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REVIEW ARTICLE

IS INTERMITTENT FASTING A GOOD DIET PLAN FOR A HEALTHIER LIFESTYLE?

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ABSTRACT

Two dietary patterns that have been shown to improve heart health include the Mediterranean Diet and Dietary Approaches to Stop Hypertension. Another common dietary method based on periodic fasting intervals is IF. Alternative diets include alternate-day fasting and time-restricted eating. Despite the lack of large, randomised clinical trials evaluating the link between IF and cardiovascular outcomes, human research suggests that this diet may lower cardiovascular disease risk by improving weight management, hypertension, dyslipidaemia, and diabetes. IF may enhance your health in a variety of ways, including reduced oxidative stress, improved circadian rhythm, and ketogenesis. This review investigating the current data about the possible cardiovascular benefits of intermittent fasting and makes areas for further research.

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INTRODUCTION

Although cardiovascular death rates have decreased, they have lately plateaued, and mortality rates among 35 to 64-year-old men and girls in the United States have risen (1). Obesity and a poor diet are important modifiable variables in the development of cardiovascular disease, with a 13 percent attributable risk of cardiovascular mortality (2). One of the dietary methods that has been shown to decrease cardiovascular risk is calorie restriction, which involves limiting calories consumed over a period of time. Weight reduction, reduced blood pressure, and better insulin sensitivity have all been related to calorie restriction in humans (3). IF is a dietary intervention that limits food intake in a similar manner to calorie restriction. IF, focuses on the time of day or week when meals may be eaten. IF is divided into two categories: alternate day fasting and time-restricted fasting. Alternative DF regimens may include 24-hour fasts followed by a 24-hour feeding period that may be repeated many times a week, such as the 5:2 technique, which alternates two fast days with five non-restrictive days. 16-hour fasts with 8-hour feeding schedules, 20-hour fasts with 4-hour meal schedules, and other forms of time-restricted fasting are examples of Time-Restricted Fasting. While both calorie restriction and intermittent fasting can lead to a reduction in total caloric intake, IF does not. In both people and animals, IF has been associated to improved glucose regulation (4, 5).On the other hand, long-term calorie restriction adherence is poor, but IF may be more promising. Because these two diets are so similar, it's conceivable that IF may also help your heart. This eating habit has also been related to a lower incidence of neurological diseases including Alzheimer's and Parkinson's disease (6). In this review, we look at the potential advantages of IF for improving health depending on dietary habits.

Health and Aging Effects of Intermittent Fasting: The emphasis of calorie restriction and intermittent fasting research until recently was on ageing and duration of life. The overarching result of almost a century of animal caloric restriction studies was that decreased food intake substantially increases life span.

In one of the first investigations of intermittent fasting, Goodrick and colleagues discovered that keeping rats on an alternate-day eating schedule that starts when they are young adults may extend their average life span by up to 80%. On the other hand, the impact of calorie restriction on health and lifespan varies and is influenced by sex, nutrition, age, and genetic factors (7). According to a meta-analysis of data from 1934 to 2012 (8), calorie restriction improves the median life span by 14 to 45 %in rats but just 4 to 27% in mice. A study of 41 recombinant inbred mouse strains showed considerable variation depending on the strain and sex, ranging from a considerably extended life duration to a significantly reduced life span (9). However, the research only looked at one caloric restriction regimen (a 40% decrease in calories) and did not look at health indicators, mortality reasons, or underlying processes. There was an inverse relationship between adiposity reduction and life span when animals were subjected to such severe caloric restriction (10), implying that animals with a shorter life span had a greater reduction in adiposity and transitioned to starvation more quickly, whereas animals with a longer life span had the least reduction in fat. The results of two major monkey studies, which contradicted each other, threw doubt on the connection between calorie restriction and improved health and longevity. The University of Wisconsin showed that calorie restriction increases both health and survival (11), whereas the National Institute on Aging found no significant decrease in mortality despite substantial improvements in overall health (12). Changes in the effects of caloric restriction on life span in the two trials could be explained by differences in daily calorie intake, the start of the intervention, meal composition, feeding protocols, sex, and genetic background. IF reduces obesity, insulin resistance, dyslipidaemia, hypertension, and inflammation in individuals (13).

IF appears to be more helpful to one's health than simply consuming fewer calories.16 healthy individuals were randomly assigned to an alternate-day fasting regimen for 22 days, and they lost 2.5 percent of their baseline weight and 4% of their fat mass, with a 57 percent decrease in fasting insulin levels (14). In two independent trials, overweight women (about 100 women) were randomly assigned to either a 5:2 IF programme or a 25% decrease in daily calorie consumption. Over the course of six months, all groups of women lost the same amount of weight, but the 5:2 IF group had a greater improvement in insulin sensitivity and a smaller waist circumference decrease (15).

Mechanism that may be used: A variety of studies have connected intermittent fasting to better cardiovascular results. Less oxidative insult is supported by the Oxidative Stress Hypothesis (16). The circadian rhythm hypothesis, which is linked to IF rather than calorie restriction and suggests a mechanism exclusive to intermittent fasting, is a second theory. Intermittent fasting induces a ketogenic state in the body, which has been associated to a decrease in cardiovascular risk factors.

Hypothesis of Oxidative Stress: According to the Oxidative Stress Hypothesis (16), calorie restriction leads mitochondria to produce less free radicals. After 8 weeks of alternate day fasting, obese individuals with asthma had reduced levels of inflammation, such as tumour necrosis factor-alpha (TNF-ALPHA) and Brain Derived Neurotrophic Factors(BNDF), as well as oxidative stress, such as nitro tyrosine, 8-isoprostane, protein carbonyls, and 4-hydroxynoneal adducts. They also exhibited higher uric acid levels, which is an antioxidant (17).

Theory of Circadian Rhythm: According to the circadian rhythm theory, physiological activities occur at the optimal period set by evolution (18). By fasting correctly, we may be able to optimise the peripheral clocks of our organs, including those situated in the liver, adipose, and skeletal tissues. As shown by a higher prevalence of cardiometabolic diseases in shift workers, dysregulation of this system raises the risk of chronic illnesses (19). Reduced insulin levels later in the day is one circadian example relevant to intermittent fasting (19). Late dinners are associated with higher postprandial glucose levels than daytime meals, increasing the risk of diabetes. Circadian misalignment causes insulin resistance in humans after just three days. 10 Consuming food late at night has been shown to impair both the quality and amount of sleep (20), as well as insulin resistance, obesity, and cardiovascular disease. The advantages of different time-restricted fasting regimens have changed according on the timing of the fast, emphasising the circadian clock's significance in this dietary pattern. Subjects who were allowed to eat throughout the day lost more weight and had better glycaemic control, cholesterol levels, and inflammatory markers (21). Glycaemic control, blood pressure, and cholesterol levels did not improve or even worsen in individuals on a time-restricted fasting programme that allowed for late afternoon or evening meals defined as those consumed after 16:00 (10). Intermittent fasting, when done correctly, may benefit one's heart health by synchronising with their circadian cycle.

Ketosis is a state of being ketogenic: The increase in hydroxybutyrate levels in fasting overweight individuals (17) suggests that intermittent fasting induces a ketogenic state. After 6–8 hours of fasting, ketone levels rise, signalling a shift from fat storage to fat utilisation, while low-density lipoproteins (LDL) levels fall and high-density lipoproteins (HDL) levels rise (12). The shift from glucose to fatty acids and ketones as a source of energy is referred to as intermittent metabolic switching. Furthermore, since the ketogenic diet requires more energy to metabolise ketones, it helps weight reduction (22). Intermittent fasting combines elements of the ketogenic diet, resulting in enhanced adipose metabolism, as well as weight and cholesterol loss. Intermittent fasting may be more beneficial than the ketogenic diet since it includes a high amount of animal fats. Excessive fat intake is related to higher levels of trimethylamine N-oxide, a metabolite that may be hazardous.metabolite associated with an increased risk of cardiovascular disease, which has been related to a ketogenic diet (23).

Hinduism's Intermittent Fasting and Feasting Spectrum: Hinduism is recognised as a way of life rather than a religion by India's Supreme Court (24). The Hindu Vedas are referred to as Sruti, while writings that interpret their meaning into a way of life (Sanatana Dharma – the ancient way) are referred to as smriti. The "smritis" sanctifies fasting as a way of life. The “smritis” also emphasise the need for “Yata Sakthi” for fasting, which means that the rigorous forms of fasting are only for the able-bodied, and that those who are infirm/ill should either not fast or follow symbolic observances. For married (unwidowed) women, total fasting is often banned. Ascetics, on the other hand, have more rigorous fasting requirements. "Nirahara" – fasting without food; "Phalahara" – fasting with fruit and milk; and "Alpahara" – fasting with

broken rice and other meals are the three types of fasting. The essence of Hindu observances is represented by a cycle of fasting and feasting, and the calendar (known as Panchanga) is jam-packed with observances, only a few of which are rigorously followed. Many traditions have been diluted to suit contemporary living, while others have vanished completely. The health consequences of IF have not been studied in this scenario. For the purpose of discussion, The fasting practises in TN may be grouped into the following categories:

- Fasting on a regular basis (fasting during the week)
- During holidays, there is fasting and feasting.

Fasting on a regular basis: The Ekadashi is the most holy fasting time for the Smritis. It is recognised by both Vaishnavites (followers of Vishnu) and "Smarthas" (followers of Adishankara's advaitic philosophy). It asks for a 36-hour fast starting after dark on the 10th day and concluding with rice, greens ("Agathi Keerai"), gooseberry (Amla), and gravy with turkey berry (Sundaikai) for breakfast on the 12th day. The ill, children, and pregnant women do not need to fast. For the length of the fast, ascetics must fast entirely and abstain from speaking. Fasting for other gods has become a tradition, and a variety of fasts for a favourite deity have sprung up as a consequence. For example, Lord Shiva's followers fast on Mondays and the 13th day of the lunar cycle (Pradosham), whereas Lord Vishnu's devotees fast on Saturday. Fasting on Tuesday is traditional in Southern India and is devoted to Mariamman (a manifestation of Shakthi). The mane fortnight and the new moon day are two instances of mane fasting rituals (pitru paksh in the North and maalaya paksha in the South). Periodic observances may also be seen in the week preceding up to the Skanda Shasti, which is extensively celebrated in Tamil Nadu since Skanda, also known as Muruga, is regarded as the Tamil God. Many of these fasts aren't strict and run from sunrise to dusk, with exceptions for drinks, fruit, and milk (referred to as oru pozhudu in Tamil). Because rice is prohibited on such days, Jains in Tamil Nadu eat broken grain for supper. Jains in Tamil Nadu fast on full moon days, Chaturdasi (the 14th day of the fortnight), and Ashtami (the 15th day of the fortnight) (8th day of the fortnight).

During festivals, people fast and feast: Kalra et al. go into considerable detail regarding the Navarathri months' fasting rites and the Karva Chauth practise. (25) Tamil Nadu observes Diwali, the "festival of lights," a day earlier than the rest of India (naraka chaturdashi). Sweets and savoury meals prepared with roasted Bengal gramme flour, rice flour, jaggery, sugar, ghee, and coconut are served during Diwali. A traditional medicine called as "Deepavali Marundhu" (in Tamil) has been created to prevent the harmful effects of excessive carbohydrate and fat consumption in light of this high-calorie snack eating. Omam (dried oregano), milagu (black pepper corns), jeeragam (cumin seeds), sukku (dried ginger), sitharathai (poudre - similar to Alpinia galanga but smaller in size), arisi-thippili (long pepper), and kanda-thippili (long pepper) are some of the components used in the marundhu (Piper retrofractum). In the month of Maargazhi, the "Thiruvathirai" event is held (mid-December to mid-January - dhanur maasa).The festivities begin five days before "Thiruvathirai," when the temple serves only exquisite coconut and bananas for breakfast. For the sake of their children's health, mothers fast on makeeram the day before Thiruvathirai. On this day, a meal called "Ettangadi" is made as a sacrifice to the goddess. This meal is prepared with eight different kinds of root vegetables and fire-roasted plantains. Thiruvathirai is a day when women and girls fast in a religious manner. They observe this for the sake of their spouses and would-be husbands. They exclusively consume grains like chama and wheat, as well as vegetables, bananas, and coconut. "Kali," a sweet dish prepared with fried rice powder (mashed flour) and jaggery known as "Thiruvathirai kali," is the festival's one-of-a-kind culinary contribution. Pongal is the most important festival in Tamil Nadu, signalling the start of harvest season or the Sun's northward march. The Pongal festival, which celebrates the beginning of a new season, is a great way to usher in the new year by cleaning out the old and welcoming in new harvests. The term "pongal" literally means "boiling over" or "spilling over" in Tamil, and it is a symbol of Indian culture's wealth and success. During this occasion, milk is boiling over as a symbol of plenty. The most anticipated part of the Pongal celebration is the preparation of the Pongal meals "Venpongal" and "Chakkarapongal." Both salt and sweet versions are made using rice, moong dhal, ghee, cashew nuts, raisins, jaggery, and spices.

January

January is the month of festivals. Bhogi, Pongal, and Maattu Pongal, or Kaanum Pongal, are three days of harvest celebrations. The feast consists mostly of dishes prepared with freshly harvested rice, jaggery, and the most recent seasonal vegetables.

February

Maha Sivarathiri People fast throughout the whole day and do not sleep for the entire night in order to honour Lord Shiva. They only eat in the AM the next day. Sweet potato is cooked with jaggery and eaten as a night meal in certain households.

March

During this month, Tamil Nadu celebrates Karadaiyaan Nonbu. Fasting is observed until the time of pooja, after which rice cakes prepared with jaggery and chilies, as well as black gramme lentil, are consumed with plenty of butter. This month also sees Telugu and Kannada New Year festivities. People only fast until the time of poojas, after which meals consisting of maida, jaggery, and ghee become an essential part of the New Year celebration.

April

The Rama Navami festival commemorates Lord Rama's birth in April. Panagam (a fragrant jaggery water), butter milk, and soaked moong dhal with coconut, cucumber, and spice are consumed. This month also marks the beginning of the Tamil New Year. Poli is also a key component in this dish. On Tamil New Year's Day, a meal consisting of raw mango chunks, neem blossoms, and jaggery symbolising many flavours of life is served as a special dish.

August

The females in the family commemorate Varalakshmi vratham in August. They fast till the time of Pooja and eat idlis, dumplings, and keers at that period. Rice isn't something

they're meant to eat. During this month, Lord Krishna's birth is commemorated. The poojas are exclusively performed in the evenings. People fast for the whole day and eat after the pooja. The primary things consumed during these holidays are oil-based dishes and basic healthful preparations such as flattened rice (aval in Tamil) with jaggery and coconut, curd, and milk.

September

During this month, Ganesh Chathurthi is celebrated. The feast includes keers, sweet and kara (spicy) lentil dumplings (vada). Many people celebrate Chathurthi, the fourth day following the full moon of each month. They fast for the whole day. They eat after the pooja in the evening.

October

During this month, Durga Pooja or Navarathri is observed. People usually fast for 9 days or until puja time and then eat what they want. Some individuals fast throughout the whole day and just eat at night, avoiding rice.

November

During this month, Deepavali is celebrated. On this day, a variety of sweets and savoury foods are consumed. As an antidote to greasy meals, a specific herbal remedy consisting of pepper, cumin seeds, ajwain, ginger, chithrathai, coriander seeds, jaggery, and ghee is consumed.

December

During this month, Karthigai Deepam is observed. On this day, items consisting of puffed rice and happamsebrated du (rice flour) are produced. Thiruvadhurai or arudra darisanam, the Chidambaram festival honouring Lord Nataraja, occurs in this month. During the beginning of the day, a “uppuma”-like dish of rice and jaggery, a sauce with lentils, and seven or nine seasonal vegetables are given to God and consumed. People usually in fasting upto 48 days for Sabarimalai Yathra.

Applications in the Clinic Conditions

Diabetes Mellitus and Obesity: In animal models, intermittent feeding increases insulin sensitivity, prevents obesity from a high-fat diet, and reduces diabetic retinopathy (26). Okinawa's traditional population practises intermittent fasting and has low obesity and diabetes mellitus rates, as well as excellent lifespan (27). Okinawans often consume a low-calorie, high-nutrient diet consisting of energy-dense but nutrient-dense foods such Okinawan sweet potatoes, different vegetables, and legumes. Members of the Calorie Restriction Society (28) who followed the CRON (Calorie Restriction with Optimal Nutrition) diet had lower incidences of diabetes, as well as lower levels of insulin-like growth factor 1, growth hormone, inflammation, and oxidative stress markers. A multicenter study showed that daily calorie restriction lowers several cardiometabolic risk factors in nonobese individuals (29). Furthermore, six short-term trials including overweight or obese individuals discovered that intermittent fasting is equally as effective for weight reduction as conventional diets (30). According to two recent studies (31), daily calorie restriction or 4:3 intermittent fasting (24-hour fasting three times a week) reduced insulin resistance in individuals with prediabetes or type 2 diabetes. Participants in both intervention groups lost weight but did not improve insulin sensitivity, cholesterol levels, or blood pressure when compared to the control group in a 12-month study comparing alternate-day fasting, daily calorie restriction, and a control diet (32).

Diseases of the Cardiovascular System: Intermittent fasting lowers blood pressure, resting heart rate, high-density and low-density lipoprotein (HDL and LDL) cholesterol, triglycerides, glucose, insulin, and insulin resistance in both animals and humans (33). In addition, intermittent fasting reduces systemic inflammation and oxidative stress, which are linked to atherosclerosis (34). Intermittent fasting improves blood pressure, resting heart rate, levels of high-density and low-density lipoprotein (HDL and LDL) cholesterol, triglycerides, glucose, and insulin, as well as insulin resistance in animals and people (31). Intermittent fasting reduces indicators of systemic inflammation and oxidative stress, two factors related to atherosclerosis (35). Varady et al. discovered that alternate-day fasting was beneficial for weight reduction and cardioprotection in normal-weight and overweight individuals. 59 Improvements in cardiovascular health markers often emerge 2 to 4 weeks after beginning alternate day fasting and fade away over many weeks after resuming to a normal diet (36).

Cancer: More than a century ago, Moreschi and Rous reported the therapeutic benefits of fasting and calorie restriction on malignancies in animals. Since then, numerous animal studies have shown that daily caloric restriction or alternate-day fasting reduces the occurrence of spontaneous tumours in rodents during normal ageing and suppresses the growth of many types of induced tumours while increasing their sensitivity to chemotherapy and irradiation (7). Intermittent fasting, meanwhile, is believed to alter cancer cells' energy metabolism, reducing their development and making them more susceptible to therapeutic therapies. (37) A reduction in insulin and growth hormone receptor signalling, as well as an increase in the transcription factors forkhead box O (FOXO) and nuclear factor erythroid 2–related factor 2, are the underlying processes (NRF2). The anticancer advantages of intermittent fasting are erased by genetic deletion of NRF2 or FOXO1, but life span is maintained, (38), while removal of FOXO3 maintains the anticancer benefits but decreases the longevity impact. Fasting for short periods of time, which activates these transcription factors and their downstream targets, may protect normal cells against cancer while simultaneously improving their stress tolerance. Clinical studies using intermittent fasting in cancer patients have been completed or are under ongoing. The bulk of the early studies were concerned with patient compliance, side effects, and biomarker identification. For example, a trial of daily calorie restriction in prostate cancer patients showed good adherence (95%) and no adverse effects (38). Intermittent fasting has been demonstrated in many case studies to decrease tumour development and extend life in glioblastoma patients (38). According to ClinicalTrials.gov, intermittent fasting is being investigated in people with breast, ovarian, prostate, endometrial, and colorectal malignancies, as well as glioblastoma. Although intermittent fasting regimens vary per research, all need intermittent fasting throughout chemotherapy. Humans have not been examined to determine whether intermittent fasting affects cancer recurrence (41).

Diseases of the Nervous System: Excessive calorie consumption has been related to an increased risk of stroke,

Alzheimer's disease, and Parkinson's disease, particularly in middle age (44). There is substantial preclinical evidence that alternate-day fasting may delay the onset and progression of disease processes in animal models of Alzheimer's disease and Parkinson's disease (45). Intermittent fasting boosts mitochondrial activity and promotes autophagy, neurotrophic factor synthesis, antioxidant defences, and DNA repair, among other activities, which increases brain stress tolerance. Intermittent fasting also enhances GABAergic inhibitory neurotransmission (i.e., -aminobutyric acid–related inhibitory neurotransmission), which may aid in the reduction of seizures and excitotoxicity (46). There are few randomised controlled studies of intermittent fasting in individuals who are at risk of or already have a neurodegenerative disease. In order to find a disease-modifying impact, an intervention should be begun early in the sickness process and continued for a lengthy period of time (e.g., a 1-year study).

Arthritis, Asthma, and Multiple Sclerosis: When obese people lose weight, their asthma symptoms improve (46). During a two-month period, patients who followed an alternate-day fasting programme had a greater blood level of ketone bodies on calorie restriction days and lost weight, reducing asthma symptoms and airway resistance (45). Significant decreases in serum markers of inflammation and oxidative stress have been related to symptom relief (45). Multiple sclerosis is an autoimmune disease that causes axon demyelination and neuronal degeneration in the central nervous system. Alternate-day fasting and periodic cycles of 3 consecutive days of calorie restriction reduce autoimmune demyelination and enhance functional outcomes in a rat model of multiple sclerosis (experimentally created autoimmune encephalomyelitis) (47,48). According to two recent pilot trials (48), patients with multiple sclerosis who adhere to intermittent-fasting regimens had decreased symptoms in as little as two months. Intermittent fasting is thought to be beneficial in rheumatoid arthritis because it reduces inflammation, and there is evidence to back up its usage in arthritis patients (48).

The Benefits and Drawbacks of the Intermittent Fasting Diet: Several human and animal studies have proven the therapeutic efficacy of the IF diet (47). It helps the circulatory system function correctly and reduces the risk of myocardial infarction by lowering body fat and bulk (49). Individuals may decrease their risk of metabolic syndrome by controlling the concentration of different metabolic markers such as insulin and glucose (44). It also reduces the likelihood of type 2 diabetes (49). According to research, following the IF diet over a long period of time may help individuals live longer (47). The IF diet has a positive effect on nervous system performance. It protects neurons against ageing caused by environmental and hereditary factors by regulating the body's free radical production and stress response mechanisms (44). Intermittent fasting is not without its drawbacks. Fasting for just a few hours in the start creates a slew of issues. Because the body needs time to adapt to utilising ketones instead of glucose, the diet is sometimes accompanied with unpleasant emotions such as fatigue or dizziness at first. For anybody suffering from reactive hypoglycaemia, this is definitely not a good diet. In addition, calorie restriction coupled with the use of anti-diabetic medicines has been linked to severe hypoglycaemia and even death (47).

In the aged, it's related to an increased risk of cardiovascular disease, arrhythmia, and stroke. Body instability is caused by fluctuations in glucose concentration, which leads to a greater frequency of falls and osteoporosis-related fractures (48). When hypoglycaemia is present, the ACCORD research showed a greater risk of cardiovascular events in both older and younger individuals (49). A greater risk of diabetic ketoacidosis is also not insignificant, particularly when insulin levels are low due to fasting or poor meal intake. Furthermore, calorie restriction leads to a disruption in hormone regulation. As a consequence of these disruptions, women's menstrual cycles may be interrupted, and men's testosterone levels may be reduced. Intermittent fasting should be avoided by children, pregnant women, and individuals who do intense physical labour (49).

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