


Review

Intermittent Fasting and Fat Mass: What Is the Clinical Magnitude?

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Abstract: Clinical studies addressing the benefits of intermittent fasting (IF) diets have evoked interest in the treatment of obesity. Herein, the overall effects of IF regimens on fat-mass loss are explained in a brief review through a recent literature update. To date, human studies show a reduction in fat mass from 0.7 to 11.3 kg after IF regimens, in which the duration of interventions ranges from two weeks to one year. In light of this, IF regimens can be considered a reasonable approach to weight (fat mass) loss. However, the benefits of IF regimens occur thanks to energy restriction and cannot hence be considered the best dietary protocol compared to conventional diets.

Keywords: intermittent fasting; fat mass; obesity; time-restricted feeding; weight loss

1. Introduction

Many types of intermittent fasting (IF) regimens have integrated therapeutic alternatives against health issues [1]. Religious, conventional, and modern protocols constitute IF regimens such as Ramadan, alternate-day fasting, and time-restricted feeding [2,3]; even skipping breakfast can be considered a type of IF depending on the fasting hours, as IF diets consist of ≥ 12 h/day of fasting [4].

Along these lines, IF emerged as a multifaceted dietary tool to manage cardiometabolic problems such as dyslipidemia, elevated blood glucose levels, hypertension, and non-alcoholic fatty liver disease [5,6]. Taken together, the mechanisms ascribed to these benefits are mainly due to the fasting-induced adenosine monophosphate-activated protein kinase (AMPK)/sirtuin 1 axis, whose enzymes activate the peroxisome proliferator-activated receptor alpha (PPAR α) and peroxisome proliferator-activated receptor-gamma coactivator 1 alpha (PGC-1 α) in skeletal muscle, adipocytes, cardiomyocytes, and hepatocytes, ultimately enhancing fatty acid oxidation and insulin sensitivity [7–11].

Thanks to these attractive mechanisms, IF has also gained massive attention as a weight loss approach, since the AMPK-sirtuin 1 signaling pathway is triggered by energy depletion [12–14]. However, it is crucial to note that weight loss per se can ameliorate metabolic aspects of cardiovascular diseases and accompanying low-grade inflammation [15–20]. Thus, a critical appraisal geared toward the general effects of IF regimens on weight loss must be done in an effort to draw pragmatic conclusions for scientists, dietitians, physicians, and other health practitioners.

Although epidemiologically relevant and ubiquitous in the general circles of medicine, body weight, body mass index, and waist circumference are measures with less specificity than body fat in understanding adiposity. In this way, clinical attention to body fat changes is a straightforward and meaningful way of inferring weight loss success, guiding professionals who cope with body composition. In 2018, I published a review regarding the general effects of IF on fat mass [21], and, fortunately, many studies were published after that [22–24]. Accordingly, in this brief review, I have updated my previous search and expanded the general effects of IF strategies on fat mass in order to underpin the current scientific state and depict the clinical magnitude.



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2. Methods

A brief literature search was performed employing MEDLINE, EMBASE, SCOPUS, and Web of Science from inception to December 2021. The following keywords were used: “intermittent fasting” OR “time-restricted feeding” OR “alternate-day fasting” OR “Ramadan” and “fat mass” OR “weight loss” OR “body composition”.

Only human studies were selected, while studies that used skinfold as a method of body composition were excluded due to notable interrater differences. Then, intragroup differences for body fat in kilograms or percentages from IF interventions were collected to provide a clear message. Following this search, a total of 20 arms (17 studies) were included.

Lastly, a viewpoint along with take-home messages for practitioners was undertaken as a means of translating the results into the clinical setting.

3. Effects of IF Diets on Fat Mass

Overall, studies in Table 1 that demonstrate significant intragroup decreases in fat mass cover a range of 0.7 to 11.3 kg after IF regimens, in which the length of interventions varied from two weeks to one year.

Table 1. Human studies that addressed changes in fat mass after intermittent fasting.

Reference	Subjects in the IF Arm	IF Protocol	Duration	Δ Fat Mass	Body Composition Method
<i>Alternate-day fasting</i>					
Carter et al., 2019 [25]	70 patients with type 2 diabetes (39 women and 31 men), 61 ± 9 y	Followed a 500–600 kcal diet for 2 non-consecutive days/week and their usual diet for 5 days/week.	12 months	↓5.1 kg *	DXA
Antoni et al., 2018 [26]	15 patients with overweight/obesity (8 women and 7 men), 42 ± 4 y	Approximately 25% (630 kcal) of their estimated energy needs for 2 days/week. On the remaining 5 days (feed days), participants’ food intake was self-selected, but they were asked to consume a eucaloric healthy diet.	2 weeks	↓3.7 kg *	BIA
Byrne et al., 2018 [27]	24 men with obesity, 40 ± 9 y	Energy intake equivalent to 67% of weight maintenance requirements.	4 months	↓9.2 kg *	BIA
Coutinho et al., 2018 [28]	18 patients with obesity (women:men ratio = 10:4), 39 ± 11 y	Patients underwent 3 non-consecutive days of partial fasting per week (550 and 660 kcal/day for women and men, respectively). For the feeding days, a diet matching energy needs was prescribed.	3 months	↓11.3 kg *	Plethysmography
Trepanowski et al., 2017 [29]	25 men with obesity, 44 ± 10 y	Alternate-day fasting (25% of energy needs on fast days instructed to be consumed between 12 p.m. and 2 p.m.; 125% of energy needs on alternating feast days).	6 months	↓4.8 kg *	DXA
Klempel et al., 2013 [30]	17 women with obesity, 42 ± 3 y	Alternate-day fasting, high-fat diet (45% fat, 40% carbohydrate and 15% protein), 25% of energy needs on the fasting day (consumed between 12 p.m. and 2 p.m.) and 125% of energy needs on the feed day.	2 months	↓5.4 kg *	DXA
Klempel et al., 2013 [30]	18 women with obesity, 43 ± 2 y	Alternate-day fasting, low-fat diet (25% fat, 60% carbohydrate and 15% protein), 25% of energy needs on the fasting day (consumed between 12 p.m. and 2 p.m.) and 125% of energy needs on the feed day.	2 months	↓4.2 kg *	DXA

Table 1. Cont.

Reference	Subjects in the IF Arm	IF Protocol	Duration	Δ Fat Mass	Body Composition Method
<i>Ramadan</i>					
Nachvak et al., 2018 [31]	152 healthy men, 39 ± 11 y	Absence of any food or fluid intake during daylight hours.	1 months	↓0.7 kg *	BIA
Hammouda et al., 2013 [32]	15 professional soccer players, 17 ± 0.3 y	Absence of any food or fluid intake during daylight hours.	1 month	↓0.7 kg	BIA
Mirzaei et al., 2012 [33]	14 male collegiate wrestlers, 20 ± 3 y	Absence of any food or fluid intake during daylight hours.	1 month	↓1.0 kg *	BIA
Sadiya et al., 2011 [34]	19 patients (14 women and 5 men) with metabolic syndrome, 37 ± 13 y	Absence of any food or fluid intake during daylight hours.	1 month	↓0.8 kg	BIA
Ibrahim et al., 2008 [35]	14 subjects (9 men and 4 healthy women), 25–58 y	Absence of any food or fluid intake during daylight hours.	1 month	↑0.4 kg	BIA
Kassab et al., 2003 [36]	6 eutrophic women, 18–45 y	Absence of any food or fluid intake during daylight hours.	1 month	↓3.6 * kg	BIA
Kassab et al., 2003 [36]	18 women with obesity, 18–45 y	Absence of any food or fluid intake during daylight hours.	1 month	↓0.2 kg	BIA
<i>Time-restricted feeding</i>					
Pureza et al., 2021 [37]	31 low-income women with obesity, 32 ± 7 y	Low-energy (500–1000 caloric deficit), time-restricted feeding of 12 h.	12 months	↓1.0%	BIA
Lowe et al., 2020 [38]	49 women and men with overweight and obesity, 47 ± 11 y	Time-restricted eating, ad libitum intake from 12 p.m. until 8 p.m. and complete abstinence from caloric intake from 8 p.m. until 12 p.m. the following day.	3 months	↓0.5 kg	DXA
Moro et al., 2020 [39]	8 young elite male cyclists, 20 ± 2 y	Time-restricted feeding with 100% of the estimated daily energy needs in an 8-h time window (from 10 a.m. to 6 p.m.).	1 month	↓1.1% *	BIA
Tinsley et al., 2019 [40]	13 resistance-trained females, 22 ± 2 y	Time-restricted feeding (16/8) with calorie intake (~1600 kcal/day) between 12 p.m. to 8 p.m.	2 months	↓0.4 kg *	DXA
Tinsley et al., 2019 [40]	13 resistance-trained females, 22 ± 3 y	Time-restricted feeding (16/8) with calorie intake (~1500 kcal/day) between 12 p.m. and 8 p.m. plus 3 g/day β-hydroxy β-methylbutyrate.	2 months	↓0.7 kg *	DXA
Moro et al., 2016 [41]	17 resistance-trained males, 30 ± 4 y	Time-restricted feeding (16/8) based on 3 meals consumed at 1 p.m., 4 p.m. and 8 p.m. Eucaloric, high-protein diet.	2 months	↓1.6 *	DXA

* statistical intragroup significance ($p < 0.05$) before and after IF as used in the original study; intragroup statistical analysis was not performed for values without superscript symbols. Fat mass values without symbols represent nonsignificant changes. BIA, bioelectrical impedance; DXA, dual-energy X-ray absorptiometry; IF, intermittent fasting.

Regarding methods for assessing fat mass, the use of bioelectrical impedance was prevalent in Ramadan studies, which are the seminal works (2003–2013) in the background of IF (Table 1).

While Ramadan studies have an observational design, fortunately, several randomized clinical trials (RCTs) employing time-restricted feeding or alternate-day fasting have emerged in recent years using dual-energy X-ray absorptiometry (DXA) for body composition analysis (Table 1).

A single study used air displacement plethysmography and, interestingly, showed a greater fat mass reduction (−11.3 kg) [28]. This study investigated an alternate-day fasting protocol with a duration of three months, in which patients followed three non-consecutive days of partial fasting per week (550 and 660 kcal/day for women and men,

respectively) or a diet matching energy needs for feeding days. Such a fat mass loss portrays clinical relevance if maintained in the long term, as epidemiological estimates show that a predicted fat mass above 21 kg is associated with an overt increase of all-cause mortality risk, confirmed by a hazard ratio of 1.22 (1.18 to 1.26) per standard deviation [42].

As the above-mentioned results are based on intragroup comparisons of IF regimens, it is crucial to consider their effects compared to continuous energy restriction. Trepanowski et al. conducted one of the best RCTs so far to respond to this clinical question [29]. Both alternate-day fasting (25% and 125% of energy needs on fast days and feast days, respectively) and continuous energy restriction (75% of energy needs every day) decreased the fat mass in patients with obesity under a 6-month weight-loss phase, without difference between groups [29]. Therefore, it cannot be affirmed that IF regimes are superior to traditional low-calorie diets, especially when calories are equalized.

4. General Clues for Clinical Practice

Individuals with obesity can benefit from IF due to its greater flexibility. For instance, it is possible to maintain high-volume meals within the eating window, which could be an interesting approach for individuals with obesity due to a likely higher stomach capacity induced by previous eating habits [43].

At least ~30 g protein per meal (or ~3 g leucine across food per meal) divided into two high-volume meals with one or two snacks can be sufficient to supply total protein needs, aiding satiety and muscle maintenance as well [41,44–46]. Supplementing with whey protein or vegetable protein (i.e., pea, soy, and rice protein isolate) along with dairy (yogurt, milk, cheese, etc.) can be useful tools for providing an adequate amount of protein and calcium in snacks. This advice is important because the central tenet of IF is to reduce the meal frequency, thereby decreasing the intake of dietary sources of calcium by excluding breakfast and snacks.

It is worth noting that it is wise to include high-fiber foods in high-volume meals in order to avoid excess calories from sugars and oils. Vegetables, fruits, seeds, whole grains are some examples of healthy foods to be included as a base. In addition, they provide micronutrients and antioxidants [47–51]. That said, incorporating small amounts of “unhealthy” foods can be accepted to maintain some of the patient’s habits, but in moderation, as flexible dieting strategies have been deemed an important weight loss approach as a means of avoiding weight regain [52].

Binge eating in patients with obesity must be monitored individually. On the one hand, IF could shorten the eating window, leading to a reduced total caloric intake; on the other hand, long hours of fasting could trigger binge eating and therefore result in a higher caloric intake even within the eating window of IF regimens.

Nowadays, due to a busy work schedule, many individuals only have the early morning hours to exercise. Thus, IF can be an approach to not shortening the hours of sleep to prepare breakfast and wait for a proper digestion time; however, exercise while fasting can be uncomfortable for many individuals, although it is metabolically viable given that muscle glycogen stores depend on the previous day’s food intake [53] and a common exercise routine (~1 h/day) does not cause hypoglycemia [54]—except in patients on hypoglycemic medications without adequate control [55].

Finally, caveats for different clinical populations cannot be ruled out. Not only patients with insulin-treated diabetes but also very elderly subjects, children, and pregnant and breastfeeding women can be more susceptible to adverse effects of fasting.

5. Conclusions

IF regimens are a useful tool targeting weight loss due to their pronounced body fat-lowering effects. In addition to aesthetic outcomes, these effects in part explain the benefits of IF in obesity-related diseases (e.g., dyslipidemia, type 2 diabetes mellitus, hypertension, and nonalcoholic fatty liver disease) due to the unifying link between adiposity and low-

grade inflammation [2,56], but further long-term RCTs are imperative to allow a better understanding of dietary adherence and primary outcomes.

At best, health professionals (dietitians, nutritionists, and physicians) who face miscellaneous challenges in the inherently complex management of obesity could consider IF diets as a worthwhile strategy. Notwithstanding the attractive mechanisms and clinical results, however, the benefits of IF diets occur thanks to energy restriction and thus cannot be considered the best dietary protocol compared to conventional methods.

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