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Review Article / Derleme

The influence of meal frequency and timing on cardiometabolic health

Öğün sıklığı ve öğün zamanlamasının kardiyometabolik sağlık üzerindeki etkisi

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ABSTRACT

Metabolic syndrome is a disease with increasing incidence, affecting large numbers of people worldwide and increasing mortality rates. Increased body weight is a major risk factor for the disease. Patients with metabolic syndrome are at increased risk of obesity-related diseases such as cardiovascular disease and type 2 diabetes. Medical nutrition therapy, which is an important part of the treatment of the disease, reaches a sustainable treatment format if it is planned by considering the medical and social status of the individual. Evidence-based medical nutrition therapy should also be shaped according to personal characteristics such as socioeconomic status, physical activity and eating habits. Nutritional habits not only vary from person to person but have also changed from past to present. In the accelerating world, living conditions have moved away from the traditional meal pattern, and meal times and numbers have changed. In order to provide sustainable and evidence-based medical nutrition therapies suitable for individuals' current living conditions, it has become necessary to know the health effects of new eating habits such as skipping meals, meal timing and hunger. In this review, the effects of new eating habits such as meal frequency, meal timing (eating in mornings, eating at nights, eating at irregular meals) and skipping meals on the emergence and pathogenesis of metabolic syndrome and its components were examined

ÖZ

Metabolik sendrom dünya çapında çok sayıda insanı etkileyen, görülme sıklığı ve ölüm oranları artan bir hastalıktır. Artmış vücut ağırlığı, hastalık için önemli bir risk faktörüdür. Metabolik sendromlu hastalar, kardiyovasküler hastalık ve tip 2 diyabet gibi obezite ile ilişkili hastalıklara yakalanma açısından artmış risk altındadır. Hastalığın tedavisinin önemli bir parçası olan tıbbi beslenme tedavisi, bireyin tıbbi ve sosyal durumu göz önünde bulundurularak planlandığında sürdürülebilir bir tedavi formatına ulaşmaktadır. Kanıta dayalı tıbbi beslenme tedavisi, sosyoekonomik durum, fiziksel aktivite ve beslenme alışkanlıkları gibi kişisel özelliklere göre de şekillendirilmelidir. Beslenme alışkanlıkları sadece kişiden kişiye değişmekle kalmayıp geçmişten günümüze de değişmiştir. Hızlanan dünyada yaşam koşulları geleneksel yemek düzeninden uzaklaşmış, yemek saatleri ve sayıları değişmiştir. Bireylerin mevcut yaşam koşullarına uygun, sürdürülebilir ve kanıta dayalı tıbbi beslenme tedavileri sunabilmek için öğün atlama, öğün zamanlaması ve açlık gibi yeni beslenme alışkanlıklarının sağlık üzerindeki etkilerinin bilinmesi gerekli hale gelmiştir. Bu derlemede, öğün sıklığı, öğün zamanlaması (sabah yeme, akşam yeme, düzensiz öğünlerde yeme) ve öğün atlama gibi yeni beslenme alışkanlıklarının metabolik sendrom ve bileşenlerinin ortaya çıkışı ve patogenezi üzerine etkileri incelenmiştir.

INTRODUCTION

Nutrition is not only an act of taking nutrients to sustain life. Individuals also use nutrition as a tool at various points in life. For example, eating at a gathering of friends to socialize, due to religious beliefs, and differentiating the number and content of meals according to working conditions are also part of the diet. Nutrition, which starts from the first moment of life, gains various characteristics according to the environment in which the individual is born and raised. Individual eating habits take shape over time. It is important that these habits are shaped correctly over time because studies show that eating habits can be as important as the health effects of nutrients and that unhealthy diet is one of the biggest risk factors for obesity, cardiovascular disease and death (Rodríguez-Monforte et al., 2017; Yusuf et al., 2014). Many factors such as the types and portions of food consumed, how food is cooked, when and how often meals are eaten, and even how they are eaten constitute individuals' dietary behaviors. Attitudes such as skipping breakfast, irregular meal times, eating only one or two meals a day, eating at night and eating small but frequent meals are eating habits related to meal timing and frequency. Each of these eating habits has a different

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effect on metabolism, but they are often confused with each other. For example, although skipping breakfast or eating breakfast late in the day have different health effects, a late breakfast can be interpreted as lunch, leading to a confusion of meaning. This situation requires scientists to make their interpretations in this context. The results of delaying the time of meals, skipping meals altogether or eating at different times each day which fall under the concept of meal timing and frequency, have not been clearly compiled. In the concept of meal, which is an important variable of eating habits, which occupies a large place in the emergence of metabolic syndrome and metabolic syndrome-related conditions; although it is important to focus on the nutrients consumed in the meal as well as when and how often they are consumed, with the idea that there is not enough information on this subject in the literature, this review, meal frequency, meal timing (eating in mornings, eating at nights, eating at irregular meals) and skipping meals aims to explicitly assess the evidence on the effects of eating habits on cardiometabolic health.

Meal Frequency

A well-defined concept of a meal can significantly influence the results of meal frequency. To date, various methods have been used to define an eating event or eating activity. Castro et al. defined the concept of a meal as an eating event that provides at least 210 kj of energy, with a minimum of 15 minutes between two consecutive eating events (De Castro, 1993). Meal frequency was historically based on the coena, which was the only main meal that took place around 16:00 in Ancient Rome, and the two accompanying snacks, ientaculum in the morning and prandium at night (Flandrin, 2003). Over time, the usual meal pattern became breakfast, lunch and dinner. Breakfast was the meal before going to work or to the club, while dinner was the last main meal before dark before artificial lighting. In recent years, dietitians have introduced the concept of snacks with the aim of regulating appetite. Many studies have been conducted with the idea that the frequency of main and intermediate meals may be related to the incidence and prognosis of various chronic diseases.

In the literature examining the effect of meal frequency on body weight and cardiometabolic health, increased meal frequency was associated with lower body weight (Howarth et al., 2007; Murakami & Livingstone, 2015) and better cardiometabolic profile (Ha & Song, 2019). Smith et al. also found that increased meal frequency in men was associated with decreased waist circumference, fasting blood glucose, fasting insulin, total cholesterol, triglyceride (TG) and low density lipoprotein cholesterol (LDL-C) levels among cardiometabolic risk factors (Smith et al., 2012). Another study found that increased meal frequency was associated with a lower prevalence of metabolic syndrome in men, but not in women (Jung et al., 2017).

In the US National Health and Nutrition Examination Survey prospective study, the risk of all-cause mortality increased by 30% and cardiovascular disease (CVD) mortality increased by approximately 80% in single-meal eaters compared to three-meal eaters. In addition, taking a new look at the health effects of meal frequency, a time interval of ≤4.5 hours between two meals despite the same number of meals was associated with higher all-cause mortality (Sun et al., 2023). In 850 adults whose total number of main and intermediate meals were categorized as five or less, six-seven and more than seven, an increase in the total number of meals and intermediate meals was found to be associated with an increase in the prevalence of metabolic syndrome. In this study, the diet quality of the participants was also examined to support the effect of the number of meals on metabolic health. Although the diet quality of the participants was high, increased eating occasion and snack increased the risk of metabolic syndrome (Azizi et al., 2022).

Although increased meal frequency is a dietary pattern that may be of concern in terms of negatively affecting postprandial blood glucose, Carlson and colleagues' randomized controlled cross-over study showed that those who ate three meals versus one meal had higher fasting glucose (Carlson et al., 2007). On the other hand, there are studies that confirm the opposite view. In a study of 50,660 adults, it was found that those who had 3 meals versus those who had 1-2 meals had a higher body mass index (BMI), and the number of main meals and snacks were positively correlated with BMI. The researchers believe that this result is not only due to the effect of meal frequency, but also to a combination of the effects of meal timing and nighttime fasting. They hypothesized that prolonging overnight fasting by reducing meal frequency may activate factors such as increased concentration of satiety hormones (leptin and ghrelin), improvement of metabolic regulators such as cAMP response element-binding protein, and reduction of oxidative stress, thereby reducing body weight (Kahleova et al., 2017). Studies suggesting that increased meal frequency may also provoke an increase in BMI suggest that this causality cannot be explained only by high energy consumption, and that food stimuli, feelings of hunger and desire to eat should also be taken into account. However, the cross-sectional design of these studies is insufficient to explain causality due to the nature of these studies, making randomized controlled studies necessary in this context. As a matter of fact,

the Dietary Guidelines Advisory Committee has not yet made a recommendation on meal frequency in the 2020-2025 Dietary Guidelines for Americans (Snetselaar et al., 2021). Although the general consensus is to maintain the usual breakfast, lunch and dinner rather than a single meal, confounding factors such as the individual's living conditions and the timing and content of meals make further research necessary for a clear judgment.

Meal Timing

In various parts of the world, meal times vary during the day. In addition to factors such as the traditional eating habits of the society, living conditions and individual preferences of individuals, even the geographical location and climatic conditions of the relevant location affect the timing of meals. For example, individuals living in countries with hot climates prefer to socialize with family or friends in the evening rather than during the day, which increases nighttime meals. Likewise, individuals who work start their day early and eat breakfast at an earlier time, while individuals who spend most of their time at home, such as housewives and retirees, start their day later and eat breakfast at a relatively later time. Having any meal at the same time often has different health effects depending on the time of day (Ha & Song, 2019). In this section of the review, the concept of mealtime will be examined under three separate headings: eating in the morning (having breakfast), eating at nights and eating irregular meals.

Eating in the morning

According to the results of What We Eat in America (WWEIA), National Health and Nutrition Examination Survey (NHANES) 2017- March 2020, the frequency of eating breakfast in the morning is 85% in individuals aged 40 to 59 years in the United States, and the energy contribution of breakfast to the daily diet is 18% on average in all individuals (Sebastian et al., 2024). In Turkey, the prevalence of individuals over 15 years of age eating breakfast is 85% (TÜRKİYE BESLENME VE SAĞLIK ARAŞTIRMASI (TBSA), n.d.). Compared to previous years, the current situation shows that the frequency of eating breakfast has been decreasing over the last four decades (Kant & Graubard, 2015a). This is an indication that daily calorie needs are met in the evening. In a study by et al. comparing two groups consuming the same calories, one group consuming high calories in the morning and the other in the evening, it was concluded that the group consuming high calories during the day was superior in terms of weight loss, serum ghrelin, insulin resistance and individual appetite sensation (Jakubowicz et al., 2013). This result brings to mind the quote "Eat like a king in the morning, a prince at noon and a peasant at dinner" by Maimonides, a thinker, physician and philosopher who lived in the millennia. Many studies have reported an inverse association between energy intake at breakfast and weight gain and incidence of cardiovascular risk factors (hypertension, increased LDL-C, decreased high density lipoprotein cholesterol (HDL-C)) (Cahill et al., 2013; Deshmukh-Taskar et al., 2013; Witbracht et al., 2015) In a cross-sectional study examining the effect of meal timing and frequency in Korean adults, it was observed that the frequency of metabolic syndrome was lower in men and women who had a morning meal (Ha & Song, 2019). A systematic review and meta-analysis of 9 different studies involving a total of 242,095 participants found that breakfast skippers had a higher risk of all-cause (HR: 1.27, 95% CI, 1.07-1.51, I2 = 77%), CVD-related (HR 1.28, 95% CI 1.10-1.50, I2 = 0%) and cancer-related (HR: 1.34, 95% CI: 1.11-1.61, I2 = 0%) deaths than regular breakfast eaters (Wang et al, 2024). To our knowledge, although there is no research that contradicts the positive relationship between breakfast and the percentage of protection from cardiovascular diseases, in the study of Dhurandhar et al. in the study of weight loss, those who ate breakfast did not achieve superiority in weight loss compared to those who did not eat breakfast (Dhurandhar et al., 2014).

Prolonging the fasting period by skipping breakfast during the day following overnight fasting increases 24-hour energy expenditure. However, skipping breakfast may lead to higher insulin concentrations and increased fat oxidation. This can lead to metabolic inflexibility resulting in low-level inflammation and impaired glucose balance (Nas et al., 2017). Therefore, breakfast meal is especially important for cardiometabolic health. It is important to include breakfast in the daily diet and to remind individuals in healthy nutrition recommendations

Eating at nights

Eating at nights will discuss the actions of eating dinner and night snacks. In a study of 8153 people aged 40-54 years who were regularly followed up in Japan, it was concluded that the risk of developing metabolic syndrome was higher in women who had a habit of eating at night than in women who did not eat at night (OR=1.68; 95% CI=1.00-2.84). In the same study, the rate of obesity in women who ate night meals was two times higher than in women who did not (OR: 2.11; 95% CI = 1.42-3.15) and 3 times higher than in men (OR: 3.02; 95% CI = 1.72-5.29) (Yoshida et al., 2018). Soga et al. examined 4912 participants and found that 32.4% of men and 15.2% of women had the habit of eating dinner within two hours before sleep, and 26.0% of men and

23.2% of women had the habit of snacking after dinner. In the study, while the risk of metabolic syndrome was associated with women who ate dinner within two hours before sleep more than three days a week, night snacking was also associated with the risk of metabolic syndrome in men and women (Tsutatani et al., 2017). When the National Health and Nutrition Examination Survey (NHANES) 2015 - 2018 results were evaluated, it was reported that the prevalence of abdominal obesity was higher in those who ate late meals (IRR, 1.12; 95% CI, 1.01-1.25) (Bernardes da Cunha et al., 2023).

However, the results of these studies do not explain the direct association of high energy intake later in the day with higher BMI or worsened cardiometabolic status. The high heterogeneity and risk of bias in these studies prevent a definitive conclusion on this issue (Fong et al., 2017).

Eating irregular meals

The concept of irregular eating can be defined as a condition in which the time and number of daily meals are not approximately the same. It is thought that individuals who eat in this way are more at risk for metabolic syndrome, and that having regular meals may be protective against insulin resistance (Sierra-Johnson et al., 2008). Nutritional habits acquired during childhood and even infancy play an important role in maintaining and improving health until old age. In Swedish young people who were included in the cohort in adolescence and followed for 27 years, it was reported that those with irregular eating habits had a higher prevalence of metabolic syndrome in adulthood and this relationship was explained by the unhealthy lifestyles that young people who had irregular eating habits in adolescence continued in middle age. Regardless of lifestyle and BMI, skipping breakfast was found to be a factor increasing the risk of metabolic syndrome (OR=1-67; 95% CI 1-00, 2-80) (Wennberg et al., 2016). Irregular eating and frequent skipping of meals are thought to be less favorable for achieving a healthy cardiometabolic profile.

Circadian rhythm is another topic that should be discussed when evaluating the cardiometabolic impact of meal timing. Circadian rhythm can be defined as an endogenous rhythm that regulates biological processes in approximately 24-hour cycles and can be briefly summarized as a daily pattern that synchronizes human physiology (Berson et al., 2002; Potter et al., 2016). While light is the main regulator of the circadian clock in the central nervous system, clocks in the periphery located in the liver, adipocytes, gut and other organs are stimulated by food intake (Berson et al., 2002; Dibner et al., 2010; Pickel & Sung, 2020). The name circadian syndrome has been proposed for the clinical picture in which disruptions in the timing of food intake lead to disruption in circadian risk and circadian disruption results in cardiometabolic diseases, sleep disturbances, depression and metabolic dysfunction-associated steatotic liver disease (MASLD) (Zimmet et al., 2019). Inappropriate mealtimes, skipping meals and shift work are risk factors for circadian syndrome (Akbar & Shi, 2024). When the relationship between meal timing and metabolic syndrome is examined, there seems to be a general tendency that the morning meal has a protective effect on metabolic syndrome, while eating at night may impair cardiometabolic health. However, the limited number of studies on nocturnal eating and metabolic syndrome and the high heterogeneity in these studies necessitate further research to fully understand this relationship.

Skipping Meals

With fast-paced living conditions, the habit of skipping meals in the usual meal pattern is increasing. In studies examining the impact of skipping meals, eating irregular meals is not a condition that can change from day to day, but rather skipping meals is the state of not taking any meal regularly. According to the results of TBSA 2017, 15% of individuals over the age of 15 in Turkey (male 16.4, female 13.7) skip breakfast. According to the results of the same survey, breakfast is the most frequently skipped main meal, followed by lunch (24.7%) and dinner (3.7%) (TÜRKİYE BESLENME VE SAĞLIK ARAŞTIRMASI (TBSA), n.d.). The results of the US National Health and Nutrition Examination Survey show that the rates of skipping breakfast, lunch and dinner are 19%, 22% and 8% for men and 19%, 21% and 7% for women, respectively. In other words, 40% of US adults skip at least one meal and at least one in five people aged 20-74 skips breakfast or lunch (Kant & Graubard, 2015b). The increasing prevalence of skipping meals has made it necessary to examine the health effects of this behavior. When the consequences of skipping breakfast, the most frequently skipped meal, are evaluated, it has been observed that skipping breakfast increases body weight, cardiovascular disease and mortality risk(Cahill et al., 2013; Kubota et al., 2016; Ma et al., 2020; Rong et al., 2019). According to the results obtained from the US National Health and Nutrition Examination Survey, skipping breakfast especially increases cardiovascular mortality, while skipping lunch and dinner increases the risk of all-cause mortality (Sun et al., 2023). Similar results were obtained in the Korea National Health and Nutrition Examination Survey (KNHANES). In men, skipping two meals, regardless of the type of meal, was associated with an increased risk of metabolic syndrome, while skipping breakfast increased fasting glucose and TG levels in women. As expected, fasting

blood glucose levels decreased in women who skipped dinner (Park et al., 2023). A study in university students reported that skipping dinner was also associated with increased risk of overweight/obesity in young women and men (1.74 (1.07-2.84) and 1.68 (1.02-2.78) women and men, respectively) (Yamamoto et al., 2021). Consistently skipping meals is thought to have an effect on the biochemical pathways that cause arterial fibrillation (Nizami et al., 2022). The cardiometabolic effect of breakfast persists in the geriatric population. In a population-based cross-sectional study of 3607 geriatric individuals over 60 years of age, regular meals were inversely associated with metabolic syndrome, insulin resistance and gamma-glutamyl transferase (Sierra-Johnson et al., 2008).

As authors, we think that the knowledge that skipping meals in adolescence increases the risk of metabolic syndrome in adulthood (Wennberg et al., 2016); and that a minimal eating habit such as skipping meals in a fragile period with many comorbidities such as the geriatric period may be associated with metabolic syndrome (Sierra-Johnson et al., 2008) once again shows how nutrition is a vital activity related to general health. Having a regular eating habit without skipping meals is an effective nutrition therapy variable in the prevention and treatment of metabolic syndrome (Kahleova et al., 2017; Sierra-Johnson et al., 2008; St-Onge et al., 2017). Skipping meals has positive effects on health independent of meal frequency. While it is also possible to explain this through biochemical pathways, it is also necessary to consider that individuals with a healthy eating pattern are likely to make relatively better food choices and lifestyle habits. However, the use of food consumption records with the 24-hour reminder method based on patient declaration in the vast majority of studies may have led to potential biases due to intentional or unintentional misrepresentation of individuals (Flegal, 1999). Further studies are needed in this field to explain the possible relationship more accurately.

CONCLUSION

Meal timing and frequency are two separate eating patterns that involve many variables. Skipping meals, having irregular meal patterns, and eating one, two or more meals comprise many intertwined eating behaviors. Although it is possible to accept the potential benefits of maintaining meal regularity, the importance of breakfast as a general opinion, the effect of each attitude should be evaluated separately. In addition to the questions of how many times, when and how often meals are eaten, it is important to answer which food, how much and how it is eaten, how the food is cooked, who, with whom, where and even in what mood these meals are made. Because nutrition is a multifactorial action and should be examined in all aspects when evaluating cardiometabolic health as in all clinical conditions. The lack of adequate research still makes it impossible to make definitive judgments on the subject.

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