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CARDIOVASCULAR DISEASE (JHY WU, SECTION EDITOR)

Cardiorenal Metabolic Consequences of Nighttime Snacking: Is it an Innocent Eating Behavior?

Mehmet Kanbay[1] · Sidar Copur[2] · Atalay Demiray[2] · Kathherine R. Tuttler[3,4]

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Abstract

Purpose of Review Health consequences of nighttime eating, as a publicly discussed eating behavior type, have been speculated lately. Nighttime eating has been linked to various metabolic outcomes including hyperlipidemia, hypertriglyceridemia, hyperglycemia, weight gain, elevated blood pressure, obesity, and metabolic syndrome, and cardiorenal outcomes such as atherosclerosis, a decline in eGFR, and proteinuria.

Recent Findings Although the exact underlying pathophysiological mechanism is not yet clear, multiple hypotheses including disrupted circadian rhythm, altered hormonal levels, and decline in cellular regeneration have been proposed.

Summary In this review, we aim to evaluate the growing literature on nighttime eating behavior in terms of metabolic and cardiorenal outcomes, pathophysiological basis, and potential therapeutic alternatives.

Keywords Nighttime snacking · Metabolic syndrome · Hypertension · Inflammation · Proteinuria · Obesity

Introduction

Metabolic syndrome and obesity have increasingly become major public health concerns in the last few decades as the global prevalence of metabolic syndrome is over 20% while the global prevalence of obesity is over 15% [1–4]. Eating behaviors including nighttime eating and skipping breakfast are important determinants of obesity in addition to energy expenditure, genetic factors, dietary intake, and caloric intake [5]. Although nighttime eating behavior has not been strictly defined, it is considered as high caloric intake later at night which is relative to the sleeping pattern of an individual [6]. On the other hand, night eating syndrome (NES) is characterized by daytime anorexia, evening hyperphagia defined as consumption of more than 25% of daily caloric intake after evening meal including nighttime awakening for food intake, and insomnia [7, 8]. The prevalence of NES is between 6 and 16% in obese individuals which is considerably higher compared to the general population with a prevalence of 1.5% [9–11]. Patients with NES are prone to develop metabolic syndrome, abdominal obesity, dyslipidemia, hyperglycemia, diabetes mellitus, hypertension, and psychiatric disorders such as binge eating disorder and sleeping disorders [12–15]. Higher energy intake before sleep is linked to higher weight gain and obesity even in individuals without NES and associated with increased frequency of skipping breakfast; nevertheless, studies in this field are limited in terms of number and detailed analysis for the comparison of various eating patterns regarding the timing and content of the meals [16–19]. Even though exact reasoning is not clear, possible explanations include altered circadian rhythm affecting hormonal balances, lower serum levels of leptin, higher total daily caloric intake, and lower rates of energy expenditure at night due to less physical activity [16, 20, 21]. In this review, we aim to discuss the health consequences of high caloric intake in the late evening including metabolic parameters, cardiovascular and endocrinological outcomes, and renal function.

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✉ Mehmet Kanbay
mkanbay@ku.edu.tr

[1] Department of Medicine, Division of Nephrology, Koc University School of Medicine, 34010 Istanbul, Turkey

[2] Department of Medicine, Koc University School of Medicine, Istanbul, Turkey

[3] Division of Nephrology, University of Washington, Seattle, WA, USA

[4] Providence Medical Research Center, Providence Health Care, Spokane, WA, USA

Hypothetical Framework

Almost all physiological and metabolic events that occur in humans, as well as many other species, are under the direct control of circadian rhythm, approximately a 24-h cycle, which is genetically pre-determined and under the influence of environmental factors such as sunlight, food, temperature, and neuro-endocrinological determinants [22]. Metabolic consequences of nighttime eating may be attributable to its effect on the biological clock. The primary physiological center for circadian rhythm is located at the suprachiasmatic nucleus of the hypothalamus which produces endogenous rhythmic oscillations with certain neurotransmitters, mainly vasoactive intestinal peptide (VIP) and arginine vasopressin (AVP) to control daily physiological activities [23]. Feeding has a direct effect on circadian rhythm through various mechanisms. First, elevated serum levels of glucose downregulate certain transcription factors, namely Period-1 (PER1) and Period-2 (PER2), in mesenchymal cells and regulate the expression of adenosine monophosphate–activated protein kinase (AMPK) [24]. Secondly, hyperinsulinemia and decreased peripheral insulin sensitivity lead to alteration of periodicity at insulin-sensitive tissues such as skeletal muscles, adipose tissue, and liver. Additionally, an imbalance between anabolic-to-catabolic reactions at the cellular level in response to insulin leads to alteration of the cellular redox state which is important in the interaction among the downstream signaling molecules of circadian rhythm signal such as the interaction between CLOCK/BMAL1 or NPAS2/BMAL1 dimers and DNA [25, 26]. Lastly, the suprachiasmatic nucleus has receptors for certain hormones and cytokines such as leptin, ghrelin, orexin, and insulin, all of which undergo changes in serum levels in response to food intake [26–28]. Notably, mice that are fed outside of their biological clock for eating gain more weight; studies in humans are contradictory [29–33].

Another crucial aspect of nighttime eating is its effects on levels of hormones and physiological responses at certain endocrine organs. Disruption of circadian rhythm following nighttime high caloric intake leads to nocturnal decline in serum leptin, ghrelin, melatonin, and cortisol levels [34–36]. Nocturnal corticotropin-releasing hormone (CRH)–induced stimulated secretion of adrenocorticotropic hormone (ACTH) and cortisol results in disruption of the hypothalamic–pituitary–adrenal axis manifested by the dampened effect of CRH or ACTH to stimulate cortisol secretion by the adrenal gland [37, 38]. A decline in melatonin and leptin in individuals with such eating behavior may be attributable to elevated CRH levels which are known to suppress the secretion of melatonin while reduced levels of leptin remove suppressive effects on CRH secretion [39–41]. A decline in nocturnal melatonin further disrupts the circadian rhythm and delays sleep cycle initiation [42]. Postprandial hyperglycemia is involved in the over-secretion of insulin and the development of reduced peripheral insulin sensitivity which may cause dysregulation of anabolic-to-catabolic reactions, impairment of cellular regeneration, disruption of protein synthesis, and DNA repair [43, 44]. Cells are more prone to develop mutations and DNA damage under the hyperglycemic environment in addition to poor DNA repair response [45–47].

Metabolic Consequences of Nighttime Eating

Multiple cross-sectional studies demonstrate significant associations between obesity and nighttime eating or NES; however, longitudinal and interventional studies in this field are limited. In a study conducted with 60,800 Japanese subjects with self-reported eating behavior, higher rates of metabolic syndrome and obesity have been observed in individuals who demonstrate the eating behavior consisted of nighttime eating and skipping breakfast but not in either group alone [48]. On the other hand, a study investigating nighttime eating behavior conducted with The Danish MONICA cohort composed of 2987 subjects with 5-year follow-up demonstrated statistically significant weight gain in obese females [49]. Additionally, obesity and metabolic syndrome were more commonly observed in nighttime workers [50]. Multiple other studies reported considerable associations between such eating behavior and weight gain while skipping breakfast and nighttime eating behaviors are interrelated and in most cases co-exist [51–57]. High nighttime caloric intake may inhibit morning eating behavior while poor early caloric intake may promote higher nighttime eating behavior, thus, creating a vicious cycle (Fig. 1).

Components of metabolic syndrome include abdominal waist circumference over 88 cm in females and 102 cm in males, hyperglycemia, hyperlipidemia, high blood pressure, and low serum high-density lipoprotein (HDL) level. Nighttime eating without breakfast skipping behavior has been linked to hyperglycemia in another cross-sectional study conducted with 61,364 healthy Japanese middle-aged adults [58]. Such eating behavior has an acute effect on diurnal blood glucose variation including elevation in postprandial hyperglycemia and average daily blood glucose level [59]. In addition to hyperglycemia, nighttime eating behavior is associated with hypertriglyceridemia in both genders in a large-scale study conducted with 8153 middle-aged adults [60]. Daily intake of 200-kcal snack at nighttime is associated with higher serum levels of low-density lipoprotein (LDL) compared to daytime intake of 200-kcal snack after

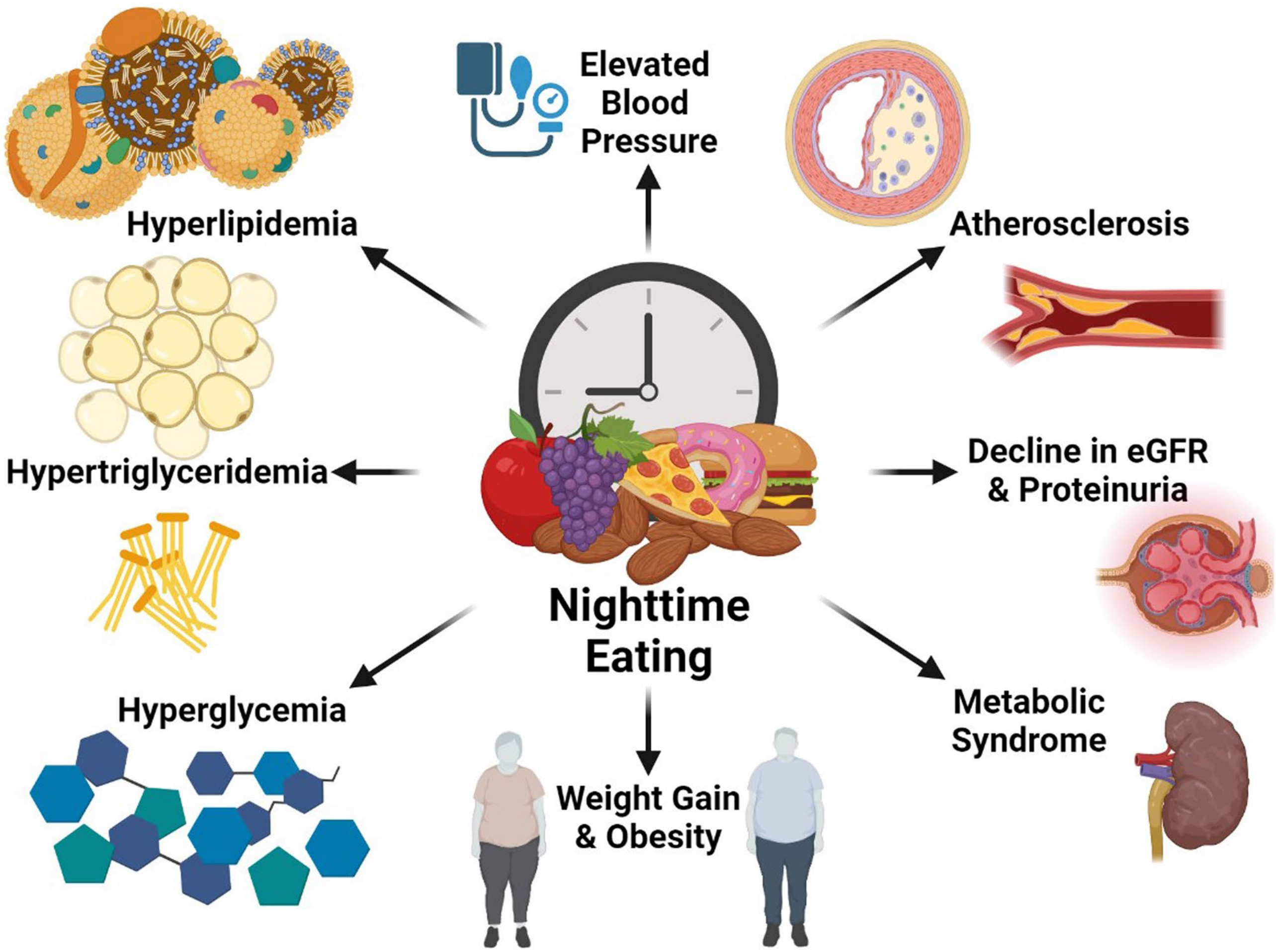

Fig. 1 The possible relationships between negative health outcomes and nighttime eating

two weeks in a randomized cross-over study which may be due to a decline in fatty acid oxidation at night [61]. Furthermore, a link between nighttime eating behavior and hypertension or atherosclerosis has been observed in multiple large-scale studies (Fig. 1) [60, 62]. However, it is important to emphasize that nighttime eaters consumed higher daily calories (mean = 4758; 95% CI = 4409–5107) compared to non-nighttime eaters (mean = 4244; 95% CI = 3971–4517) in a statistically significant manner (p value = 0.01) [16].

Although the exact underlying mechanism underlying weight gain observed in individuals with such eating behavior is not clear, various hypotheses have been proposed. First, it has been hypothesized that nighttime eaters (NEs) ingest higher daily calories compared to non-NEs which has been validated in a study conducted with 154 subjects in which no statistically significant difference in terms of baseline body mass index or body fat percentage is present, whereas, no difference in the distribution of macronutrients such as carbohydrates, proteins, or fat has been detected [16]. Second, altered eating behaviors lead to endocrinological and circadian changes in individuals altering energy expenditure, thermogenesis, and anabolic and catabolic biochemical processes. Postprandial hyperglycemia observed after nighttime snack leads to an elevation in insulin secretion and decrease in peripheral insulin sensitivity which causes a decline in the activation of lipoprotein lipase, an enzyme involved in the degradation and metabolism of lipoproteins and chylomicrons, and thus elevation of serum triglyceride levels [63, 64]. Also, secretion of certain hormones such as resistin and tumor necrosis factor-α from adipocytes or decline in the secretion of adiponectin plays a crucial role in the metabolic dysfunction [65]. Lastly, nighttime energy expenditure is considerably lower compared to daytime energy expenditure. Higher serum levels of ghrelin and lower levels of leptin observed in NEs may explain the disrupted balance between energy expenditure and intake (Fig. 2) [34, 36].

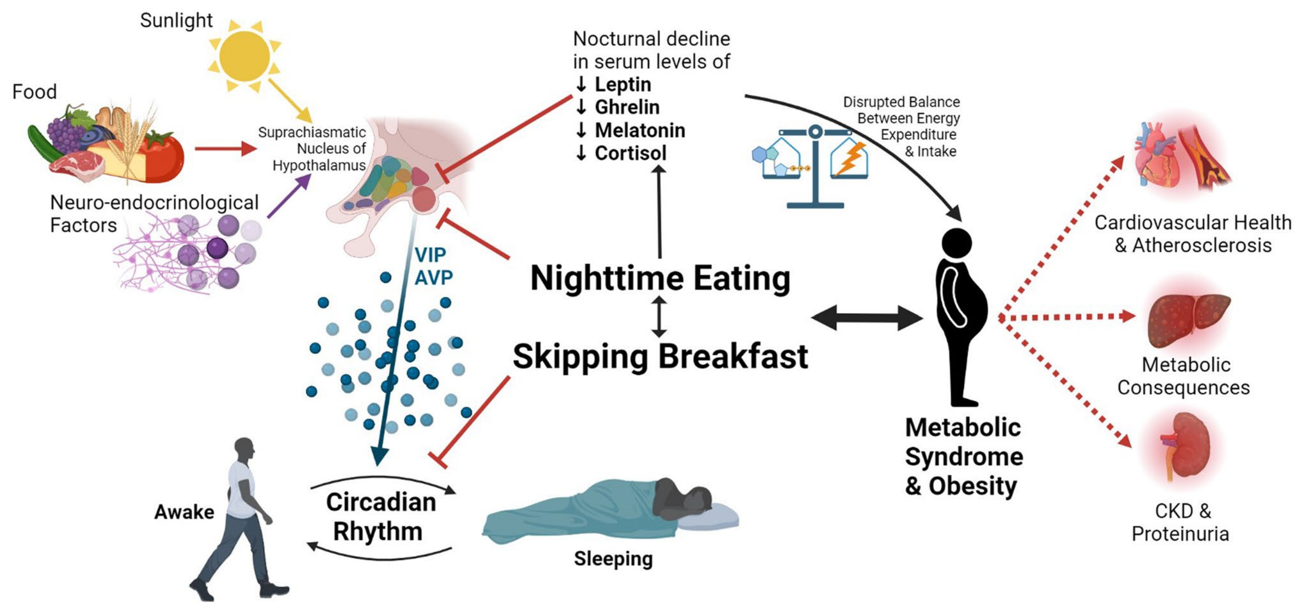

Fig. 2 The disrupted circadian rhythm due to nighttime eating and skipping breakfast and its relations with metabolic syndrome and obesity. VIP, vasoactive intestinal peptide; AVP, arginine vasopressin; CKD, chronic kidney disease

Nighttime Eating and Cardiorenal Outcomes

Effect of dietary intake of macronutrients and percentage of macronutrients in daily diet, as well as dietary frequency, have long been investigated for their cardiovascular effects. Studies have indicated small high-frequency meals are associated with improved cardiovascular health in most cases [66–68]; nevertheless, only a few studies have investigated the effect of nighttime eating on cardiovascular health [54, 68]. Metabolic consequences of nighttime eating include elevation of serum LDL and triglyceride levels, hyperglycemia, and blood pressure, all of which increase the risk of adverse cardiovascular outcomes in NEs compared to non-NEs. However, the limited number of studies in this field revealed variable findings. Poor cardiovascular health scores have been reported in NEs in a cross-sectional study conducted with the Kardiovize Brno 2030 cohort including 1659 subjects and in another study conducted with 26,902 subjects with a 16-year follow-up period while contradictory findings are observed in a national survey study [69–71]. Furthermore, a few studies reported neither a positive nor negative relationship between cardiovascular health and nighttime eating [17, 72]. The absence of that expected association may be attributable to the short duration of follow-up in most studies for the development of cardiovascular outcomes, self-reported eating behaviors, and the absence of long-term interventional studies. Poor cardiovascular consequences associated with nighttime eating behavior are more evident in terms of high blood pressure and atherosclerosis (Fig. 2) [17, 62, 73].

Similar to expected cardiovascular outcomes in NEs, a decline in kidney function may occur in those individuals due to effects of hyperglycemia and a decrease in insulin sensitivity, hypertension, and ischemia caused by atherosclerosis of the renal vasculature. Additionally, higher incidences of proteinuria and chronic kidney disease are reported in obese individuals [74]. Higher rates of chronic kidney disease have been detected in individuals with eating behavior including nighttime eating or bedtime snacking in a study conducted with 316 male subjects in addition to higher rates of proteinuria detected on the dipstick in another study conducted with 60,800 Japanese adults [48, 75]. Furthermore, disruption of the circadian rhythm leads to higher plasma glucose levels with upregulated gluconeogenesis in the kidneys of diabetic mice.

Future Directions

Many of the metabolic and cardiovascular consequences of nighttime caloric intake have been identified in recent years, whereas, studies investigating therapeutic alternatives to reverse such conditions are limited. A nighttime eating syndrome is a psychiatric condition with relation to other sleep and mood disorders; thus, pharmacotherapeutic alternatives include selective serotonin reuptake inhibitors such as escitalopram (clinical trial ID: NCT00636649 and NCT01401595) and melatonin (clinical trial ID: NCT02500017) or cognitive behavioral therapy (clinical trial ID: NCT03094000). On the other hand, no therapeutic

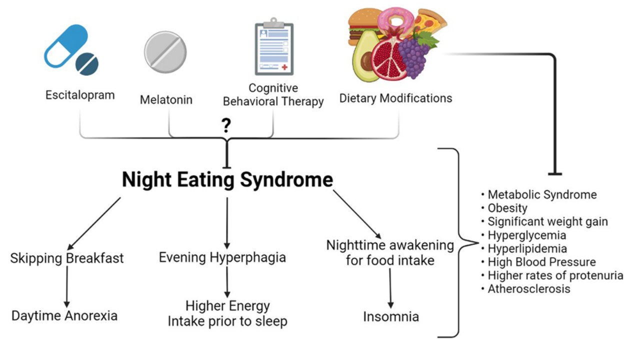

Fig. 3 The possible treatment options for night eating syndrome

alternative has yet been investigated for nighttime eaters rather than NE while a single clinical trial (clinical trial ID: NCT04182867) aims to explore the effect of dietary modifications on cardiometabolic outcomes in nighttime workers. Additionally, another clinical trial (clinical trial ID: NCT03803345) aims to detect the metabolic effects, primarily glucose tolerance, of nighttime eating in pregnant females (Fig. 3). Future studies conducted with a higher number of participants and longer follow-up periods are needed to expand the knowledge and understanding of this topic. Studies investigating the cardiometabolic consequences of such eating behaviors should also analyze the nutritional content of the food consumed at that time of a day and assess how much of the effect is attributable to the timing of the meal rather than the nutritional content. Furthermore, studies including the comparative analysis of different time periods with regard to sleeping time should be performed to assess and determine the safer and healthier meal periods for the patients and the general population.

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Compliance with Ethical Standards

Conflict of Interest Authors declare that they have no conflict of interest.

Human and Animal Rights and Informed Consent This article does not contain any studies with human or animal subjects performed by any of the authors.

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