabolic syndrome--a new world-wide definition. A Consensus Statement from the International Diabetes Federation. Diabet Med J Br Diabet Assoc 2006;23:469–80. https://doi.org/10.1111/j.1464-5491.2006.01858.x.
10. American Diabetes Association. 2. Classification and Diagnosis of Diabetes: Standards of Medical Care in Diabetes—2021. Diabetes Care 2021;44:S15–33. https://doi.org/10.2337/dc21-S002.
11. Alberti KGMM, Eckel RH, Grundy SM, Zimmet PZ, Cleeman JI, Donato KA, et al. Harmonizing the Metabolic Syndrome: A Joint Interim Statement of the International Diabetes Federation Task Force on Epidemiology and Prevention; National Heart, Lung, and Blood Institute; American Heart Association; World Heart Federation; International Atherosclerosis Society; and International Association for the Study of Obesity. Circulation 2009;120:1640–5. https://doi.org/10.1161/CIRCULATIONAHA.109.192644.
12. Chow LS, Manoogian ENC, Alvear A, Fleischer JG, Thor H, Dietsche K, et al. Time-Restricted Eating Effects on Body Composition and Metabolic Measures in Humans who are Overweight: A Feasibility Study. Obesity 2020;28:860–9. https://doi.org/10.1002/oby.22756.
13. Kahleova H, Belinova L, Malinska H, Oliyarnyk O, Trnovska J, Skop V, et al. Eating two larger meals a day (breakfast and lunch) is more effective than six smaller meals in a reduced-energy regimen for patients with type 2 diabetes: a randomised crossover study. Diabetologia 2014;57:1552–60. https://doi.org/10.1007/s00125-014-3253-5.
14. Stanek A, Brożyna-Tkaczyk K, Zolghadri S, Cholewka A, Myśliński W. The Role of Intermittent Energy Restriction Diet on Metabolic Profile and Weight Loss among Obese Adults. Nutrients 2022;14:1509. https://doi.org/10.3390/nu14071509.
15. Lowe DA, Wu N, Rohdin-Bibby L, Moore AH, Kelly N, Liu YE, et al. Effects of Time-Restricted Eating on Weight Loss and Other Metabolic Parameters in Women and Men With Overweight and Obesity: The TREAT Randomized Clinical Trial. JAMA Intern Med 2020;180:1491. https://doi.org/10.1001/jamainternmed.2020.4153.
16. Kunduraci YE, Ozbek H. Does the Energy Restriction Intermittent Fasting Diet Alleviate Metabolic Syndrome Biomarkers? A Randomized Controlled Trial. Nutrients 2020;12:3213. https://doi.org/10.3390/nu12103213.
17. Anton SD, Moehl K, Donahoo WT, Marosi K, Lee SA, Mainous AG, et al. Flipping the Metabolic Switch: Understanding and Applying the Health Benefits of Fasting: Flipping the Metabolic Switch. Obesity 2018;26:254–68. https://doi.org/10.1002/oby.22065.
18. Sutton EF, Beyl R, Early KS, Cefalu WT, Ravussin E, Peterson CM. Early Time-Restricted Feeding Improves Insulin Sensitivity, Blood Pressure, and Oxidative Stress Even without Weight Loss in Men with Prediabetes. Cell Metab 2018;27:1212-1221.e3. https://doi.org/10.1016/j.cmet.2018.04.010.
19. Chaix A, Zarrinpar A, Miu P, Panda S. Time-Restricted Feeding Is a Preventative and Therapeutic Intervention against Diverse Nutritional Challenges. Cell Metab 2014;20:991–1005. https://doi.org/10.1016/j.cmet.2014.11.001.
20. Zarrinpar A, Chaix A, Yooseph S, Panda S. Diet and feeding pattern affect the diurnal dynamics of the gut microbiome. Cell Metab 2014;20:1006–17. https://doi.org/10.1016/j.cmet.2014.11.008.
21. García-Luna C, Soberanes-Chávez P, de Gortari P. Prepuberal light phase feeding induces neuroendocrine alterations in adult rats. J Endocrinol 2017;232:15–28. https://doi.org/10.1530/JOE-16-0402.
22. Gill S, Panda S. A Smartphone App Reveals Erratic Diurnal Eating Patterns in Humans that Can Be Modulated for Health Benefits. Cell Metab 2015;22:789–98. https://doi.org/10.1016/j.cmet.2015.09.005.
23. Jakubowicz D, Barnea M, Wainstein J, Froy O. Effects of caloric intake timing on insulin resistance and hyperandrogenism in lean women with polycystic ovary syndrome. Clin Sci Lond Engl 1979 2013;125:423–32. https://doi.org/10.1042/CS20130071.
24. Jakubowicz D, Barnea M, Wainstein J, Froy O. High caloric intake at breakfast vs. dinner differentially influences weight loss of overweight and obese women. Obes Silver Spring Md 2013;21:2504–12. https://doi.org/10.1002/oby.20460.
25. Welsh DK, Takahashi JS, Kay SA. Suprachiasmatic nucleus: cell autonomy and network properties. Annu Rev Physiol 2010;72:551–77. https://doi.org/10.1146/annurev-physiol-021909-135919.
26. Herzog ED, Hermanstyne T, Smyllie NJ, Hastings MH. Regulating the Suprachiasmatic Nucleus (SCN) Circadian Clockwork: Interplay between Cell-Autonomous and Circuit-Level Mechanisms. Cold Spring Harb Perspect Biol 2017;9:a027706. https://doi.org/10.1101/cshperspect.a027706.
27. Espelund U, Hansen TK, Højlund K, Beck-Nielsen H, Clausen JT, Hansen BS, et al. Fasting unmasks a strong inverse association between ghrelin and cortisol in serum: studies in obese and normal-weight subjects. J Clin Endocrinol Metab 2005;90:741–6. https://doi.org/10.1210/jc.2004-0604.
28. Manoogian ENC, Panda S. Circadian rhythms, time-restricted feeding, and healthy aging. Ageing Res Rev 2017;39:59–67. https://doi.org/10.1016/j.arr.2016.12.006.
29. Boden G, Ruiz J, Urbain JL, Chen X. Evidence for a circadian rhythm of insulin secretion. Am J Physiol 1996;271:E246-252. https://doi.org/10.1152/ajpendo.1996.271.2.E246.
30. Charlot A, Hutt F, Sabatier E, Zoll J. Beneficial Effects of Early Time-Restricted Feeding on Metabolic Diseases: Importance of Aligning Food Habits with the Circadian Clock. Nutrients 2021;13:1405. https://doi.org/10.3390/nu13051405.