REVIEW ARTICLE

Impact of Circadian-Aligned Meal Timing and Sleep Rhythm on Cardiovascular Health: A Comprehensive Review

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Abstract

Cardiovascular health is influenced not only by the quality of diet but also by the timing of meals. Circadian rhythms, the body's internal biological clock, regulate physiological processes, including metabolism, hormone secretion and cardiovascular function. Disruptions in these rhythms, such as irregular meal timing, have been linked to an increased risk of cardiovascular diseases (CVD). There is a strong association between delayed meal timing, particularly late-night eating and breakfast skipping and heightened cardiovascular and cerebrovascular risks. A large-scale European study has suggested that prolonged overnight fasting may lower the risk of CVD and stroke. Emerging dietary approaches, such as time-restricted eating (TRE) and chrono-nutrition, have gained attention for their potential in mitigating metabolic disorders and promoting cardiovascular health. This review explores the intricate relationship between circadian-regulated meal timing and cardiovascular outcomes, analysing molecular mechanisms, clinical evidence and possible dietary interventions. By understanding the role of chrono-nutrition, this review aimed to provide insights into optimising meal schedules to enhance cardiovascular well-being and reduce disease risk. In addition to melatonin's endogenous regulation, dietary sources of melatonin and chronobiotic nutrients (eg, walnuts, tart cherries, oats) may help support circadian alignment. Strategic intake of these foods, especially during evening hours, could enhance melatonin levels and improve cardiovascular outcomes. Moreover, the timing of other compounds like caffeine has emerged as a modifiable factor, with studies showing that morning coffee consumption may reduce cardiovascular and cancer mortality. While intermittent fasting and caloric restriction both reduce caloric intake, these operate through distinct mechanisms. Caloric restriction focuses on reducing total energy consumption, whereas meal timing strategies emphasise aligning food intake with circadian rhythms without necessarily altering caloric quantity. This distinction is critical, as it supports the view on circadian physiology in metabolic regulation.

Key words: Circadian rhythm; Meals, time; Cardiovascular system; Molecular mechanism.

Introduction

Cardiovascular diseases (CVDs) remain the leading cause of morbidity and mortality worldwide, accounting for a significant burden on public health systems. Traditionally, the focus of cardiovascular health research has centred on dietary composition, emphasising the intake of specif-

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ic nutrients, caloric balance and overall dietary quality. However, recent scientific advancements have highlighted the importance of not only what we eat but also when we eat. Meal timing, an essential component of chrono-nutrition, plays a critical role in modulating various physiological processes that influence metabolic health and cardiovascular function. Emerging evidence suggests that aligning meal schedules with the body's circadian rhythms may have profound implications for cardiovascular well-being.[1] Circadian rhythms are endogenous, approximately 24-hour cycles that regulate numerous biological processes, including sleep-wake patterns, hormone secretion, metabolism and cardiovascular function. These rhythms are synchronised by external environmental cues, primarily the light-dark cycle, but are also influenced by behavioural factors such as eating patterns, sleep schedules and physical activity. The disruption of circadian rhythms due to modern lifestyle habits such as shift work, irregular sleep patterns and late-night eating has been strongly associated with metabolic disorders, obesity, diabetes and increased risk of CVD.[2]

Recent investigation indicates that irregular meal timing, particularly late-night eating and breakfast skipping, disrupts the natural metabolic rhythm, leading to insulin resistance, dyslipidaemia, inflammation and endothelial dysfunction, all of which are risk factors for cardiovascular diseases. Extensive research has demonstrated a strong association between skipping breakfast and unfavourable cardiovascular outcomes. A large-scale prospective cohort study conducted in Japan found that individuals who habitually omitted breakfast had a significantly elevated risk of developing atherosclerotic plaques and subclinical coronary artery disease, independent of conventional cardiovascular risk factors.[3] In a similar vein, a study based on NHANES data by Rong and associates revealed that breakfast skipping was linked to an 87 % increased risk of death from cardiovascular causes, emphasising the crucial role of breakfast in cardiovascular protection.[4]

A recent nutritional epidemiology study reinforced these findings by demonstrating that habitual breakfast consumption was associated with improved cardiometabolic markers and lower systemic inflammation, suggesting a mechanistic link through modulation of postprandial glucose and lipid metabolism.[5] For instance, delayed meal intake has been shown to interfere with glucose homeostasis and lipid metabolism, thereby exacerbating the risk of hypertension and atherosclerosis. A large-scale European study has further demonstrated that prolonged overnight fasting, ensuring a sufficient fasting window between the last meal of the day and breakfast, can reduce the risk of cardiovascular diseases and stroke. These findings underscore the potential benefits of structured meal timing as a preventive strategy against CVD. Time-restricted eating (TRE) has emerged as a promising dietary approach that aligns food intake with circadian rhythms. TRE involves consuming all meals within a defined window, typically ranging from 6 to 10 hours, allowing for an extended fasting period overnight suggested that TRE enhances cardiometabolic health by improving lipid profiles, reducing oxidative stress, modulating inflammatory pathways and optimising glucose metabolism. Similarly, chrono-nutrition, which integrates meal timing with circadian biology, has gained attention for its potential in mitigating cardiovascular and metabolic disorders.[6-8]

Given the growing body of evidence supporting the role of circadian meal timing in cardiovascular health, this review aims to explore the intricate interplay between meal schedules and cardiovascular outcomes.[7, 8] By examining the molecular mechanisms, clinical evidence and potential dietary interventions, this article provides a thorough understanding of how circadian-aligned meal timing may be used as a preventative or therapeutic approach to cardiovascular disease by synthesising a wide range of new evidence from the disciplines of chronobiology, molecular cardiology, nutritional science and circadian medicine. This paper also explores the intricate relationship between hormone fluctuations, clock gene expression and metabolic regulation as it is influenced by meal timing. Additionally, it highlights the importance of chronotypes in determining how each person reacts to chrono-nutritional strategies and the impact of genetic polymorphisms, such as those affecting melatonin receptors. Furthermore, this study proposes future directions for customised chrono-nutrition and chronotherapy in cardiovascular risk reduction by integrating results from epidemiological research, clinical interventions and experimental models.

Methods

This is a narrative (non-systematic) review conducted through a comprehensive literature search using *PubMed, Scopus* and *Google Scholar*, covering publications available up to March 2025. Search terms included: "circadian rhythm," "meal timing," "chrono-nutrition," "intermittent fasting," "cardiovascular health," "melatonin," and "time-restricted eating." Eligible studies included original research articles, clinical trials, meta-analyses and observational studies examining the influence of meal timing, circadian rhythm alignment or disruption, sleep patterns, or chrono-nutritional interventions on cardiovascular and metabolic health outcomes. Studies focused exclusively on caloric intake without addressing timing aspects were excluded. A total of approximately 66 studies were included in this review after applying inclusion criteria and relevance screening. Preference was given to studies involving human participants, although mechanistic insights from relevant animal models were also incorporated. References were selected via manual screening based on scientific rigor and relevance. Additional sources were identified by reviewing bibliographies of key articles.

Molecular basis of circadian rhythms

At the molecular level, circadian rhythms are regulated by a network of clock genes and their protein products. These molecular oscillations influence nutrient metabolism and their disruption, as seen with mistimed meals, may contribute to cardiovascular risk factors.[1] The circadian clock comprises a network of core clock genes, including Period (Per), Cryptochrome (Cry), Clock and Bmal1. These genes, expressed rhythmically, form transcription-translation feedback loops that generate oscillations with a period of approximately 24 hours. Clock genes are expressed not only in the central circadian pacemaker (the suprachiasmatic nucleus) but also in peripheral tissues, including the heart and vasculature. In fact, the molecular clock regulates key processes such as myocardial contractility, vascular tone and blood pressure.[2, 6]

The circadian clock exerts a profound influence on metabolic pathways, impacting lipid and glucose metabolism. Dysregulation of metabolic processes linked to the circadian clock contributes significantly to the development of cardiovascular risk factors, thereby establishing a connection between circadian disruption, metabolic syndrome and atherosclerosis. Disruptions in circadian rhythms, whether caused by shift work, irregular sleep patterns, or genetic mutations affecting clock genes, are consistently associated with an elevated risk of cardiovascular diseases. These perturbations can lead to endothelial dysfunction, systemic inflammation and adverse cardiac remodelling, further exacerbating cardiovascular pathology.[7] Perturbations in the circadian clock can lead to endothelial dysfunction, inflammation and adverse cardiac remodelling. Recent evidence suggests that the timing of meals throughout the day may have implications for cardiovascular health. Consuming a substantial portion of daily caloric intake during the morning hours, aligning with the body's natural circadian rhythm, appears to positively influence metabolic parameters associated with cardiovascular well-being.[8]

Meal timing is an important factor in mitigating cardiovascular risks. Delay in the first meal of the day is directly linked to an elevated risk of heart disease, while eating late at night is also linked to a higher risk of cardiovascular disease. Optimising meal timing, including adopting earlier eating patterns and a prolonged nighttime fasting period, could significantly benefit cardiovascular health.[7] Circadian meal timing influences glucose metabolism, insulin sensitivity and lipid profiles. Irregular meal patterns, such as late-night eating, have been associated with adverse metabolic outcomes, potentially contributing to the development of cardiovascular risk factors therefore, disruption in circadian rhythm leads to circadian misalignment and disturbances in clock gene mechanism occurring due to unhealthy and disturbed meal timings, leading to physiological disturbances, oxidative stress, inflammation and autonomic nervous system disturbances that directly gives rise to hypertension, stroke, cardiomyopathy, Myocardial Infarction leading to cardiovascular disease risk factors[8] (Figure 1).

Irregularities in sleeping and in eating schedules lead to circadian misalignment and can result in adverse health outcomes, particularly concerning vascular health. Variability in the placement of calories across the 24 hours was found to be strongly associated with carotid artery thick-

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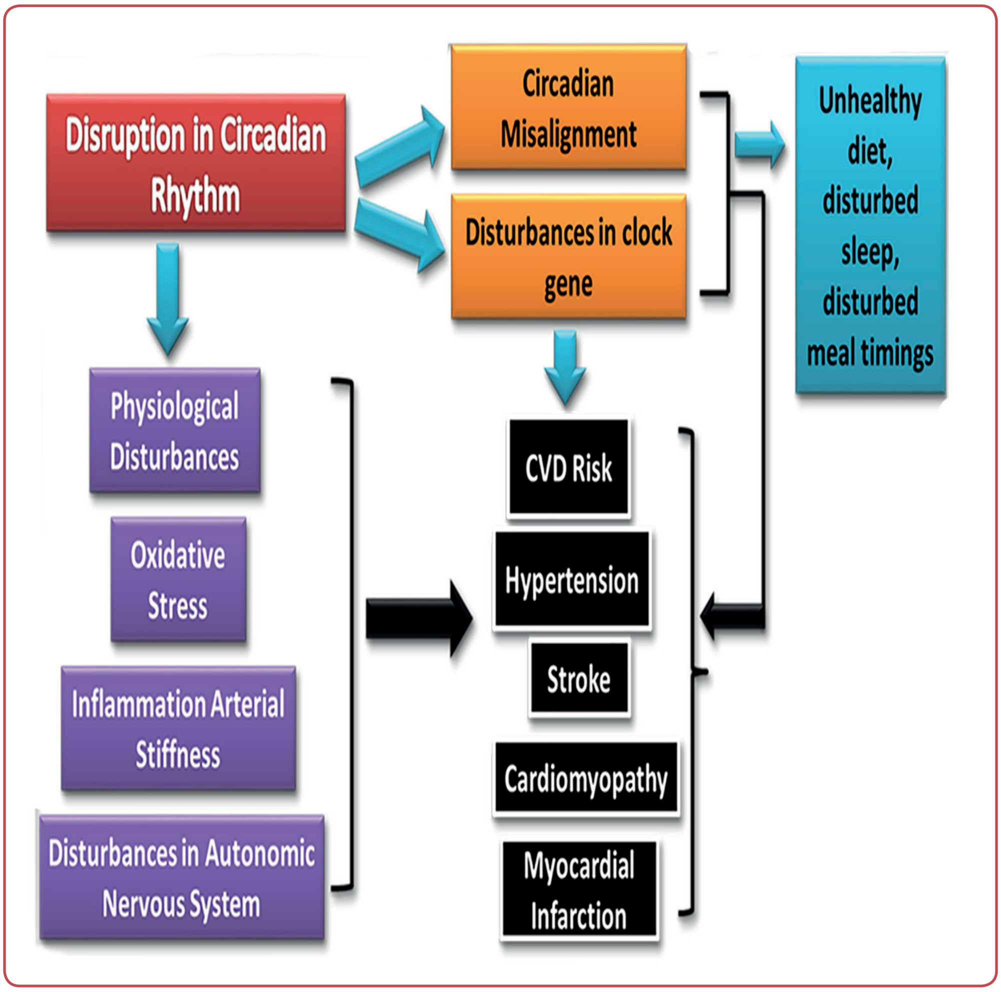

Figure 1: ***Circadian misalignment leading to cardiovascular risk factors:*** *Disruption in circadian rhythm leading to circadian misalignment and disturbances in clock gene mechanism occurring due to unhealthy and disturbed meal timings, leading to physiological disturbances, oxidative stress, inflammation and autonomic nervous system disturbances that directly gives rise to hypertension, stroke, cardiomyopathy, myocardial infarction.*

ness, highlighting its impact on vascular health.[9] Understanding the molecular basis of circadian rhythms opens avenues for potential therapeutic interventions. Chronotherapy, which considers the circadian timing of drug administration, is an emerging strategy with implications for optimising cardiovascular medications. Future research should focus on elucidating the precise mechanisms by which the circadian clock influences cardiovascular health and exploring innovative therapeutic approaches that leverage circadian biology for cardiovascular disease prevention and management. The molecular basis of circadian rhythms intertwines with cardiovascular health, liver and kidney health, as well as influencing a myriad of processes critical for overall health.[10] Unravelling intricate molecular clockwork holds promise for advancing our understanding of cardiovascular diseases and developing innovative therapeutic strategies.

Chrono-nutrition and cardiovascular risk factors

Chrono-nutrition, an emerging field within nutritional science, focuses on the temporal aspects of dietary patterns and their impact on health. Understanding of chrono-nutrition, with a specific emphasis on its influence on cardiovascular risk factors, is pertinent to cardiovascular health. The intricate interplay between meal timing, circadian rhythms and cardiovascular health is offering insights into potential strategies for cardiovascular disease prevention and management. Chrono-nutrition emphasises the importance of when we eat in addition to what we eat. Aligning meal timing with the body's internal clock may improve blood pressure regulation, lipid metabolism and overall metabolic health, thereby mitigating cardiovascular risks.[11] Observational studies have provided insights into the association between meal timing and cardiovascular outcomes. Individuals who adhere to a pattern of consuming larger meals earlier in the day tend to exhibit a lower prevalence of cardiovascular risk factors, highlighting the potential benefits of circadian-aligned eating. The timing of food consumption exerts a powerful influence on circadian rhythmicity. Chrono-nutrition has attracted considerable interest for possible beneficial effects on cardiovascular health. Human studies on chrono-nutrition-based dietary interventions could reduce the risk for cardiovascular disease by improving weight control, hypertension, dyslipidaemia and diabetes.[12] However, meta-analysis of randomised control trials in this present varying and somehow conflicting results. Even the traditional association of breakfast skipping with adverse cardiovascular outcomes is nowadays controversial.[13]

Circadian rhythms govern metabolic processes, influencing nutrient utilisation, insulin sensitivity and lipid metabolism. Understanding the molecular basis of circadian rhythms provides a foundation for exploring how chrono-nutrition can modulate these processes and impact cardiovascular health. Chrono-nutrition has been associated with alterations in lipid profiles, indicating that distributing dietary fat intake appropriately throughout the day may positively influence cholesterol levels, boost immune function, improve heart rhythm and reduce the risk of atherosclerosis and cardiovascular events[14] (Figure 2). Meal timing influences blood pressure regulation; chrono-nutritional approaches, such as time-restricted feeding, may contribute to the maintenance of a healthy blood pressure profile, a critical factor in cardiovascular health. Chrono-nutritional interventions also appear to improve lipid profiles. A 2020 meta-analysis showed that time-restricted eating and early-time feeding reduced LDL-C concentrations by an average of 7.2 mg/dL compared to controls, particularly in overweight and

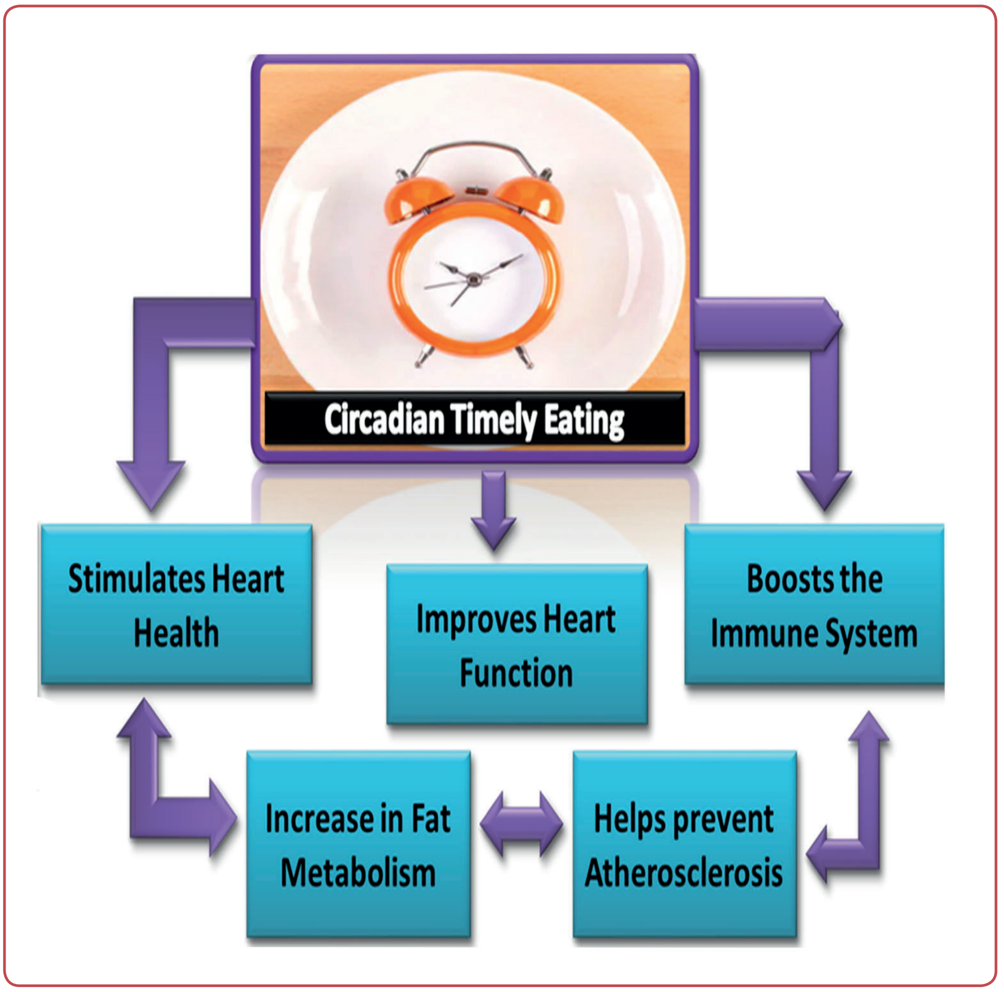

Figure 2: ***Circadian eating timely:*** *Proper meal timings may help in stimulating the heart health by improving immune system function, improving blood pressure and increasing in boy's fat metabolism*

obese populations.[15] Similarly, a 2023 systematic review highlighted that skipping late-night meals and following early feeding schedules led to significant improvements in HDL-C and triglyceride levels,[16] suggesting chrono-nutrition can be an effective strategy for lipid management and cardiovascular prevention. A summary of key studies evaluating the impact of circadian rhythms, meal timing and sleep patterns on cardiovascular outcomes is provided in Table 1.

The temporal distribution of meals has been linked to inflammatory markers. Chrono-nutritional interventions may mitigate chronic inflam-

Table 1: Key studies on circadian rhythm, meal timing and cardiovascular health

SN	Study reference	Category	Population / model	Study type	Key findings
1	*Durgan and Young, 2010*	Circadian biology	Cardiomyocytes (animal)	Review	Circadian variation influences timing of CV events like MI and stroke.
2	*Curtis and Fitzgerald, 2006*	Central/ peripheral clocks	Review	Review	Central and peripheral clocks influence vascular tone, inflammation.
3	*Cahill et al, 2013*	Breakfast skipping	US male health professionals	Prospective cohort	Skipping breakfast associated with increased risk of coronary heart disease.
4	*Rong et al, 2019*	Breakfast skipping	US adults	Cohort study	Skipping breakfast linked to higher cardiovascular and all-cause mortality.
5	*Wang et al, 2024*	Breakfast skipping	Adults (meta-analysis)	Systematic review	Breakfast skipping associated with increased all-cause, CV and cancer mortality.
6	*Takeda and Maemura, 2016*	Circadian onset of CV events	Review	Review	Circadian variation influences timing of CV events like MI and stroke.
7	*Jamshed et al, 2022*	Intermittent fasting	Adults with obesity	Randomised trial	Early time-restricted eating improved weight loss and cardiometabolic outcomes.
8	*Fatima et al, 2021*	Shift work and circadian risk	Nurses	Observational	Shift work and circadian rhythm disruption increase CV risk factors.
9	*Fatima et al, 2021*	Sleep and metabolism	Review	Narrative review	Sleep deprivation linked to higher risk of metabolic syndrome and diabetes.
10	*Zhang et al, 2014*	Clock genes and metabolism	Mice	Experimental (animal)	BMAL1 promotes lipogenesis via insulin-AKT-mTORC2 pathway; tied to metabolic regulation.
11	*Zhu et al, 2023*	Melatonin gene and diabetes	Genetic analysis	Review	MTNR1B gene connects circadian regulation to T2DM; evolutionary insights into circadian health.
12	*Pot et al, 2016*	Meal irregularity	Review of human studies	Mixed methods	Irregular eating associated with adverse cardiometabolic outcomes.
13	*Garaulet et al, 2013*	Food timing and weight loss	Obese individuals	Intervention study	Late lunch eaters lost less weight than early eaters, despite same calorie intake.
14	*Katsi et al, 2022*	Chrono-nutrition	Review	Narrative review	Emphasises role of chrono-nutrition in managing cardiometabolic disorders.
15	*Bonnet et al, 2020*	Breakfast skipping	Adults (RCTs, meta-analysis)	Meta-analysis	Breakfast skipping linked to higher BMI and adverse cardiometabolic profiles.
16	*Yu et al, 2023*	Breakfast skipping	Mixed cohorts	Systematic review/ meta-analysis	Breakfast omission negatively affects CV risk factors; need for guidance on optimal timing.

CV: cardiovascular; T2DM: type 2 diabetes mellitus; MI: myocardial infarction; BMI: body mass index;

mation, thereby reducing the risk of endothelial dysfunction and atherosclerosis. Time-restricted feeding, a chrono-nutritional approach, involves confining daily food intake to specific time windows.[17] Studies suggest that this approach may confer cardiovascular benefits by improving metabolic health, reducing oxidative stress and enhancing circadian rhythms.[14, 17, 18] Recognising individual variability in circadian rhythms and lifestyle patterns is essential when considering chrono-nutritional recommendations. Personalised approaches that consider an individual's chronotype, daily schedule and preferences are crucial for successful implementation.[19] While chrono-nutrition shows promise for cardiovascular health, challenges such as work schedules and lifestyle constraints need consideration. Long-term effects of chrono-nutritional interventions and refine guidelines for optimal implementation must be explored.

Melatonin, a pineal hormone tightly regulated by the light-dark cycle, plays a pivotal role in synchronising circadian rhythms, including those involved in glucose metabolism, blood pressure regulation and insulin secretion. While melatonin is briefly mentioned, its implications for cardio-metabolic health deserve greater emphasis. Recent studies have elucidated that melatonin acts through specific G-protein-coupled receptors, MT1 and MT2 (encoded by MTNR1A and MTNR1B), which are expressed in pancreatic β-cells and vascular tissues. Polymorphisms in the MTNR1 B gene, particularly rs10830963, have been strongly associated with impaired insulin secretion, increased risk of type 2 diabetes and adverse lipid profiles.[20] This genetic variant appears to enhance melatonin signalling, thereby worsening the metabolic impact of late-night eating, when melatonin levels are naturally elevated and insulin sensitivity is reduced. A clinical study demonstrated that late dinner timing led to impaired glucose tolerance in MTNR1B variant carriers compared to non-carriers, suggesting a gene-diet timing interaction.[21] Moreover, melatonin has been shown to lower nighttime blood pressure, modulate sympathetic activity and reduce oxidative stress, making it an important chrono-biotic factor in cardiovascular protection. Its role in the interplay between light exposure, food intake and hormonal rhythms is increasingly recognised, especially with findings that melatonin receptor sensitivity influences the risk of circadian misalignment-induced metabolic dysfunction.[11] Finally, a recent review highlighted that melatonin-rich foods such as cherries, walnuts and oats can potentially reinforce circadian alignment and improve cardiometabolic health outcomes, especially when consumed in a time-restricted manner.[22] These findings open new avenues for personalised chrono-nutrition, where both genetic background and meal composition may influence therapeutic outcomes.

Metabolic processes, such as the digestion and utilisation of carbohydrates, lipids and proteins, display circadian variation and respond differently based on the time of food intake. Morning hours are associated with greater insulin sensitivity and glucose tolerance, which supports more efficient carbohydrate metabolism, whereas late-night eating is linked to impaired lipid oxidation and elevated postprandial glucose levels. Protein metabolism also exhibits time-of-day differences, with improved nitrogen retention during daytime consumption. In addition, oxidative stress and inflammatory responses are time-sensitive. Studies indicate that pro-inflammatory cytokine levels are typically lower in the morning and increase during the evening, suggesting that late-night meals may intensify systemic inflammation. Furthermore, limited but growing evidence has linked circadian misalignment with the accumulation of advanced glycation end-products (AGEs) toxic metabolites formed from the non-enzymatic reaction between sugars and proteins or fats. Elevated AGE levels, commonly observed in diabetes and atherosclerosis, are influenced by disrupted glycemic control during circadian misalignment. Although direct human studies remain sparse, experimental data indicate that meal timing and circadian regulation play a key role in modulating AGE formation and vascular aging, making it a promising avenue for further investigation in chrono-nutritional interventions.

Morning preference and cardiovascular health

Some studies indicate that individuals who have a preference for morning activities and consume a larger portion of their daily caloric intake earlier in the day may have better cardiovascular health. This pattern is thought to align with the body's natural circadian rhythm, where metabolic processes are more efficient during the day. There has been ongoing research into the association between morning preference (morning chronotype) and cardiovascular health.[23]

a) - Morning preference and metabolic health

Morning preference, characterised by an inclination towards morning activities and an earlier wake-up time, has been associated with various aspects of metabolic health. Individuals with a preference for morning activities, often referred to as "morning larks" or having a morning chronotype, tend to wake up and be more active earlier in the day. Some studies suggest that morning preference is associated with better metabolic health, including improved insulin sensitivity and lower risk factors for cardiovascular diseases.[23] The molecular clock, comprising core clock genes, orchestrates these rhythmic metabolic activities. Understanding the circadian regulation of metabolism sets the stage for exploring the relationship with morning preference. Epidemiological studies suggest that individuals with a morning chronotype may exhibit better insulin sensitivity.[23, 24] The evidence linking morning preference to improved glucose metabolism, reduced risk of insulin resistance and lower incidence of type 2 diabetes.[25] Morning preferences is amalgamated with specific dietary patterns, exploring the choices and timing of meals among morning-oriented individuals provides insights into the potential impact on overall caloric intake, nutrient distribution and metabolic outcomes. Research indicates that morning-oriented individuals may be more successful in weight management efforts.[26] Morning chronotype has been linked to more favourable physical activity patterns. Understanding how morning-oriented individuals engage in regular physical activity provides context for the observed metabolic benefits and overall health advantages. Morning preference often aligns with better sleep quality and there is a bidirectional relationship between morning chronotype, sleep duration and the influence on metabolic health outcomes.[27] Practical applications of chrono-nutrition, such as time-restricted feeding and optimising meal timing, may complement morning preference to enhance metabolic health. Morning preference emerges as a valuable marker associated with improved metabolic health and cardiovascular health, early breakfast in the morning helps retain the body's healthy circadian rhythm, by maintaining the time of eating throughout the day and keeping in pace the balanced micro-biome giving rise to healthy heart functioning, whereas the late night dinner causes disrupted circadian rhythm by inconsistency in the daily meal timings leading to disturbed rhythmic pattern of heart causing high cardiovascular risk[28] (Figure 3).

b) - Meal timings and circadian rhythm and cardiovascular health

The timing of meals, intricately linked to the body's circadian rhythms, has gained attention as a potential modifiable factor influencing cardiovascular health. The body's circadian rhythm influences various physiological processes, including metabolism. There is evidence to suggest that aligning meal timing with the body's natural circadian rhythm may have positive effects on metabolic health.[28-30] Shift work and irregular meal patterns associated with circadian disruption have been linked to increased cardiovascular risks.[31] Breakfast is the most important meal of the day and it is also traditionally included in the concept of 'Community-specific healthy eating' worldwide. A decline in breakfast consumption has been witnessed in recent decades. Consuming a larger portion of daily caloric intake earlier in the day may be beneficial for weight management and insulin sensitivity. While the connection between morning preference and cardiovascular health is still an active area of research, some studies propose that individuals with a morning chronotype may have a lower risk of cardiovascular diseases.[32]

Regular meal times are as important as what we eat due to the impact on the body's internal clock. Interestingly, eating breakfast tend to have reduced rates of heart disease, low cholesterol and low blood pressure with normal blood sugar levels.[29] Skipping breakfast is more likely to eat throughout the day and it also results in poor nutrition that may lead to obesity and diabetes. Those who do not eat breakfast have a 27 % increased risk of heart disease and 18 % more likely to have a stroke. Factors such as lower rates of obesity, healthier dietary patterns and improved sleep quality associated with morning preference may contribute to cardiovascular benefits.[32] Understanding the molecular mechanisms underlying the relationship between meal timings, circadian rhythms and cardiovascular health opens avenues for chrono-therapeutic interventions.

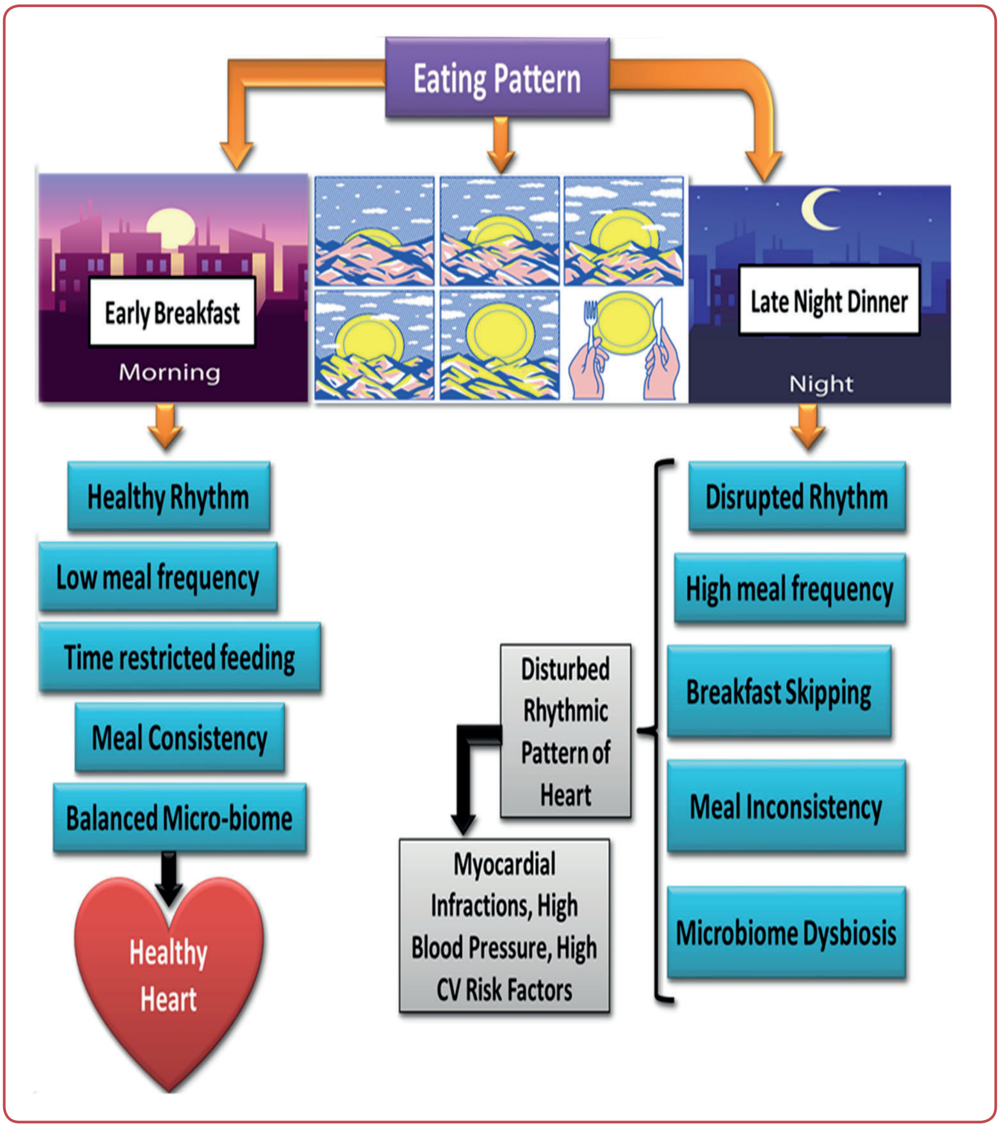

Figure 3: ***Eating pattern and physiological wellbeing:*** *This diagram depicts the early breakfast timings and late night dinner; early breakfast in the morning helps retain the body's healthy circadian rhythm, by maintaining the time of eating throughout the day and keeping in pace the balanced micro-biome giving rise to healthy heart functioning, whereas the late night dinner causes disrupted circadian rhythm by inconsistency in the daily meal timings leading to disturbed rhythmic pattern of heart causing high blood pressure, myocardial infarction and high cardiovascular risk.*

Meal timings, intricately connected to circadian rhythms, play a significant role in cardiovascular health. Circadian rhythm eating and fasting pattern shows the time-restricted pattern of circadian rhythm eating, 7 am-7 pm eating and fasting time. Avoid artificial lights and eating late at night (Figure 4).

c) Sleep quality and cardiovascular health

Sleep quality is a fundamental aspect of overall health and its relationship with cardiovascular well-being has garnered increasing attention. Adequate and high-quality sleep is crucial for overall health, including cardiovascular health. Poor sleep patterns, especially those associated with evening chronotypes or irregular sleep schedules, have been linked to an increased risk of cardiovascular diseases. Numerous epidemiological studies have established associations between poor sleep quality and an increased risk of cardiovascular diseases.[33] Understanding the influence of sleep on cardiovascular parameters is crucial. Common sleep disorders, such as obstructive sleep apnoea (OSA) and insomnia, have been linked to heightened cardiovascular risk.[34] Chronic sleep disturbances contribute to sys-

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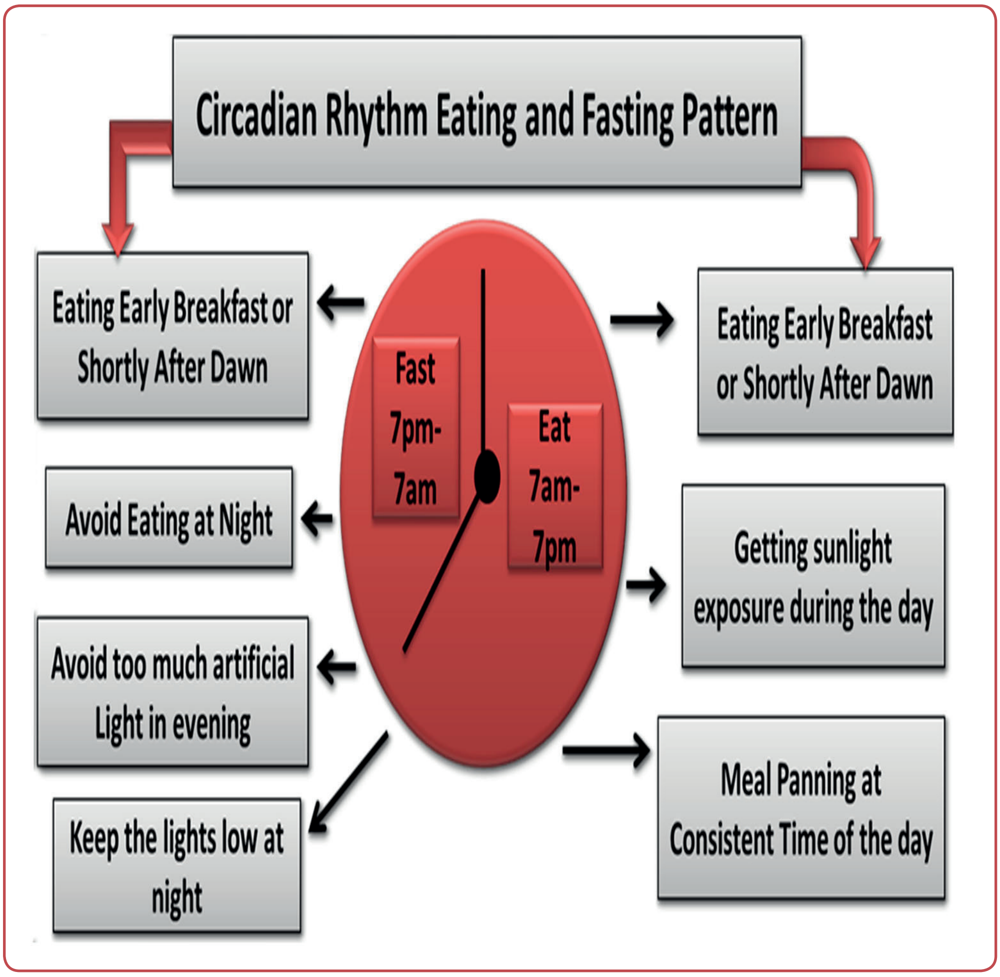

Figure 4: ***Circadian rhythm eating and fasting pattern:*** *This diagram shows the time-restricted pattern of circadian rhythm eating, 7 am-7 pm eating and fasting time. Artificial lights and eating late at night should be avoided.*

temic inflammation and oxidative stress, both of which are implicated in the pathogenesis of cardiovascular diseases. Sleep quality influences metabolic processes, including glucose metabolism and insulin sensitivity. The disturbances in sleep architecture may contribute to the development of metabolic syndrome and type 2 diabetes, both of which elevate cardiovascular risk. Both insufficient and excessive sleep duration have been associated with adverse cardiovascular outcomes. The U-shaped relationship between sleep duration and the risk of cardiovascular diseases emphasises the importance of optimal sleep duration for cardiovascular health.[34]

Sufficient quality of sleep is important for maintaining cardiovascular health. However, most previous studies focused on sleep duration. A growing number of studies have demonstrated that short sleep duration elevates the risk of cardiovascular disease.[35, 36] Some studies have also shown that poor sleep quality was found to be associated with a greater risk of cardiovascular disease,[35-38] while other studies have argued that the quality of sleep is more important than the duration of sleep.[39, 40] However, there are limited data about the joint effects of quality of sleep and duration of sleep on the risk of cardiovascular disease, especially from large, prospective cohort studies. The bidirectional relationship between sleep quality and mental health is also important and plays a direct role in cardiovascular health. Mental health conditions, such as depression and anxiety, are not only consequences of poor sleep but also independent risk factors for cardiovascular diseases.[41] Interventions aimed at improving sleep quality, including cognitive-behavioural therapy for insomnia (CBT-I) and continuous positive airway pressure (CPAP) for sleep apnoea, have shown promise in mitigating cardiovascular risks. Sleep quality stands as a critical determinant of cardiovascular health, with bidirectional influences between the two. The multifaceted relationship emphasises the importance of prioritising sleep for overall cardiovascular well-being.[42]

Late-night eating and metabolic effects

Late-night eating has become prevalent in modern societies, raising concerns about its potential impact on metabolic health and cardiovascular well-being. Eating late at night, especially large or heavy meals, may have adverse effects on cardiovascular health. Late-night eating, characterised by the consumption of meals close to bedtime, has become a common dietary pattern. This is because the body's metabolic processes tend to slow down during the nighttime. Late-night eating has been associated with metabolic syndrome, obesity and other cardiovascular risk factors.[43] Late eating can predispose to obesity and metabolic syndrome through several potential mechanisms. Because sleep decreases metabolic rate.[44, 45] Eating close to bedtime may reduce the rate of oxidation of ingested nutrients. Late-night eating can disrupt circadian rhythms, affecting the natural oscillations of metabolic processes. Studies have indicated that late-night eating may adversely affect glucose metabolism and insulin sensitivity. Chronic inflammation is a known contributor to cardiovascular diseases. Late-night eating may activate inflammatory pathways, fostering a pro-inflammatory environment.[46] Late-night eating may have implications for metabolic health and, subsequently, cardiovascular health. However, it's important to note that the relationship between late-night eating and cardiovascular outcomes is complex and findings can vary among individuals. Eating late at night may disrupt the body's circadian rhythm and natural metabolic processes. The body's metabolic rate tends to slow down during the evening and night. Late-night eating has been associated with poorer glucose tolerance, insulin resistance and disturbances in lipid. Some studies have suggested that consuming a significant portion of daily caloric intake during the late evening or night may contribute to weight gain and obesity. Obesity is a well-established risk factor for cardiovascular diseases, including hypertension, coronary artery disease and heart failure.[47]

Late-night eating can also impact sleep quality. Digesting a large meal close to bedtime may lead to discomfort and disrupt sleep patterns. The body's ability to process and metabolise nutrients may be less efficient during the nighttime compared to daytime. Poor sleep quality is associated with various cardiovascular risk factors, including obesity, insulin resistance and hypertension. Disruption of the circadian rhythm, including irregular meal timing, has been linked to adverse metabolic effects and an increased risk of cardiovascular diseases.[48]

Intermittent fasting and cardiovascular benefits

Intermittent fasting, an eating pattern characterised by alternating periods of eating and fasting, has emerged as a popular dietary strategy with potential implications for cardiovascular health. Intermittent fasting is a dietary intervention just like caloric restriction, working on the principle of restricting food intake. It focuses on the timing of when meals can be consumed, either within a day or a week. Two types of intermittent fasting are alternate-day fasting and time-restricted fasting. In alternative day fasting, the subset may consist of 24-hour fasts followed by a 24-hour period of eating that can be done several times a week, such as a 5:2 strategy, where there are 2 fast days mixed into 5 non-restrictive days.[49] For time-restricted eating, variations include 16-hour fasting with 8-hour feeding times, 20-hour fasts with 4-hour feeding times, or other similar versions. While both caloric restriction and intermittent fasting may result in overall low caloric intake. Many other dietary interventions have been shown to improve cardiovascular risk, including caloric restriction, which involves limiting calories during a given period. Most of the people in developed and developing countries adopted a Western lifestyle of work, eating and sleeping, which includes eating several high-calorie meals throughout the day, therefore leading to cardiometabolic complications and early onset of many chronic diseases.[50] A growing number of clinical trials examining the consequences of different forms of intermittent fasting, such as restricting food intake every other day or limiting it to a short window during the day (known as alternate-day fasting and time-restricted eating, respectively), indicate that the amount of food as well as the duration of time spent eating every day are important determinants of the effects of diet on our health and lifespan, the benefits of Intermittent fasting promotes active weight loss and long term intermittent fasting has promising results in improving overall cardiovascular health[49-51] (Figure 5).

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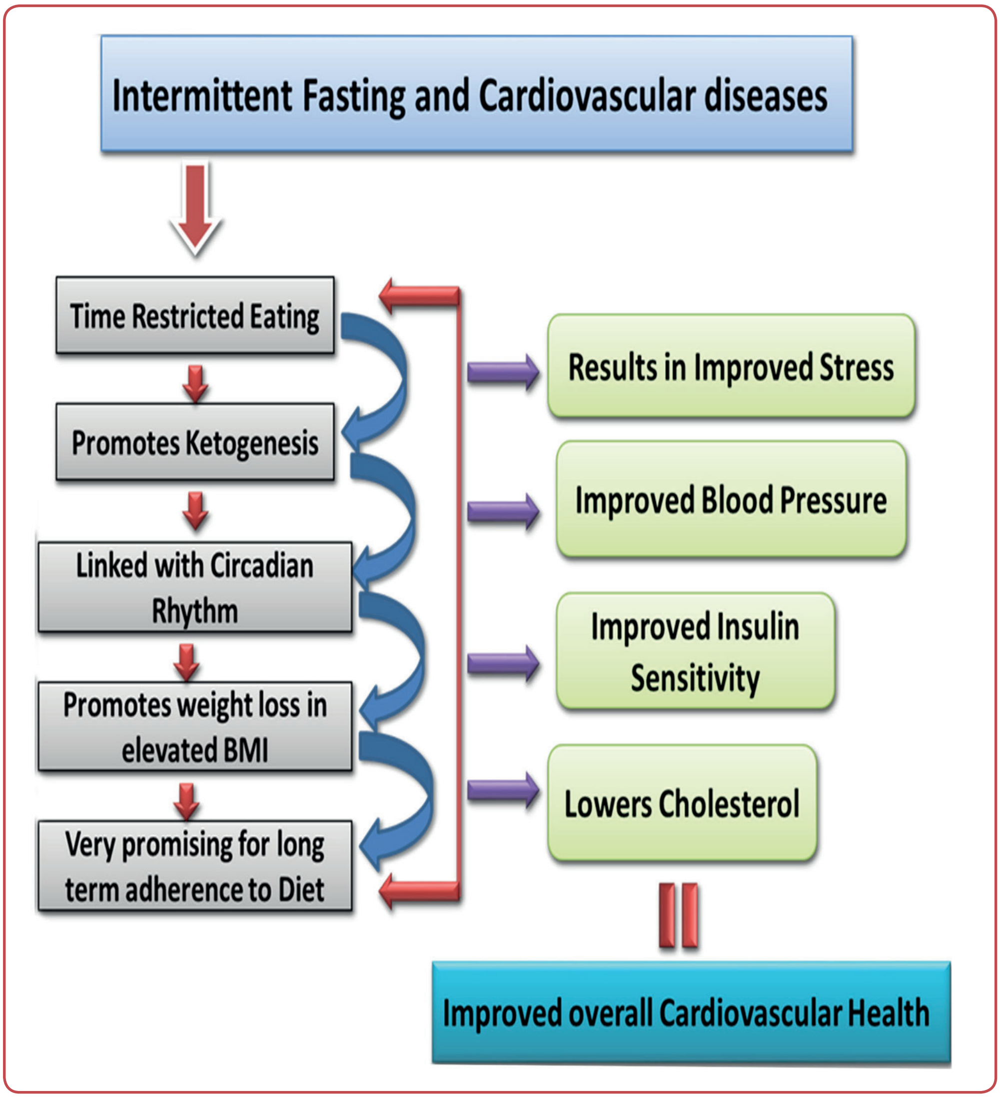

Figure 5: ***Intermittent fasting and cardiovascular disease risk:*** *The figure shows the benefits of intermittent fasting that promote active weight loss and those who stick to intermittent fasting have promising results in improving overall cardiovascular health*

Caloric restriction is linked to improvement in weight, blood pressure and insulin sensitivity.[49] Numerous studies have investigated the effects of intermittent fasting on cardiovascular risk factors such as blood pressure, lipid profiles and glycaemic control.[50] Autophagy, a vital cellular maintenance mechanism has been identified as a key pathway through which time-restricted feeding (TRF) promotes cardiovascular health. This process involves the breakdown and recycling of damaged proteins and organelles via lysosomes, thereby enhancing metabolic adaptability, lowering inflammation and supporting the repair of cardiovascular tissues. A randomised crossover study revealed that limiting food intake to a 6-hour window, with dinner consumed before 3 p.m., led to significant improvements in insulin sensitivity, reductions in oxidative stress and lower blood pressure. These benefits are likely linked to increased autophagic activity.[7, 52] Additionally, a clinical review highlighted that fasting periods longer than 12–14 hours activate the AMPK and SIRT1 signalling pathways, which boost autophagy and mitophagy, processes critical for preserving vascular integrity, decreasing arterial stiffness and preventing the development of atherosclerotic plaques.[53] Autophagy holds particular importance in the heart, where it safeguards against ischemic damage and cardiac hypertrophy. Consequently, extended fasting intervals may serve as a molecular reset mechanism, reinforcing cardiovascular resilience while aligning with the circadian regulation of metabolism. These insights suggest that TRF should be regarded not merely as a dietary regimen, but as a form of chronotherapy that capitalises on bio-

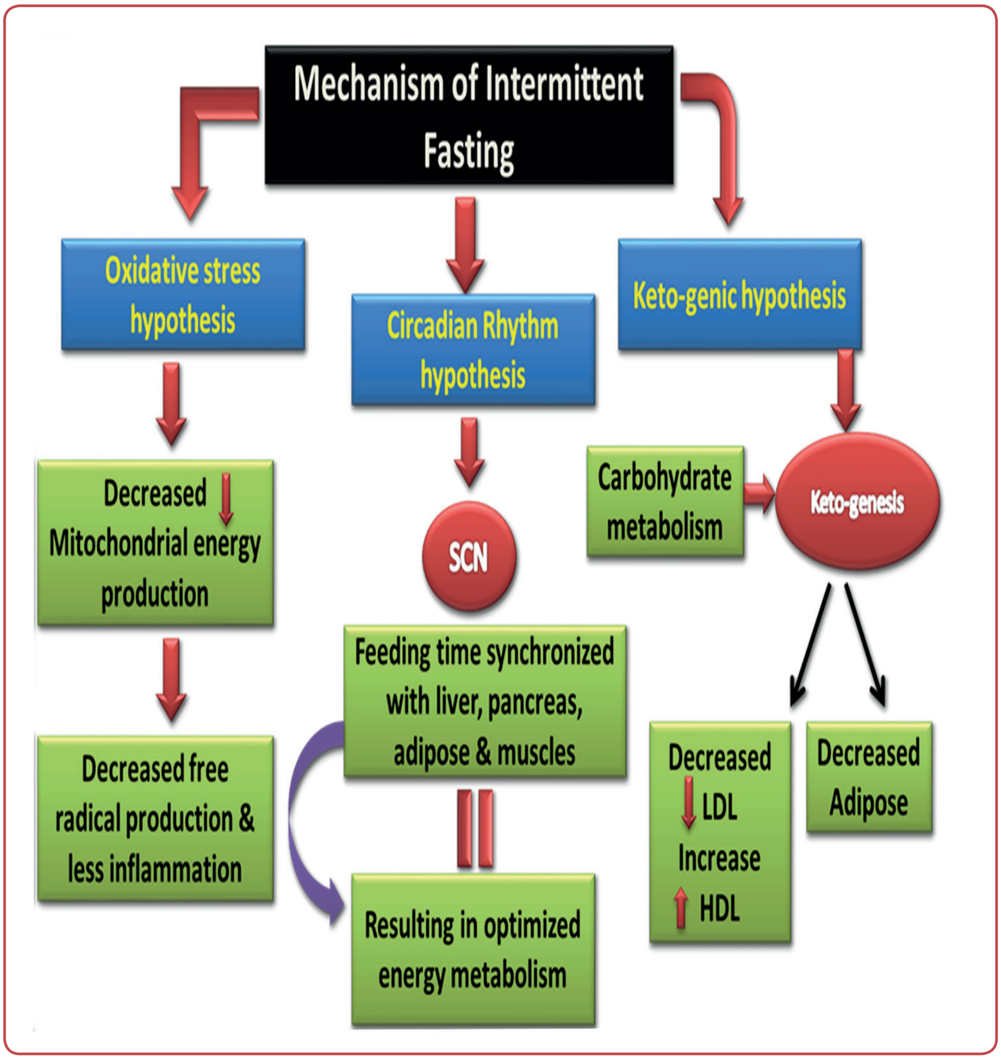

Figure 6: ***Mechanism of intermittent fasting:*** *1-The oxidative stress hypothesis postulates that fasting reduces stress leading to fewer free radicals with less mitochondrial energy production ultimately lowering the body's oxidative stress. 2- The circadian rhythm component focuses on syncing eating periods to the organ's circadian rhythm, optimising glucose and fat utilisation. 3- Ketogenic state, recognises that intermittent fasting induces ketogenesis, which decreases blood pressure and adipose tissue.*

logical timing to enhance cellular repair and cardiovascular function.[51]

There are several theories for how intermittent fasting could lead to better cardiovascular outcomes; the three main theories are discussed here: the oxidative stress hypothesis, circadian rhythm and ketogenic state. The oxidative stress hypothesis postulates that fasting reduces stress, leading to fewer free radicals with less mitochondrial energy production, ultimately lowering the body's oxidative stress.[54] The circadian rhythm component focuses on syncing eating periods to the organ's circadian rhythm, optimising glucose and fat utilisation.[55] The third mechanism, ketogenic state, recognises that intermittent fasting induces ketogenesis, which decreases blood pressure and adipose tissue. Specifically, intermittent fasting forces the body to rely on a fatty acid diet, derived from adipose tissue breakdown, instead of on a rich diet, which is particularly reintroduced only during the eating periods. In support of this, higher circulating levels of the ketone body β-hydroxybutyrate and polyunsaturated free fatty acids have been brought into the studies. Such metabolic shifts occur periodically during intermittent fasting, thus improving cellular metabolic flexibility and bioenergetic efficiency. Indeed, an elevated ketogenesis through ketogenic diet (ie, without fasting) is suggested to exert a cardioprotective role, at least in animals, by improving cardiac energetics and activating survival signalling pathways that promote health and prolong lifespan[56] (Figure 6).

Fatima et al. Scr Med. 2025 Jul-Aug;56(4):743-63.

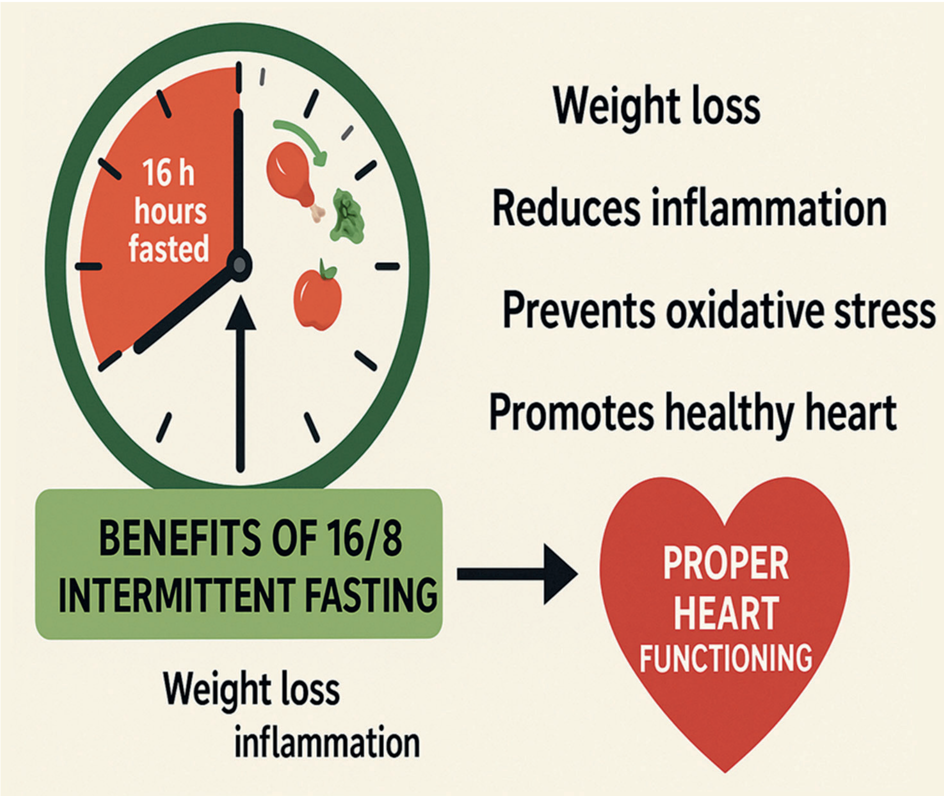

Figure 7: ***Benefits of intermittent fasting leading to proper heart functioning:*** *Intermittent fasting enhances weight loss, reduces inflammation, prevent oxidative stress promoting healthy heart*

Several studies suggest that intermittent fasting may contribute to improved metabolic health and weight management.[54-56] Positive effects on insulin sensitivity, blood glucose levels and lipid profiles have been reported, all of which are relevant to cardiovascular risk factors. Intermittent fasting induces metabolic adaptations, including changes in insulin sensitivity, lipid metabolism and autophagy.[43] Understanding these adaptations is crucial for deciphering the potential cardiovascular benefits of intermittent fasting. Chronic inflammation and oxidative stress are implicated in cardiovascular diseases. Intermittent fasting has been suggested to reduce inflammatory markers and oxidative stress.[54] Intermittent fasting may influence lipid metabolism, leading to favourable changes in cholesterol levels and triglycerides. These lipid profile improvements are associated with a lower risk of atherosclerosis and coronary artery disease.[57] Limited studies suggest that intermittent fasting may have a positive impact on blood pressure regulation.[52, 57] Reductions in blood pressure are crucial for preventing hypertension, a major cardiovascular risk factor. Some research indicates that intermittent fasting may enhance endothelial function, which is essential for maintaining healthy blood vessels. Improved endothelial function contributes to better cardiovascular health by promoting proper blood flow and preventing atherosclerosis[52] (Figure 7). Long-term studies are needed to better understand the sustained cardiovascular benefits of intermittent fasting. It's essential to acknowledge the variability in individual responses to intermittent fasting. Intermittent fasting holds promise as a dietary strategy with potential cardiovascular benefits. Factors such as adherence, overall diet quality and individual health conditions can influence outcomes.

Circadian disruption and cardiovascular risks

The link between circadian disruption and cardiovascular risk involves complex interactions among molecular mechanisms, epidemiological patterns and potential therapeutic strategies. The circadian system governed by the master clock in the suprachiasmatic nucleus of the brain regulates critical physiological processes such as the sleep-wake cycle, hormone secretion and metabolic function. Disruption of this finely tuned system, due to factors like irregular sleep patterns, shift work, or misaligned dietary habits, has been implicated in the development of cardiovascular diseases.[58] Chronic circadian misalignment can lead to metabolic disturbances, insulin resistance, systemic inflammation and endothelial dysfunction, all of which contribute to cardiovascular pathology. Epidemiological studies further support a heightened incidence of adverse cardiovascular events during the early morning hours (6:00 AM to 12:00 PM), a period considered particularly vulnerable due to circadian-driven fluctuations in blood pressure, heart rate and coagulation activity.[59]

At the molecular level, circadian rhythms are governed by a series of clock genes and their protein products. Disruptions in these molecular oscillations, often induced by irregular sleep patterns, shift work, or artificial light exposure during the night, can perturb the finely tuned balance and contribute to cardiovascular dysfunction. Numerous studies have highlighted the association between circadian disruption and an increased risk of cardiovascular diseases. Epidemiologic studies report a morning peak in adverse cardiovascular events.[58-60] While both intermittent fasting and caloric restriction may reduce caloric intake, they operate via different mechanisms. Caloric restriction focuses on reducing the total quantity of food consumed, whereas circadian-aligned meal timing emphasises when food is consumed to align with the body's biological clock without necessarily altering calorie count.[61]

Circadian disruption profoundly influences blood pressure regulation. The circadian rhythm tightly regulates blood pressure, characterised by a predictable pattern of fluctuations throughout the day and night. Circadian clocks are present not only in the central pacemaker (the suprachiasmatic nucleus) but also in peripheral tissues, including the vasculature and kidneys. These clocks coordinate to modulate blood pressure and maintain cardiovascular homeostasis. The nocturnal dip in blood pressure, a protective mechanism against cardiovascular events, is often blunted in individuals with irregular sleep patterns, contributing to sustained hypertension and increased cardiovascular risks.[60] External factors, such as shift work, irregular sleep patterns and lifestyle choices, can disrupt circadian rhythms. Circadian disruption influences blood pressure, including alterations in sympathetic nervous system activity, hormonal fluctuations and endothelial dysfunction. Epidemiological studies have consistently demonstrated associations between circadian disruption and an increased risk of hypertension.[62] Evidence links shift work, irregular sleep and circadian misalignment to elevated blood pressure and the development of hypertension.[61] Circadian disruption may impair endothelial function, a critical determinant of blood pressure regulation and its often associated with a blunted or altered nocturnal dip in blood pressure, a phenomenon linked to adverse cardiovascular outcomes.[58]

Circadian disruption, characterised by disturbances in the natural sleep-wake cycle, has been linked to chronic inflammation, a key factor in the development and progression of cardiovascular diseases. Circadian rhythms govern various physiological processes, including the immune system and inflammatory responses.[63] The circadian clock tightly regulates immune responses, impacting the rhythmic expression of pro-inflammatory and anti-inflammatory mediators. Circadian disruption, often induced by irregular sleep patterns and shift work, is associated with alterations in inflammatory markers. The evidence linking circadian disruption to changes in cytokines, acute-phase reactants and other inflammatory molecules implicated in cardiovascular diseases. Circadian disruption may foster endothelial inflammation, impair vascular function and contribute to atherosclerosis. Inflammatory processes contribute to endothelial dysfunction, a critical event in the pathogenesis of cardiovascular diseases.[64]

Elevated levels of inflammatory markers contribute to endothelial dysfunction and plaque formation, critical elements in the progression of cardiovascular diseases.[64] Oxidative stress and inflammation are interconnected processes in cardiovascular diseases. Circadian disruption may contribute to a pro-oxidative and pro-inflammatory environment, amplifying the cross-talk between these pathways. Shift work-induced circadian disruption may contribute to chronic low-grade inflammation and cardiovascular risks.[8] Shift work, a common cause of circadian disruption, has been linked to an imbalance in inflammatory responses. Chrono-modulation strategies, such as timing interventions based

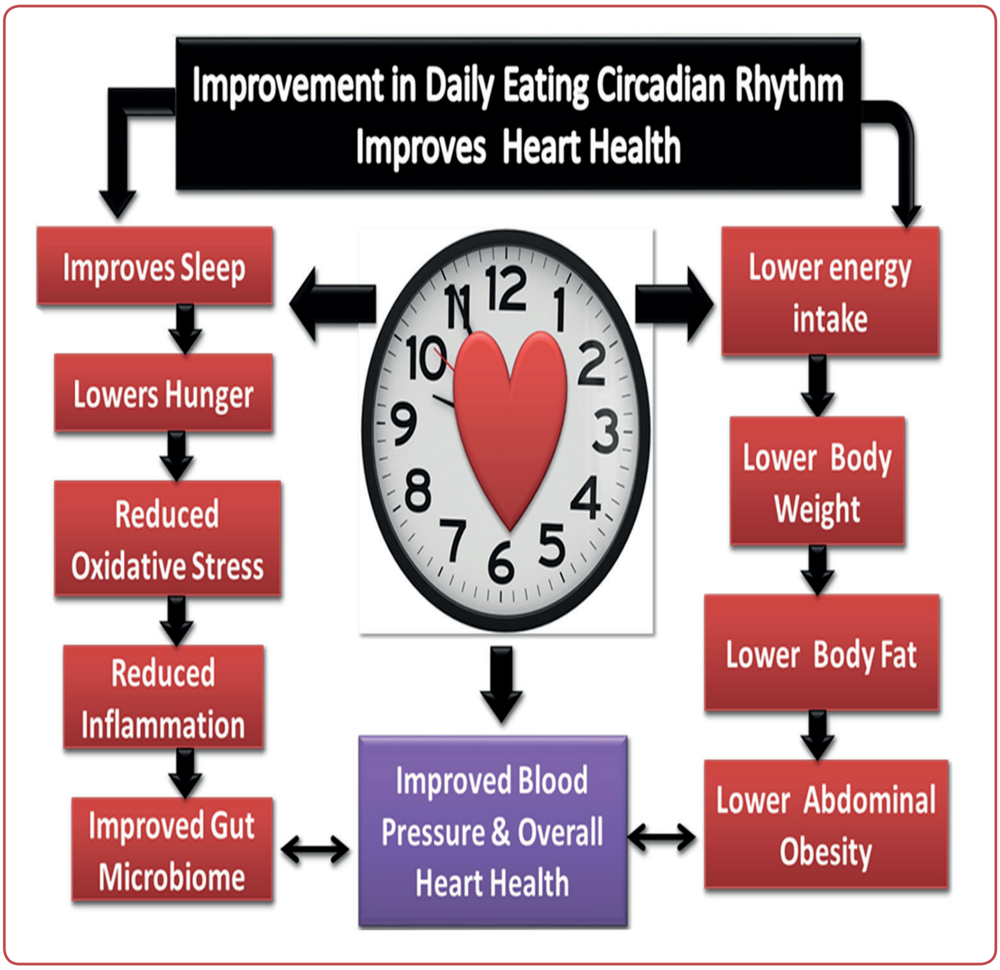

Figure 8: ***Circadian daily eating rhythm improves heart functioning:*** *Improved and time restricted feeding improves sleep, hunger, reduces oxidative stress and improves gut microbiome leading to improved cardiovascular functioning*

on circadian rhythms, have shown promise in modulating inflammatory responses. Circadian disruption, arising from factors such as irregular sleep patterns and shift work, has been implicated in adverse cardiovascular outcomes. Circadian disruption can activate the sympathetic nervous system, influencing cardiovascular parameters. Melatonin, a hormone regulated by the circadian clock, possesses cardiovascular protective properties.[7] The role of melatonin in mitigating the adverse effects of circadian disruption on cardiovascular health and potential therapeutic applications is very pertinent. Chrono-therapeutic interventions involve aligning therapeutic strategies with circadian rhythms. The potential benefits of chrono-therapeutic approaches in managing circadian disruption-associated cardiovascular risks emphasise the importance of timing in the treatment of CVD.[7] Strategies such as optimising sleep hygiene, implementing chronotherapy and developing pharmaceutical agents targeting circadian pathways are under investigation as potential approaches to mitigate cardiovascular risks associated with circadian disruption.[65] Circadian daily eating rhythm improves heart functioning: Improved rhythm and time-restricted feeding improve sleep, hunger, reduce oxidative stress and improve gut microbiome, leading to improved cardiovascular functioning (Figure 8).

Chronobiotic nutrients and dietary timing

Beyond the basic components of diet such as macronutrients and meal timing, emerging evidence has identified specific foods and bioactive compounds such as coffee, melatonin-rich foods and polyphenols as chronobiotics. These are agents capable of modulating the timing (phase) and strength (amplitude) of circadian rhythms. When consumed in accordance with the body's internal biological clock, these substances can positively influence cardiometabolic health. A well-studied example is coffee, which not only functions as a central nervous system stimulant but also exhibits chronobiotic properties. Its key active ingredients, including caffeine and chlorogenic acids, have been shown to affect vital metabolic and hormonal processes, such as cortisol release, insulin sensitivity and lipid metabolism. Supporting this, a large-scale cohort study published in the *European Heart Journal* found that individuals who consumed coffee before 9 am had a lower risk of mortality from all causes, including cardiovascular disease and cancer, compared to those who consumed it later in the day. These health benefits are thought to be linked to coffee's interaction with circadian-regulated processes, including hepatic glucose production and sympathetic nervous system activity.[66]

Additionally, certain chrono-nutrients such as omega-3 fatty acids, vitamin B6, tryptophan and various flavonoids are known to influence the expression of circadian genes and the synthesis of melatonin, a hormone critical for sleep-wake regulation. Foods naturally high in melatonin or its precursors, including oats, bananas, cherries and walnuts, may promote better circadian alignment, particularly when ingested during the evening hours. This dietary approach could provide a cost-effective strategy for enhancing circadian rhythm stability in individuals affected by circadian misalignment, such as shift workers or those experiencing social jet lag. Collectively, these insights support the concept of chronotherapy through diet, where the timing of nutrient intake is strategically planned to synchronise with biological rhythms. Personalised nutritional interventions of this kind may significantly enhance the effectiveness of chrono-nutritional strategies and warrant further investigation in future clinical research.

Future directions

Future investigations should aim to clarify the intricate biological pathways through which circadian disruption contributes to the development of cardiovascular diseases. Advancing this understanding will require robust methodologies, including longitudinal cohort studies, randomised controlled trials and translational research that assess the impact of targeted circadian-based interventions. Among these, intermittent fasting has emerged as a promising approach, demonstrating beneficial effects on cardiovascular risk factors such as obesity, hypertension, dyslipidaemia and diabetes. However, the underlying mechanisms driving these improvements remain incompletely understood. Circadian misalignment primarily resulting from modern lifestyle behaviours, has become an increasingly recognised but modifiable determinant of cardiovascular risk. Acknowledging the multifaceted nature of this relationship creates new opportunities for innovative preventive and therapeutic strategies. Notably, aligning nutritional intake with the body's internal circadian rhythms offers substantial potential for intervention. Future research should focus on identifying the most effective meal timing patterns tailored to diverse populations. High-quality randomised trials and long-duration studies will be vital in confirming causal relationships and shaping practical, evidence-based dietary guidelines. Ultimately, a deeper understanding of how meal timing interacts with circadian and metabolic processes could lead to more precise and impactful strategies for promoting cardiovascular health.

Conclusion

This review consolidates a significant body of evidence linking late-night eating and breakfast omission with metabolic imbalances and increased cardiovascular risk. It underscores the role of circadian-aligned meal timing in promoting cardiovascular health. Approaches such as time-restricted feeding and chrono-nutrition are highlighted as effective, non-pharmacological strategies that harness circadian biology to enhance both metabolic and cardiovascular outcomes. By incorporating emerging insights into melatonin regulation, clock gene activity and individual chronotypes, this review offers a personalised perspective on dietary timing interventions. Nonetheless, further randomised controlled trials and long-term observational studies are necessary to validate these associations and refine clinical guidelines for circadian-based nutritional therapies.

Despite the growing body of evidence linking circadian-aligned eating patterns to improved cardiometabolic outcomes, formal dietary guidelines on meal timing remain limited. The American Heart Association, in its 2017 scientific statement, highlighted the potential benefits of regular meal timing and frequency for cardiovascular health, emphasising the importance of consuming breakfast and avoiding late-night eating. However, no global or universally adopted guidelines currently exist that specifically address optimal meal timing as part of cardiovascular disease prevention. Given the emerging evidence from clinical trials and observational studies, there is a critical need for comprehensive, evidence-based guidelines from health authorities to integrate chrono-nutrition principles into public health recommendations and clinical practice.

Ethics

This study was a secondary analysis based on the currently existing data and did not directly involve with human participants or experimental animals. Therefore, the ethics approval was not required in this paper.

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Conflicts of interest

The authors declare that there is no conflict of interest.

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Data access

The data that support the findings of this study are available from the corresponding author upon reasonable individual request.

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