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The impact of Intermittent Fasting on Weight Loss and Metabolic Health - a review of latest research

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Abstract

Introduction and purpose

Intermittent fasting (IF) is a dietary pattern that alternates between periods of fasting or reduced caloric intake and periods of unrestricted eating. There are three primary types of IF: Alternate Day Fasting (ADF), Time-Restricted Eating (TRE), and Periodic Fasting (PF). This review article summarizes the impact of IF on weight loss. Additionally, it examines the broader health effects of IF, including its influence on cardiovascular risk, diabetes management, and neurodegenerative diseases.

Description of the state of knowledge

Fasting, the practice of abstaining from or limiting food intake for a specified period, has been a cultural and religious tradition worldwide for centuries. Common IF methods alternating 24-hour periods of fasting with days of eating, TRE restricts eating to specific windows of time each day, and PF includes patterns such as the 5:2 diet, where fasting occurs on two days each week.

Conclusions

The analysis of the review article demonstrates that intermittent fasting (IF) leads to weight loss, aiding in the treatment of obesity. Moreover, IF reduces glycated hemoglobin levels and increases periods of normoglycemia, potentially benefiting diabetes patients. Nonetheless, there is a lack of sufficient research to confirm the safety of IF for diabetics, given the risk of hypoglycemia. Research also indicates that IF positively impacts cardiovascular risk factors by lowering total cholesterol, LDL-C, and triglyceride levels. Additionally, while IF might reduce the risk of certain cancers by addressing obesity, it is not advised for cancer patients due to inadequate scientific evidence. Furthermore, some studies indicate that IF could be advantageous in managing certain neurological diseases.

Keywords: Intermittent fasting; obesity; cardiovascular risk factors; diabetes; cancer

Introduction and purpose

The phenomenon of intermittent fasting has garnered considerable attention in recent years, both from the scientific community and the general public, as a potential strategy for weight management and health improvement. Intermittent fasting is a dietary pattern characterized by alternating periods of fasting or decreased calorie consumption with periods of unrestricted eating [1]. This dietary pattern encompasses three primary forms: Alternate Day Fasting, Time-Restricted Eating, and Periodic Fasting. Alternate Day Fasting involves alternating between 24-hour periods of fasting and eating [2]. This regimen encompasses two types: Complete alternate-day fasting, characterized by total intermittent energy restriction with no caloric intake on fasting days, and Modified alternate-day fasting, which permits consumption of up to 25% of daily calorie needs on fasting days [3]. Time-Restricted Eating encompasses various patterns, such as fasting for 16 hours with an 8-hour window for eating, fasting for 20 hours with a 4-hour feeding period, or comparable alternatives [2]. Periodic fasting, exemplified by the 5:2 diet, involves alternating between two fasting days and five days of regular eating per week. With the 5:2 diet, individuals maintain their usual eating habits for five days a week and then engage in fasting or reduced caloric intake on two consecutive or nonconsecutive days [3].

The presented study aimed to evaluate the impact of intermittent fasting on weight loss and its effects on overall health including changes in body weight, body composition, and metabolic parameters. Additionally, we aim to investigate the broader impact of intermittent fasting on various aspects of health, such as diabetes-related parameters, cardiovascular factors, cancer treatment, and the nervous system.

Description of the State of knowledge

Fasting, the practice of abstaining from food consumption or limiting food intake for a specified period, has been observed across various cultures and religions worldwide for centuries. Many religions have their own traditions associated with fasting, which may be mandatory during specific periods, such as Lent in Christianity, Ramadan in Islam, Yom Kippur in Judaism, and others. There are various motivations for fasting. Some cultures and religious traditions view fasting as a means of purifying the body and soul, as well as

detoxifying the body from toxins. Today, fasting is still practiced by some individuals as a means to improve health.

It is crucial to emphasize the differentiation between intermittent fasting (IF) and calorie restriction (CR) when considering dietary interventions. While CR involves the sustained reduction of total calorie intake over time, IF encompasses a wider range of eating patterns [4,5]. Intermittent fasting involves alternating periods of fasting or minimal energy intake, ensuring the intake of essential nutrients, interspersed with periods of unrestricted eating. Common IF approaches include periodic fasting in the 5:2 diet example (fasting 2 days per week), time-restricted feeding (emphasizes the timing of meals in alignment with diurnal circadian rhythms, permitting ad libitum energy intake during a restricted eating window each day), and alternate-day fasting (alternating between fasting and non-fasting days) [5,6,7,44]. Understanding this distinction is paramount for comprehending the unique physiological responses and potential health implications associated with each dietary strategy.

Intermittent fasting, by facilitating weight loss, offers several health advantages such as better lipid profiles and decreases the risk of developing chronic diseases like type 2 diabetes and heart disease as well as reduces the risk of certain cancers. Furthermore, intermittent fasting may have additional benefits, such as potential therapeutic effects in treating neurodegenerative diseases, managing pain. However, these additional benefits are not yet conclusively proven, and more extensive research is necessary to definitively assess the full impact of intermittent fasting on these conditions.

Material and methods

A search was conducted on the PubMed database for literature published between 2019 and 2024. Using the keyword “Intermittent fasting” 1508 articles were initially identified. Ultimately, 19 original papers relevant to the study’s topic were included in the review. These comprised six studies on weight loss, four on diabetes, four on cardiovascular risk factors, two on cancer treatment, three on nervous system diseases. Each paragraph comprises the findings derived from the conducted research.

Results

Obesity

Obesity, a chronic disease, arises from the excessive accumulation of body fat due to prolonged surplus energy intake over expenditure. Various factors contribute to obesity, some of which are modifiable, such as physical inactivity and excessive caloric intake, while others, like genetic predisposition and certain medications, may be non-modifiable. [8]. The basic test to diagnose obesity is body mass index (BMI), where a BMI greater than 30 kg/m² indicates obesity [9]. This simple calculation considers an individual's weight in relation to their height, serving as a preliminary screening tool to identify elevated levels of body fat. Although BMI has its limitations, it remains a widely used tool in clinical settings to assess weight status and identify potential health risks associated with obesity, prompting intervention strategies to improve overall health outcomes. The complications of obesity are multitude, ranging from cardiovascular diseases like hypertension and coronary artery disease to metabolic disorders such as type 2 diabetes and fatty liver disease [10]. Moreover, there is a link between obesity and mental health disorders such as depression and anxiety, as well as an increased risk of cancer [11,12]. Obesity treatment is comprehensive and consists of 4 forms of treatment: lifestyle modification (ie, diet and exercise), cognitive behavioral therapy, pharmacotherapy, and bariatric surgery [13, 14]. For all treatment approaches, behavior change techniques, reduction in energy intake, and increasing energy expenditure are required [15]. In order to maintain a healthy lifestyle it is advised that adults engage in physical activity for 150-300 minutes of moderate intensity or 75-150 minutes of vigorous intensity per week [16]. Additionally, it is recommended to incorporate strength training exercises ≥ 2 times/week, targeting all major muscle groups at moderate or vigorous intensity. For individuals with a BMI over 35 kg/m², opting for activities that are gentler on the musculoskeletal system, such as swimming or using a stationary bike, is suggested for lifestyle improvement [35]. Cognitive behavioral therapy (CBT) is a proven form of obesity treatment. The underlying assumptions of CBT treatments are that behaviors can be learned, unlearned, modified, and replaced by other behaviors through different strategies, some of which include goal setting, problem solving, stimulus control and self-monitoring. CBT treatments can contribute to lifestyle modification, weight loss, and weight maintenance [17]. In pharmacological treatment medications such as orlistat, naltrexone-bupropion, GLP-1 agonists (liraglutide,

semaglutide) are used [18,19]. The last treatment tier for managing obesity is bariatric surgery, which supplements other treatment approaches [20]. The types of obesity surgery most commonly is Roux-en-Y gastric bypass and sleeve gastrectomy, lead to an excess weight loss of 27-69% \geq 10 years after the procedure [21]. This surgical approach alters the digestive system to restrict food intake or alter nutrient absorption, aiming to facilitate weight loss and improve overall health outcomes for individuals struggling with severe obesity.

The randomized controlled trial (RCT) conducted by Paul J Arciero et al. aimed to evaluate the impact of intermittent fasting one day or two consecutive days per week on optimal body weight loss. Over a 4-week period, 42 participants received weekly dietary guidance and monitoring of compliance from a registered dietitian. Measurements were taken at the start (week 0) and end (week 5) of the study. The results showed a decrease in body weight in both groups, with a more significant reduction observed in the two consecutive days of the fasting group (-29%) [22].

In another study, Felicia L. Steger conducted a randomized controlled trial to examine the effects of Intermittent Energy Restriction (IER) and Continuous Energy Restriction (CONT) on weight loss. Thirty-five overweight or obese adults were assigned to either the CONT or IER group for 24 weeks, consisting of a 12-week weight loss phase and a 12-week weight maintenance phase. The diet plans were part of a comprehensive weight management program that included weekly group sessions with a registered dietitian, increased physical activity, and lifestyle changes. After 24 weeks, statistically significant and clinically significant weight loss was observed in both groups: an average of 11.38% in the CONT group and 9.37% in the IER group. The success rate for achieving a 5% weight loss was 82% for the CONT group and 61% for the IER group [23].

Przemysław Domaszewski et al. carried out an RCT to investigate the effects of six weeks of time-restricted eating (TRE) on weight loss, body composition, and visceral fat. A total of 116 participants were randomly assigned to either the TRE group or an educational control group. Those in the TRE group were instructed to consume calorie-containing beverages or food only between 8:00 PM and 12:00 PM. The control group followed a meal plan based on their usual eating habits. After the six-week intervention, there was a significant decrease in body weight, with men losing 1.8 kg and women losing 1.3 kg [24].

Felicia L. Steger and colleagues conducted a randomized controlled trial to examine the effects of early time-restricted eating (eTRE) on weight, metabolic health, mood, and sleep in participants who adhered to the regimen. Ninety obese individuals aged 25 to 75 were randomized to either the eTRE group, with an 8-hour eating window from 7:00 AM to 3:00

PM, or a control group with a 12-hour or longer eating window, for 14 weeks. Those who adhered to eTRE for at least 5 days per week showed greater improvements in body weight, body fat, heart rate, insulin resistance, and glucose levels compared to those who adhered to the control schedule [25].

Paloma Elortegui Pascual and colleagues conducted a meta-analysis to compare the effectiveness of different intermittent fasting (IF) regimens on weight loss in the general population, as well as to compare these regimens to traditional caloric energy restriction (CER). They searched three databases for randomized controlled trials (RCTs) from 2011 to June 2021 that assessed weight loss through IF methods, including alternate day fasting (ADF), the 5:2 diet, and time-restricted eating (TRE). The analysis found that the three main forms of IF are effective for weight loss, producing reductions ranging from 1% to 13% over 2 to 52 weeks. ADF was the most effective for weight loss, followed by CER and TRE, while no clear conclusions could be drawn about the effectiveness of the 5:2 diet [26].

Quing Zhang et al. performed a systematic review and meta-analysis of randomized clinical trials and pilot studies to evaluate the effectiveness of intermittent fasting (IF) versus continuous calorie restriction (CCR) in individuals who are overweight or obese. They conducted a thorough search in PubMed, Embase, the Cochrane Library, and Web of Science up until January 2022 and 11 articles with 705 patients were included. Their findings indicated that IF was more effective than CCR for weight loss, but there was no significant difference in BMI improvement between the two methods [27].

Diabetes

Diabetes mellitus is a chronic condition characterized by high blood sugar levels (hyperglycemia) and increased levels of glycated hemoglobin (HbA1c). The main objectives of managing diabetes are to keep blood glucose levels within the normal range and to lower HbA1c levels. Poorly controlled diabetes can lead to various complications, such as cardiovascular diseases, neuropathy, retinopathy, and nephropathy [28]. Intermittent fasting (IF), which promotes weight loss, has shown potential in improving certain laboratory measurements such as glucose level. Some research indicates that IF can reduce HbA1c levels and increase the time spent with normoglycemic range. However, more substantial evidence is needed to make definitive conclusions, underscoring the need for further investigation. It's crucial to recognize that using IF in diabetic patients carries the risk of hypoglycemia, which can pose significant health risks.

Jong Han Choi et al. conducted a meta-analysis to evaluate the effect of intermittent fasting on type 2 diabetics. This study included randomized controlled trials from January 1, 2000 to June 8, 2021. The results of this study suggest a strong recommendation against IF in patients with type 2 diabetes due to the lack of evidence on its benefits and harms, and risk of hypoglycemia [29].

In a study led by Charlotte Andriessen et al., 14 adults with type 2 diabetes followed a time-restricted eating plan, consuming all their food within a 10-hour window each day for three weeks. They monitored hepatic glycogen levels, insulin sensitivity, and glucose homeostasis using 24-hour continuous glucose monitoring devices. The study found that participants spent more time in the normoglycemic range and had lower fasting and 24-hour glucose levels. However, these improvements were not linked to changes in insulin sensitivity or hepatic glycogen levels [30].

Anna Obermayer et al. conducted a randomized controlled trial to evaluate the safety and feasibility of intermittent fasting (three nonconsecutive days per week) over a 12-week period in individuals with insulin-treated type 2 diabetes. Forty-three participants were assigned either to an intermittent fasting group or a control group, with both groups receiving dietary counseling and continuous glucose monitoring. The intermittent fasting group experienced a significant reduction in HbA1c levels compared to the control group over the 12 weeks, along with a decrease in the total daily insulin dose needed for those with insulin-treated type 2 diabetes [31].

Randomized Controlled Trial conducted by Vasiliki Pavlou et. al assess the effect of time-restricted eating (TRE) on weight reduction and glycemic control. This six-month, parallel-group trial, conducted from January 25, 2022, to April 1, 2023, involved 75 participants who were assigned to one of three groups: 8-hour TRE (eating from 12 to 8 pm without calorie counting), calorie restriction (CR) with a 25% daily energy reduction, or a control group. Both the TRE and CR groups showed a decrease in HbA1c levels compared to the control group, with no significant differences between the TRE and CR groups. Other measures, such as time in the euglycemic range, medication effect score, blood pressure, and plasma lipid levels, did not differ among the groups [32].

Cardiovascular risk factors

Cardiovascular risk factors are crucial indicators that can significantly impact overall heart health. These factors include high blood pressure (hypertension), elevated levels of low-density lipoprotein cholesterol (LDL-C), high total cholesterol, elevated triglycerides, obesity, insulin resistance or diabetes, smoking, and a sedentary lifestyle [33,34]. These conditions can lead to the development of atherosclerosis, heart attacks, strokes, and other cardiovascular diseases. Therefore, it is vital to manage these parameters within normal ranges to reduce the risk of severe cardiovascular events. Intermittent fasting has been shown to reduce the risk of cardiovascular events. Research indicates that intermittent fasting can lead to significant improvements in various cardiovascular risk factors, including reductions in body weight, lipid profiles, such as lower levels of total cholesterol, LDL-C, and triglycerides. By positively influencing these parameters, intermittent fasting can effectively decrease the likelihood of developing conditions such as atherosclerosis, heart attacks, and strokes. Therefore, incorporating intermittent fasting into one's lifestyle may serve as a beneficial strategy for mitigating cardiovascular risk.

Sek Ying Chair et al. conducted a Randomized Controlled Trial to investigate the effects of alternate-day fasting (ADF) and 16/8 time-restricted fasting (16/8 TRF) on weight loss, blood glucose, and lipid profiles in overweight and obese adults with prediabetes. The study included 101 participants who were randomly assigned to either the ADF group, the 16/8 TRF group, or a control group, with the intervention lasting for 3 weeks. Data were collected at the beginning of the study, at the end of the intervention, and at a 3-month follow-up. The findings suggest that incorporating intermittent fasting regimens into regular diets may help reduce the risk of diabetes and cardiovascular disease in this population. Compared to the usual diet approach, ADF significantly improved HDL-C levels and lowered blood glucose over time, while 16/8 TRF was particularly effective in reducing triglyceride levels. ADF was more effective than 16/8 TRF in reducing body weight and BMI but was less effective in lowering triglycerides. Both fasting methods had similar effects on reducing blood glucose and LDL-C levels [35].

Yi Guo et al. in a Randomized Controlled Trial investigate the impact of intermittent fasting (IF) on cardiometabolic risk factors in individuals with metabolic syndrome (MS). The study included 39 patients with MS, with 21 participants in the IF group and 18 in the control group. On fasting days, those in the IF group reduced their calorie intake by 69% compared to

non-fasting days. Over an 8-week period, IF significantly decreased fat mass, reduced oxidative stress, modulated inflammatory cytokines, and improved vasodilatory parameters. These results suggest that IF can help mitigate cardiometabolic risk factors [36].

Stephen Keenan et al. conducted a study to present secondary outcomes from a 12-week randomized controlled trial that examined the effects of isocaloric 5:2 intermittent fasting (IF) and continuous energy restriction (CER) diets, combined with resistance training, on cardiometabolic health markers. This analysis included data from 34 healthy participants who underwent a 12-week intervention with either a twice-weekly fast (5:2 IF; IFT group) or CER (CERT group) paired with resistance exercise. Both dietary approaches led to significant reductions in total cholesterol, low-density lipoprotein cholesterol, and high-density lipoprotein cholesterol. The reductions in TC and LDL-C were more pronounced in the IFT group after adjusting for baseline levels and weight changes [37].

Tatiana Moro et al. conducted a study to evaluate the long-term effects of intermittent fasting (IF) on cardiovascular risk factors. This single-blind randomized study included twenty healthy subjects who followed either a time-restricted eating (TRE) diet or a normal diet (ND) protocol for 12 months, combined with resistance training. Participants in the TRE group ate three meals within an 8-hour window each day (at 1 pm, 4 pm, and 8 pm), while those in the ND group had three meals at 8 am, 1 pm, and 8 pm. After 12 months, the TRE group showed significant reductions in body mass, fat mass, insulin-like growth factor 1, and testosterone compared to the ND group. Additionally, TRE resulted in significant improvements in inflammatory markers (interleukin 6, interleukin 1 β , and tumor necrosis factor α), insulin sensitivity (fasting glucose, insulin, and homeostatic model assessment for insulin resistance index), and lipid profiles (cholesterol, HDL, and LDL) compared to the ND group [38].

Cancer treatment

Obesity is a known risk factor for the development of various cancers, including breast, colorectal, endometrial, kidney, and pancreatic cancers. Intermittent fasting, by promoting weight loss, has the potential to reduce the risk of cancer development. However, there is currently insufficient scientific evidence to determine the impact of intermittent fasting on individuals who already have cancer. Further research is needed to explore the effects and potential benefits of intermittent fasting in cancer patients.

A review study by Katherine K. Clifton and colleagues investigated the impact of intermittent fasting on cancer prevention and treatment. The findings indicated that there is insufficient evidence regarding the effects of intermittent fasting on cancer incidence and outcomes after diagnosis due to a scarcity of human studies. Consequently, the study advises against intermittent fasting for patients actively undergoing cancer treatment. Additionally, rodent studies show inconsistent results, with some suggesting that intermittent fasting could be harmful in certain cancer conditions [39].

A study led by Yvelise Ferro aimed to assess the available evidence regarding the effect of a variety of fasting-like regimens on preventing chemotherapy-related side effects. Studies were selected from PubMed, Scopus, and Embase for this review, which concluded on November 24, 2022. The systematic review and meta-analysis found no evidence that therapeutic fasting is more effective than non-fasting in reducing chemotherapy toxicity. Despite the common belief that fasting-like diets can alleviate treatment side effects, this review underscores the absence of an evidence-based approach. The limited literature on the topic makes it impossible to confirm the effectiveness of therapeutic fasting during chemotherapy [40].

Nervous system diseases

Intermittent fasting (IF) has garnered significant interest for its potential effects on the nervous system and its role in managing neurological disorders. Research indicates that IF induces various molecular and cellular adaptations in neurons, enhancing cellular stress resistance, synaptic plasticity, and neurogenesis. These adaptations not only improve cognitive function but also offer therapeutic potential for neurological diseases such as Alzheimer's, Parkinson's, and multiple sclerosis. Intermittent fasting (IF) is also emerging as a potential therapy for pain management. The studies suggest that IF could enhance the effectiveness of chronic pain treatments, offering a novel approach to pain management that warrants further exploration in larger clinical trials. This potential application of IF adds to its growing list of benefits and underscores the need for more research into its mechanisms and long-term effects on pain relief.

A review study led by Jip Gudden and colleagues investigated the impact of intermittent fasting (IF) on brain and cognitive function. The study found no definitive short-term cognitive benefits of IF in healthy individuals. However, clinical research indicates that IF can be beneficial for managing symptoms and progression of epilepsy, Alzheimer's disease, and multiple sclerosis. Animal studies suggest potential mechanisms by which IF might help with

Parkinson's disease, ischemic stroke, autism spectrum disorder, and mood and anxiety disorders [41].

In a review study by Alex Brocchi et al., the effects of intermittent fasting (IF) on brain metabolism are explored, highlighting key molecular players such as ketone bodies, BDNF, GABA, GH/IGF-1, FGF2, sirtuin-3, mTOR, and gut microbiota. The study suggests that IF induces numerous molecular and cellular adaptations in neurons, which collectively enhance cellular stress resistance, synaptic plasticity, and neurogenesis. Despite these promising findings, the lack of standardized guidelines for IF application in patients limits its widespread use in clinical practice. Further research is required to better understand the various IF protocols and their long-term effects on brain metabolism before IF can be widely prescribed. Additionally, IF approaches in animal models have shown improvements in cognitive function and several neurological disorders, including neurodegenerative diseases [42].

Steven Pratscher and colleagues conducted a randomized controlled trial to assess the feasibility and acceptability of combining intermittent fasting and glucose administration with relaxation and guided imagery, a recognized pain treatment activity. The pilot study involved 32 adults aged 50 to 85 who had experienced chronic knee pain for at least three months. Participants completed four sessions over roughly two weeks. The study found that intermittent fasting and glucose administration could potentially enhance chronic pain treatments. The results demonstrated that the trial was feasible and acceptable, supporting the need for a larger clinical trial [43].

Author's contribution Statement

Conceptualization, Marta J. Gonciarz, Dominika K. Adamiec ;methodology, Anna Dąbrowska; software, Magdalena Czach; check, Agnieszka A. Strojny and Natalia Padaszyńska; formal analysis, Monika A. Kamińska; investigation, Anna Dąbrowska, and Adrianna Kraszkieicz; resources, Marta J. Gonciarz; data curation, Monika A. Kamińska, and Monika K. Do; writing - rough preparation, Marta J. Gonciarz; writing - review and editing, Marta J. Gonciarz and Dominika K. Adamiec; visualization, Dominika Zaliwska; supervision, Marta J. Gonciarz ; project administration, Agnieszka A. Strojny

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