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Review Article

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Dietary Strategies for Metabolic Syndrome: A Review

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Abstract

Metabolic syndrome is a cluster of metabolic abnormalities that includes abdominal obesity, atherogenic dyslipemia (elevated plasma triglycerides and reduced high-density lipoprotein cholesterol), elevated blood pressure and insulin resistance, which can manifest as elevated fasting plasma glucose. Patients classified as having metabolic syndrome are at increased risk for developing chronic diseases, including type 2 diabetes mellitus and cardiovascular diseases. Lifestyle modification is generally recognized as a key intervention in metabolic syndrome; however, the complex nature of this condition complicates treatment strategies. Specific dietary alterations have been shown to improve the metabolic derangements that constitute metabolic syndrome therefore dietary intervention is a primary focus of treatment. Nonetheless, the most effective dietary pattern for the treatment of metabolic syndrome has not yet been established. On the other hand, within the context of the overweight and obesity epidemic that is currently a global public health crisis, reducing caloric intake and increasing physical activity to achieve weight loss can improve the metabolic abnormalities observed in metabolic syndrome. The present review aims to analyze different dietary patterns with potential benefits on metabolic syndrome status in order to identify efficient strategies to fight against metabolic syndrome and associated diseases.

Keywords

Metabolic syndrome; Cholesterol; Food pattern

Abbreviations: MetS: Metabolic Syndrome; LFD: Low Fat Diet; MedDiet: Mediterranean Diet; VLCD : Very Low Carbohydrates Diets; KD: Ketogenic Diets; HPD : High Protein Diet; CH : Carbohydrates; DASH diet: Dietary Approaches To Stop Hypertension Diet; ND: Nordic Diet; SAD: Standard American Diet; VCAM-1: Vascular Cell Adhesion Molecule 1; ICAM-1: Intercellular Adhesion Molecule 1; LDL: Low Density Lipoprotein; HDL: High Density Lipoprotein; CVD : Cardiovascular Disease; T2DM: Type 2 Diabetes Mellitus; FBG: Fasting Blood Glucose; BP: Blood Pressure; MUFA: Monounsaturated Fatty Acids; PUFA: Polyunsaturated Fatty Acids; EVOO: Extra Virgin Olive Oil; LDL-c: Low Density Lipoprotein Cholesterol; HDL-c: High Density Lipoprotein Cholesterol; HbA1c: Glycated Hemoglobin; BMI: Body Mass Index; RCT: Randomized Controlled Trial

Introduction

Unhealthy dietary patterns and a sedentary lifestyle have an important role in human health, especially nowadays, when non-communicable diseases such as obesity, cardiovascular disease (CVD) and type 2 diabetes mellitus (T2DM) have somewhat unseated communicable diseases practically worldwide, despite the incidence of the former being higher in developed and developing countries [1].

In this context, high blood pressure (BP), altered blood lipid levels, excessive weight characterized by central adiposity, and abnormally high fasting blood glucose (FBG) concentrations are a cluster of metabolic risk factors that often appear together or in different combinations. In 1998 the World Health Organization WHO and subsequently, other health organizations defined this group of metabolic risk factors as metabolic syndrome (MetS), and with the exception of some details the criterial definitions of these organizations coincide [2-4]. MetS is met when at least three of five of the following factors are present: elevated triglycerides (≥ 150 mg/dL), reduced high-density lipoprotein cholesterol (HDL-c; <40 mg/dL in males and <50 mg/dL in females), elevated FBG (≥ 100 mg/dL), elevated BP (systolic BP ≥ 130 and/or diastolic BP ≥ 85 mm Hg), and elevated waist circumference (with country-specific definitions). In addition, pharmacologic treatment of any of these criteria (except waist circumference) must also be taken in account [4].

The prevalence of this complex health condition is high [5]. Studies in the last years have reported that MetS affects around 20-30% of the population [6-9]. These data are worrisome considering the relationship between MetS and the increased risk to develop other diseases. Indeed, Dragsbæk et al. described a 6.3-fold increase in the risk of developing T2DM and a 1.7-fold increase in the risk of CVD in older women with MetS while older women without MetS had a 3.6-fold and 1.3-fold increase, respectively, being these results similar to those described by Alberti et al. MetS has also been associated with depressive disorders, alterations in circadian rhythm, erectile dysfunction and colorectal cancer [4,10-15]. Although the etiology of MetS remains unknown, it has been described as being dependent on other factors such as genetic background, age, sex, ethnicity, environmental factors (urban or rural settings), socioeconomic status, physical activity, smoking habit, education and diet [16,17].

Treatment of MetS is focused on improving lifestyle by following a healthier dietary pattern and promoting physical activity. In their meta-analysis Yamaoka and Tango concluded that lifestyle intervention is effective in achieving a significant reduction in systolic and diastolic BP, triglyceride levels, waist circumference and FBG [18]. They suggested that dietary modifications could be a more effective intervention than physical activity [18]. Taking into account the relevance of MetS in health status, the aim of this review was to describe the potential benefits of different dietary patterns on MetS status in order to identify efficient strategies for its prevention, management and control of associated diseases.

Dietary patterns

Specific dietary alterations have shown to improve the metabolic derangements that constitute MetS. Therefore dietary intervention is a primary focus of treatment, even though the most effective dietary pattern for the treatment of MetS has not yet been established. Table 1 shows the different diets implemented and their positive effect on MetS criteria.

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Table 1: Dietary patterns and the potential positive effect on MetS criterias.

Dietary Pattern	Nutritional Distribution	Improvements In Mets Criteria	Ref.
Low-fat diet	■ <30% kcal/d from total fat (<10% of saturated fat)	Weight-loss and reduction of abdominal obesity	[19]
		Decreased BP (systolic and diastolic)	[20]
		Decreased LDL-c	[19,20,55]
The Mediterranean diet	■ 45-50% kcal/d from carbohydrates ■ 30-35% kcal/d from total fat (main source are EVOO and nuts) ■ 20% kcal/d from protein	Improved insulin resistance	[27]
		Reduction of the incidence of T2DM	[29]
		Decreased BP (systolic and diastolic)	[56]
		Improvements in dyslipemia	[56]
Very low carbohydrate diets or Ketogenic diet	■ <10% kcal/d from CH ■ High protein (20-30% kcal/d) ■ High fat intake (60-70% kcal/d)	Weight-loss and weight-loss maintenance	[33]
		Reduction of DBP	[33]
		Reduction of LDL-c and triglycerides levels	[33]
		Improvements in FBG	[33,34]
		Improvements in insulin resistance	[35]
		Reduction of HbA1c levels	[33,34]
High protein diet	■ High protein (20-30% kcal/d) or 1.34 g/Kg body weight/d from protein ■ Low carbohydrate (40-50% kcal/d)	Weight- loss	[38,39,40,42]
DASH diet	■ Total fats 27% kcal/d ■ Saturated fats 6% kcal/d ■ MUFA13% kcal/d ■ PUFA 8% kcal/d ■ Carbohydrates 55% kcal/d ■ Proteins 18% kcal/d	Reduction of diastolic BP	[47,50]
		Reduction of systolic BP	[48]
		Reduction of insulin levels	[47,50]
		Reduction of triglycerides, FBG, weight	[50]
		Increment of HDL-c	[50]
Nordic diet	■ Total fats 30% kcal/d ■ Saturated fats <10% kcal/d ■ Carbohydrates 50-60% kcal/d ■ Refined sugars <10% kcal/d ■ Proteins 10-20% kcal/d	Reduction of diastolic BP	[54]

Metabolic syndrome, MetS; blood pressure, BP; low-density lipoprotein cholesterol, LDL-c; high-density lipoprotein cholesterol, HDL-c, type 2 diabetes mellitus, T2DM; glycated hemoglobin, HbA1c; monounsaturated fatty acids, MUFA; polyunsaturated fatty acids, PUFA; fasting blood glucose, FBG.

Low-Fat Diet

Low-fat diet (LFD) is the leading dietary intervention to reduce the complications related to MetS. In fact, the dietary recommendations for weight loss of the American Heart Association and the National Institute of Health emphasize the importance of low-fat and high-carbohydrate dietary patterns [19]. By definition, LFD comprises <30% kcal/day from total fat, and the profile of this fat is <10% saturated fat, 12-14% monounsaturated fatty acids (MUFA) and 6-8% polyunsaturated fatty acids (PUFA). This reduction in fat is substituted by high-carbohydrate intake or high-PUFA fatty acid diets. In the scientific statement for the diagnosis and management of the MetS of the American Heart Association and National Heart, Lung, and Blood Institute [20], the atherogenic diet was proposed in patients with MetS. This diet reduces the fat content to 25-35% of total calories and includes <7% of saturated fat, <200 mg/d of dietary cholesterol and a reduction of *trans* fat intake. Although LFD is the leading nutritional strategy for MetS treatment, a very LFD should be avoided if elevated triglycerides or low HDL-c levels are present [19].

In the Women's Health Initiative (WHI), 48,835 postmenopausal women aged 50-79 years were randomized into two intervention groups: one following a LFD (<20% of kcal/d from fat) and another without a dietary intervention [20,21]. The LFD was significantly associated with improvement in the components of MetS at 1 year of intervention but not during the remainder of the follow-up (at 3 and 6 years). On the other hand, the need for cholesterol-lowering or hypertension medication was significantly reduced in the intervention group. Despite the improvement in MetS status the first year of the LFD intervention, this dietary approach resulted in no cardiovascular benefit in the long term [22].

On the other hand, other randomized clinical trials, including the PREDIMED study [23], have compared different dietary strategies with a LFD and found greater long-term cardiometabolic benefits (insulin resistance, BP and dyslipidemia) with the other dietary interventions.

Mediterranean Diet

The Mediterranean diet (MedDiet) is characterized by a high consumption of food of vegetable origin, such as fruits, vegetables, legumes, nuts and whole-grain cereals; with extra virgin olive oil (EVOO) as the principal source of fat; consumption of low-to-moderate amounts of fish and poultry; low consumption of red meat; moderate consumption of red wine; normally with meals, and tomato sauce with garlic, onion and EVOO used for meal preparation [24]. High adherence to a Mediterranean-style diet has been consistently linked to favorable health outcomes and has a beneficial influence on the metabolic pathways leading to MetS and T2DM, as well as CVD [25].

As the main key foods of the MedDiet, EVOO is a lipid extract from olives, whereas nuts are whole foods that provide additional non-lipid nutrients, including fiber; arginine, the precursor of the endogenous vasodilator nitric oxide; and minerals, such as potassium, calcium and magnesium [26]. Besides EVOO and nuts, the high content of vegetables and fresh fruits of the MedDiet, together with a moderate consumption of wine, guarantees a high intake of antioxidant vitamins and phenolic compounds. Indeed, previous reports from the PREDIMED trial (Prevención con Dieta Mediterránea), a parallel-group, multicenter, randomized trial including individuals aged 55-80 years at high risk of cardiovascular disease, showed that MedDiets are associated with improved insulin resistance and decreased oxidative

damage to low-density lipoprotein cholesterol (LDL-c) [27]. The decreased oxidative stress promoted by the MedDiet concurs with the reduction in inflammatory markers such as C-reactive protein, IL-6, vascular cell adhesion molecule 1 (VCAM-1) and intercellular adhesion molecule 1 (ICAM-1), E- and P-Selectin [28]. Therefore, a reduced inflammatory state might account for an important part of the beneficial effects of the MedDiet on MetS status. In the case of classic cardiovascular risk factors, the MedDiet supplemented with EVOO and nuts group showed a significant reduction in systolic BP of 6 mmHg and in diastolic BP of 3 mmHg. Additionally, the total-cholesterol level was significantly reduced in both groups (around 7%), and the reduction in LDL-c was greater in the EVOO compared to the nuts group (9% vs. 5%, respectively) after 1-year of intervention [28]. Moreover, several reviews on MetS and T2DM concluded that MetS status can recover after a MedDiet supplemented with EVOO or nuts [25]. In the PREDIMED trial, a subgroup of 418 non-diabetic volunteers were followed during 4 years, and it was found that when the EVOO and nuts groups of the MedDiet were analyzed, the risk to develop T2DM reduced 52% [29].

Very Low Carbohydrate Diets or Ketogenic Diets

Ketogenic diets are characterized by a reduction of carbohydrate (CH) intake, with usually less than 50g/day, representing approximately 10% of the kcal/day. It requires a proportional increase in the dietary fat and protein intake. Recent research has shown that the therapeutic use of a ketogenic diet has beneficial effects on cardiometabolic abnormalities such as T2DM and MetS [30,31]. Moreover, according to Buenos et al. the ketogenic diet seems to achieve better long-term body weight maintenance compared to the LFD [32]. In their meta-analysis they found that diastolic BP, triglycerides, LDL-c and HDL-c also improved with the ketogenic diet compared to the LFD, and other studies have described an improvement in FBG and glycated hemoglobin (HbA1c) [32,33]. Concerning MetS, a randomized interventional study including 88 patients of 18-65 years of age with MetS, pre-diabetes or T2DM demonstrated the benefits of a ketogenic diet (<30g CH/d) compared to two Standard American Diet (SAD) groups: one group with physical activity intervention and the other without. A significant reduction was observed in weight, body mass index (BMI), and HbAc1 ($P<0.001$) with the ketogenic diet while the two control groups showed no differences. It seems that the ketogenic diet induced the oxidation of fat by modulating insulin secretion [34]. This regulation of insulin levels enables tissues to become metabolically flexible and use fatty acids and ketone bodies as primary fuel sources helping to restore cellular signaling, especially insulin signaling [35,36].

Although the long-term benefits of this dietary pattern seem to be greater than those of conventional therapies, more randomized clinical trials are needed to confirm the benefits of this dietary pattern in long-term interventions. Health care professionals must take into account the difficulties in following a ketogenic diet and the alteration that this dietary pattern may have on daily habits. Furthermore, ketogenic regimens are known to potentially result in electrolyte imbalances and an increase in uric acid concentrations [37]. However, these complications can be avoided with nutritional supplementation. Therefore, a rehabilitation program to restart a balanced diet, which considers carbohydrates as the main source of calories, must be well defined to avoid adverse effects.

High Protein-Diet

High protein diets are novel dietary strategies for weight loss and seem to have beneficial effects on the comorbidities associated with MetS. A high protein diet provides approximately 20-30% kcal of the total kcal/d, which can be translated to 1.34g/Kg body weight/day from protein [38-40]. This dietary pattern may contribute to the maintenance of lean body mass during a period of energy restriction, helping to preserve resting energy expenditure and increase the thermic effect of feeding [39,41].

In a recent randomized controlled study comparing a high protein diet with a standard protein diet (0.8g/Kg body weight/day) in the treatment of the MetS, no significant differences were observed except in weight loss. It has been reported that a high protein diet does not affect insulin sensitivity, and even with an increase of physical activity, a study including overweight and obese middle- aged adults showed no significant changes in the MetS-related parameters [38,40,42].

In another study including women at risk of developing MetS, significant improvements were observed in those who followed a high protein weight-loss diet (500-900 kcal restriction per day) compared to a high fiber intake diet. This was further demonstrated in a second analysis of the original study in which a double- blind, placebo-controlled, community- based 36-week intervention was performed in women at risk of MetS [43]. Blood pressure as well as total and LDL-c levels decreased and insulin sensitivity increased, but no significant differences were observed between the two intervention groups [39].

However, according to the results of a randomized 3-period crossover feeding trial [complementary study of the Omni Heart trial [38], and a randomized 24-month intervention study in the US, there is some controversy about the effect that a high protein diet may have on the glomerular filtration rate and the possibility of presenting long-term consequences in kidney function [41,44]. Further studies are needed to confirm the safety of this dietary pattern.

DASH Diet

The Dietary Approach to Stop Hypertension (DASH diet) has demonstrated to be effective in BP management [45]. This diet is characterized by a high intake of fruits and vegetables and a low consumption of high-fat dairy products [45,46]. This diet has a reduced content fat, especially of saturated fats and dietary cholesterol, and sodium intake is reduced to approximately 3g per day [45,46].

A randomized cross-over clinical trial in female adolescents diagnosed with MetS found a significant reduction of diastolic BP (-1.9% vs +4.4% respectively, $P=0.01$) insulin levels (-10.4%, $P=0.04$) when the DASH diet was followed during 6 weeks compared to the usual dietary recommendations. However, there were no differences in insulin levels between the two interventions, and weight, waist circumference, BMI and systolic BP remained unchanged [47]. Conversely, on analyzing a subgroup of individuals with the MetS from the DASH trial, Hikmat and Appel reported that systolic BP was significantly lower following the DASH diet compared to the control diet (4.9 mm Hg, $P=0.006$) but not diastolic BP (1.9 mm Hg, $P=0.15$) [47]. A randomized controlled trial (RCT) involving a tailored DASH nutritional intervention with the supplementation of ω-3 fatty acids in elderly women, showed a significant decrease in LDL-c levels in the women receiving the intervention but no differences in the control group [48]. In a randomized, parallel study Hill et al. compared three modified DASH diets associated with calorie restriction with the American diet (high in total and saturated fat, cholesterol, sodium and lower in fiber, potassium, calcium and magnesium) [49]. They found improvements in MetS components with the three calorie-restricted diets compared to the American diet but there were no

differences between the three intervention diets. On the other hand, a RCT in 116 adult male and female patients with MetS showed a significant reduction ($P<0.05$) in triglyceride levels (8.9% and 6.0%, respectively), systolic and diastolic BP (8.3% and 6.9% and 7.7% and 8.2%, respectively), weight (18.4% and 5.3%, respectively), and waist circumference (6.7% and 19.7%, respectively). Changes in FBG were also observed in both men and women on the DASH diet for 6 months (13.4% and -10.4%, respectively), with a significant increase in HDL-c (21.1% and 33.3%, respectively). The prevalence of MetS was reduced 35% in patients in the DASH diet group, 19% in those on the weight-reduction diet and 0% in the control group ($P<0.05$) [50]. Accordingly, the DASH diet seems to be effective in MetS management, especially in relation to high BP levels.

Nordic Diet

The Nordic diet comprises a high content of whole-grain and high-fiber products (rye, barley, oat, unpolished rice), has a substantial quantity of fruits, vegetables, berries and nuts, is rapeseed oil-based, includes low-fat dairy products, and it is characterized by an elevated fish and shellfish intake [51,52]. Total fats make up approximately 30% of the total energy intake, saturated fats must not exceed 10% of total energy, carbohydrates represent 50-60% of energy intake, the refined sugar intake is less than 10% of total energy intake, and the protein content is between 10-20% of daily total energy intake [51]. This diet has been related to improvement in CVD risk factors [53].

In a study including 18 subjects with MetS undergoing a 3-month intervention with the Nordic diet compared to controls, a significant improvements was observed in diastolic BP (-4.4 mm Hg, $P=0.001$) and mean arterial pressure (-4.2 mm Hg, $P=0.006$) in the intervention group, but systolic BP showed no significant improvement (-3.5 mm Hg, $P=0.122$) [54]. On the contrary, in another study, after 18-24 weeks of intervention with Nordic diet, 96 subjects showed no significant differences in systolic and diastolic BP ($P=0.28$ and $P=0.29$ respectively) or weight loss ($P=0.097$) [52]. Nevertheless, significant improvements were observed in non-HDL-c (-68.5 mg/dL, $P=0.004$) [52]. In view of the lack of scientific evidence related to the benefits of the Nordic diet, more RCTs are needed.

Conclusion

The results of several studies suggest the potential benefits of healthy dietary patterns and lifestyle modification on MetS status. The protective effect of energy-restricted diets on MetS status seems to be due to the sum of small changes in individual components of MetS rather than a large effect on any single component. This lifestyle intervention must be focused on modification in weight-loss and physical activity in order to achieve significant improvements. The aim of this review was to describe different nutritional patterns with potential benefits in MetS status in order to facilitate new dietary strategies, which have obvious implications for the primary prevention of major cardiovascular events and provide a good public health strategy to fight against MetS and overweight.

On comparing the LFD, which is the gold standard dietary pattern for MetS treatment, with other dietary patterns, the scientific evidence in favor of the MedDiet may make this diet a new paradigm for MetS treatment. The nutritional composition of the MedDiet pattern, the fat content, the composition of fatty acids and the quality of the carbohydrates allows health professionals to provide easy-to-follow nutritional advice and avoid the use of restricted diets.

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