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Effects of Different Intermittent Fasting Regimens on Core Indicators of Metabolic Syndrome: Body Weight, Glycemia, Blood Lipids, and Blood Pressure

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Abstract. Body weight, glycemia, lipids and blood pressure are interconnected factors of metabolic syndrome, which is a public health problem worldwide and, therefore, should be managed in an integrated way. Intermittent fasting (IF) is gaining more and more popularity as a potential non-pharmacological approach. This review brings up to date evidence for the effects of major IF methods, such as time-restricted eating (TRE), alternate-day fasting (ADF) and weekly/fasting methods (e.g. 5:2 and 4:3) on major indicators of metabolic syndrome. The majority of IF diets tend to be weight loss diets, with ADF and 5:2/4:3 having more impact on weight loss than TRE, though ADF might lead to more lean mass loss amongst normal weight individuals. Glycemic effects are better established in overweight/obese people and in patients with prediabetes or type 2 diabetes but the studies in metabolically healthy people are inconsistent. The lipid response seems to be regimen dependent; 5:2 with meal replacement is favourable for triglyceride reduction, ADF may be more beneficial in reducing total cholesterol and LDL-C and TRE may be more favourable in increasing HDL-C, while the blood pressure response is less consistent, with most short- to medium-term studies showing limited results. IF in general can be helpful in the management of metabolic syndrome, but dependent on the regimen, outcome and population. There is still a need for long-term high-quality studies.

Keywords: Intermittent fasting regimens, Metabolic syndrome, Body weight, Glycemia

1. Introduction

Tissue inability to respond to insulin signals, elevated blood triglyceride readings, raised circulating cholesterol values, persistent elevated blood pressure, reduced high-density lipoprotein cholesterol (HDL-C) concentrations, plus abdominal fat accumulation form a cluster of body metabolic irregularities which frequently manifest simultaneously and carry the medical label of metabolic syndrome (MS). This harmful physical condition bears strong biological links to greater odds of developing heart and vessel illnesses alongside adult-onset glucose metabolism disorder named type 2 diabetes mellitus (T2DM). The prevalence of MS has continued to increase in the world in recent years. In 2023, an estimated 1.54 billion people aged 18 years and older across the world were meeting the criteria for MS, significantly up from 2000 [1]. The MS is also very common in China,

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particularly in adults and the prevalence is increasing in health examination subjects in economically developed areas. It therefore represents a significant public health problem and should be addressed on an ongoing and long-term basis.

No single indicator can be used to prevent and/or manage MS. It is a multidimensional disease that requires a weight management, glycemic management, lipid management and blood pressure management approach. Intermittent fasting (IF) has received some degree of practicality in recent years and has started to find research interest in the field of metabolic disease interventions. Some of the most popular types of fasting are time-restricted eating (TRE), alternate day fasting (ADF), and weekly diets, which include 5:2 or 4:3. Past thorough literature syntheses and pooled statistical assessments point out that body weight, circulating glucose states, serum lipid compositions, and arterial pressure measurements can receive separate modulating effects from diverse IF schedules. These schedules encompass shortened daily feeding intervals, rearrangements for the schedule of calorie consumption, and physiological metabolic shifts that develop after sustained dietary intervention routines. Yet, given the variation in study populations, intervention periods, and how the energy is restricted, it is unclear how the results from each of these studies compare and how effective each IF intervention is compared with the other core components of metabolic syndrome.

The core objective behind this literature overview lies in organized collection of outcome data from publicly released study works spanning recent multi-year periods which explore how diverse IF regimens act upon the primary pathological markers that make up full presentations of metabolic syndrome. Specific focus is placed on body weight, glycemia, blood lipids and blood pressure differences between various protocols (including TRE, ADF) and on potential clinical applicability to offer more precise guidance to dietary intervention strategies in metabolic syndrome.

2. Body weight

In almost all RCTs, IF was correlated with weight loss, however with significant differences between protocols. The effect of TRE seems to be largely influenced by whether there is caloric reduction in conjunction with TRE. A 4-week time-restricted eating (TRE) intervention in non-obese adults reduced daily energy intake by approximately 15% and body weight by 0.75 kg [2], while the same intervention with energy deficit had a greater impact on individuals with obesity. Comparisons within relevant controlled trials of early TRE display body weight variations which emerge between states with matched calorie deficits and ordinary routine conditions [3], which long-term grouped tests targeting people with abnormal blood glucose metabolism reveal that fixed eating intervals can deliver obvious effects for body weight regulation. Approaches which rely merely on persistent control of calorie intake struggle to widen gaps of physical weight improvement that exist relative to blank control groups [4]. In the same fashion, implementation of TRE 3 days per week was shown to result in a roughly 34% decrease in body weight of type 2 diabetic obese patients [5]. For overall physiological outcomes, TRE delivers its strongest positive impacts once this practice builds steady caloric shortfalls which sustained dietary limitation of daily feeding intervals without lowered total calorie consumption fails to generate meaningful health improvements for human physical states.

Across typical participant groups, ADF delivers larger drops in bodily mass which rigorous ADF protocols show to create obvious declines in body weight relative to control groups and TRE regimens for grown individuals who do not carry excess fatty tissue across major body regions. A 4-month study with modified ADF found a 6.43 kg weight loss as opposed to a 4.11 kg weight loss in a daily caloric restriction group with metabolic syndrome [6]. In non-alcoholic fatty liver disease (NAFLD) patients, ADF for 3 months resulted in a 5.06% decrease in body weight, which was significant as compared to exercise alone group and control group [6]. But in healthy lean adults a

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strict ADF for 3 weeks resulted in only 1.6 kg of weight loss, of which about 50% was attributed to lean mass [7]. Furthermore, a loss of body weight is possible when ADF is used in conjunction with protein supplementation, however, maintenance of muscle mass is limited. ADF carries verified practical potency that supports the shrinkage of body weight which applies to adult groups that display excess body fat storage or meet clinical markers defined for obese physical status. However, its effectiveness is less in normal weight individuals and it may be associated with loss of lean tissue.

The 5:2 pattern of IF combined with formulated substitute food servings generates more obvious declines in body mass which outperform the mass-lowering outcomes produced by metformin and empagliflozin for people who receive fresh clinical diagnoses of T2DM disorder. The overweight/obese adults in the 4:3 regimen experienced a 7.7-kg body weight decrease [8], while the daily caloric restriction group experienced a 4.8-kg decrease; importantly, the 4:3 group had a lower dropout rate (19%) than did the daily caloric restriction group (29.6%). These results indicate that a structured dietary plan or meal replacement during 2- to 3-day per week fasting can maintain beneficial weight reduction effects in up to 12-month weight reduction programs. Overall, weight loss is higher when used in combination with TRE compared to using only TRE or ADF without any other diet changes.

To sum it up, IF is a great way to lose weight. When one examines mainstream dietary regimes, overall, alternate-day fasting and regimens structured as 5 to 2 or 4 to 3 yield more substantial calorie reduction on the condition that a consistent energy deficit gets sustained. Preservation of lean mass should also be taken into account, particularly when ADF is tight and for long-term interventions in weight loss.

3. Glycemia

There is substantial population variation in the effect of the various IF protocols on glycemia. The benefit is more prominent in patients with prediabetes, T2DM or metabolic syndrome, and less or even detrimental in metabolically healthy individuals.

TRE do not seem to have any effect on improving the fasting glucose among metabolically healthy subjects. A 6-month 8-hour TRE intervention led to a decrease in glycated hemoglobin (HbA1c) of 0.91% [4], which was comparable to the decrease in the daily caloric restriction group (0.94%) and both were greater than the control group. In comparison, although early TRE induced more weight loss [3], there was no significant difference compared to the control group for fasting glucose, insulin or Homeostatic Model Assessment of Insulin Resistance (HOMA-IR). Consequently, the glycemic effects of TRE are primarily observed in individuals who have poor glucose control and seem to depend on the length of the intervention period or energy restriction.

Likewise, the glycemic effects of ADF have been restricted to insulin-resistant and/or glucose-disordered subjects and no effect – and perhaps detrimental effect – has been seen in metabolically healthy subjects. The glucose levels at fast were slightly higher in the ADF group (0.12 mmol/L higher) than in the control group of adults without obesity [4]. However, modified ADF was more effective than daily caloric restriction to improve fasting glucose and HOMA-IR in patients with MS after 4 months [9]. ADF is a strategy that lowers fasting glucose and improves HOMA-IR in obese type 2 diabetic patients, which is not significantly different than a Mediterranean diet. The 3 months of ADF also improved the fasting insulin and HOMA-IR in patients with NAFLD [6]. However, 3 weeks of strict ADF did not significantly affect glycemic parameters in lean healthy adults [7].

The 5:2 protocol with meal replacement is the most effective glucose lowering regimen compared to all other regimens, with the greatest decrease in HbA1c seen with the 5:2 protocol with meal

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replacement, compared to metformin or empagliflozin. Although not statistically significant, 12-month point estimates for fasting glucose and HOMA-IR were better for the 4:3 group than daily caloric restriction in study [8]. Measured study outcomes point toward periodic fasting sessions arranged over several weekly cycles which pair well with nutrient-balanced substitute food servings to generate prominent favorable influences that sustain stable blood sugar regulation across extended time spans for affected metabolic groups.

In general, the blood sugar-lowering effects of IF are very individual. For overweight or obese people with insulin resistance, prediabetes or T2DM, all three TRE, ADF and 5:2 regimens can be beneficial for glycemic outcomes; and the 5:2 with meal replacement can be more effective than traditional oral glucose-lowering drugs. But for people who are metabolically healthy and have normal glucose levels, using IF as a means of further optimising glycemic levels is not recommended.

4. Blood lipids

The key clinical marker that defines abnormal blood lipid profiles covers elevated circulating triglyceride concentrations, lowered high-density lipoprotein cholesterol values, and raised low-density lipoprotein cholesterol readings which available research data relating to how diverse intermittent fasting regimens act upon lipid metabolism show distinct differences tied to different measured biological endpoints.

The main benefit of TRE is to reduce triglyceride levels, and it has minimal impact on cholesterol metabolism. Triglyceride levels have been found to be lowered by several studies involving TRE. The 16:8 or 14:10 TRE protocol was able to significantly decrease triglycerides after 3 weeks [5], and this was more effective than in the control group. Long-term intervention which follows the 8-hour TRE schedule can lower triglycerides slightly yet carries shifts which lack statistical distinctions, which this dietary mode delivers weak overall regulatory power for multiple cholesterol markers and nearly no obvious gaps of lipid parameters exist among separate groups across diverse research projects.

Strict ADF displays a visually larger range for reducing lipid indicators but fails to form statistical differences relative to TRE and control cohorts [4], which modified ADF can optimize cholesterol levels with triglyceride improvement degrees that stay close to standard calorie control plans [9]. ADF brings no obvious lipid regulation effects that target people with fatty liver disease, which this pattern even creates rising tendencies of triglycerides when applied to obese crowds with impaired glucose tolerance [10]. The lipid conditioning effects which ADF produces rely heavily on population types and intervention cycles, and the overall capacity which improves cholesterol-related markers stands above that of TRE plans.

The 5:2 diet program, along with meal replacement, was effective in reducing the triglycerides and improving HDL-C levels, but it had no significant effect on LDL-C. After 12 months of the 4:3 regimen [8], however, the changes in total cholesterol, LDL-C, and triglycerides were not significantly different and the changes in HDL-C was even slightly less favorable than the changes under daily caloric restriction. Thus, it is not inevitable that the 5:2 diet will provide a greater lipid benefit than the 4:3 diet, but rather just because the meal replacement includes omega-3 fatty acids or medium-chain fatty acids, among other ingredients.

To conclude, the various types of IF have various effects on lipids. TRE seems to be more beneficial on the reduction of triglycerides, ADF is more advantageous in reducing total cholesterol and LDL-C and the 5:2 diet with meal replacement may be useful in reducing triglycerides and

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HDL-C. Thus, it seems logical to choose a different regimen according to the predominant type of dyslipidemia in the clinical setting.

5. Blood pressure

Measured data gathered from blind comparative clinical test frameworks which adopt random group assignment display inconsistent shifts in arterial pressure metrics that stem from physiological adjustments triggered by different styles of intermittent fasting intervention schedules. None of the studies found much antihypertensive effect, and only a few treatments showed some slight trends of improvement in certain groups.

There was no apparent blood pressure benefit from three studies on TRE. For a 4-week TRE intervention (eating window 12:00 to 20:04), there were no significant differences in systolic or diastolic blood pressure between the TRE and control group. Early and late time restricted feeding (8:00–16:00 and 14:00–22:00, respectively) both with the same daily energy deficit as a MED have no significant difference in their effects on systolic or diastolic blood pressure. A separate clinical research project which ran through extended observation periods shows that morning TRE regimens paired with steady daily caloric shortfalls produce more substantial drops in whole-body mass which comparative checks for systolic blood pressure across separate participant cohorts fail to show meaningful gaps while minor downward adjustments appear within diastolic blood pressure readings for all monitored volunteers. Overall, it seems that the effect of short- to medium-term TRE on blood pressure is quite small and evidence for TRE as a primary blood pressure lowering tool is lacking.

Most research projects which relate to ADF fail to verify that this pattern can lower human blood pressure remarkably, which blood pressure stays stable for healthy non-obese crowds that follow standard ADF, and obese groups that adopt revised fasting methods see no substantive improvements that target systolic and diastolic markers. Multiple trials with long and short cycles plus combined intervention research which adds physical activity cannot create obvious gaps of blood pressure between fasting cohorts and control groups, and only a few groups hold mild favorable tendencies. The regulatory performance which ADF provides for blood pressure shows uneven results, and most existing short-to-medium term tests cannot detect effective functions that reduce blood pressure levels.

Among intermittent fasting schedules which get matched with meal substitute supplies, the 5:2 pattern can deliver bidirectional adjustment that targets two blood pressure markers for crowds with newly developed diabetes and experimental evidence exists to back up such beneficial outcomes. It should also be noted, however, that in this study, meal replacement products were used and the intervention was rather intensive, so the antihypertensive effect could have been a result of the overall lifestyle modification and not only the fasting. In comparison, the 4:3 regimen produced more weight reduction than did the daily caloric restriction [8], but this was not statistically significant for blood pressure. Other than the 5:2 fasting and meal replacement specific protocol, the data on the benefits of weekly fasting for blood pressure are still weak.

In general, the results of most studies have not supported the effectiveness of short- to medium-term TRE or ADF in reducing blood pressure. The few positive results are from a highly intensive 5:2 meal replacement intervention, where the benefit of this intervention is unclear from the weight loss or overall lifestyle changes. Thus, this alternative method of nutrition IF, which is a non-pharmacological practice, should not be considered a first-line approach to blood pressure management at this time (Table 1).

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Table 1. Comparison of the effects of different IF regimens on core indicators of metabolic syndrome

Items	weight/BMI	blood sugar	TG	TC/LDL - C	HDL - C	blood pressure
TRE	++	++	++	+	±	/
ADF	+++	++	±	++	±	/
5:2	+++	+++	++	+	++	+
4:3	++	+	±	±	±	±

6. Conclusion

This review systematically summarizes intervention effects of diverse intermittent fasting regimens on core indicators of metabolic syndrome including body weight, blood glucose, blood lipids and blood pressure. For body weight management, weight loss can be achieved under nearly all fasting regimens while efficacy varies greatly. ADF and weekly fasting regimens such as the 5:2 and 4:3 patterns deliver larger weight reduction compared with time-restricted feeding and suit overweight or obese populations optimally. Strict ADF may trigger lean mass loss in individuals with normal body weight. Extents of benefits in blood glucose regulation show strong dependence on population traits. Three major fasting regimens generate favorable outcomes for patients diagnosed with prediabetes, T2DM or MS. The glucose-lowering capacity of 5:2 fasting combined with meal replacement surpasses that of classic oral hypoglycemic agents. Fasting brings no improvement to glycemic homeostasis and may impose mild impairment on such balance for metabolically healthy individuals. Lipid metabolic responses carry regimen-specific properties. Time-restricted feeding mainly reduces triglyceride levels. ADF presents greater strengths in lowering total cholesterol and low-density lipoprotein cholesterol. The combination of 5:2 fasting and meal replacement decreases triglyceride concentrations and raises high-density lipoprotein cholesterol levels simultaneously. Evidence supporting blood pressure regulation ranks the weakest across all measured endpoints. Most medium-term and short-term studies detect no definite hypotensive effects from time-restricted feeding or ADF. Intensive intervention combining 5:2 fasting and meal replacement displays a slight favorable trend, yet such benefits cannot be fully attributed to fasting practice. Overall, intermittent fasting functions as an effective adjunct non-pharmacological therapy for metabolic syndrome. Final therapeutic outcomes are closely determined by fasting regimens, targeted endpoints and receiving populations (Table 1).

Future advancement of this field requires gradual transformation from uniform one-size-fits-all models toward personalized precision nutrition strategies. The most compatible fasting patterns are selected according to patient metabolic phenotypes, gut microbiota profiles and lifestyle conditions. Additional large-sample long-term prospective trials are required to assess safety profiles, adherence levels and influences on hard cardiovascular endpoints of different fasting protocols. Synergistic mechanisms between intermittent fasting, conventional medications, exercise interventions and digital health technologies including continuous glucose monitoring and wearable devices require further exploration. Real-time feedback and dynamic adjustment can be realized to improve sustainability of interventions. Transition from merely effective status to applicable, optimizable and durable performance under evidence-based frameworks allows full integration of intermittent fasting into standardized prevention and treatment workflows for metabolic syndrome.

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