REVIEW ARTICLE

DIETARY INTERVENTIONS IN THE TREATMENT OF METABOLIC SYNDROME AS A CARDIOVASCULAR DISEASE RISK-INDUCING FACTOR. A REVIEW

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ABSTRACT

Metabolic syndrome (MetS) is a concept which refers to a simultaneous occurrence of clinically significant cardiovascular disease (CVD) risk factors that increase the risk of atherosclerosis and type 2 diabetes as well as their vascular complications. The metabolic syndrome is a complex disorder, therefore its treatment should be multifactorial and intensive. MetS occurs due to a combination of genetic and environmental factors. Each of MetS components is a well-known risk factor of atherosclerosis.

Such modifications to the lifestyle as increasing physical activity, introducing a well-balanced diet and reducing the body mass are associated with reduced occurrence of MetS and its individual components.

It is necessary to implement proper dietary processes, a physical training program and pharmacological treatment. The treatment of MetS should begin with weight loss, which affects the occurrence of abdominal obesity, as well as increased physical activity, leading to an increased tissue sensitivity to insulin. It is recommended to introduce a low-energy, individually balanced diet that will lead to a 7-10% weight loss over the course of 6-12 months. Patients are also advised to quit smoking and limit the consumption of salt and alcohol.

Key words: *metabolic syndrome, diet, dietary interventions, obesity*

STRESZCZENIE

Pojęcie zespołu metabolicznego (ZM) odnosi się do wspólnego występowania istotnych klinicznie czynników ryzyka chorób sercowo-naczyniowych (ChSN), zwiększających ryzyko rozwoju miażdżycy i cukrzycy typu 2 oraz ich powikłań naczyniowych. Zespół metaboliczny jest zaburzeniem złożonym, dlatego jego leczenie powinno być wieloczynnikowe oraz intensywne. Na występowanie ZM składa się skojarzenie czynników genetycznych i środowiskowych. Każda ze składowych ZM jest dobrze poznanym czynnikiem ryzyka wystąpienia miażdżycy. Modyfikacje stylu życia, takie jak zwiększenie aktywności fizycznej, wprowadzenie prawidłowo zbilansowanej diety oraz redukcja masy ciała są związane ze zmniejszeniem częstości występowania ZM oraz jego poszczególnych składowych. Niezbędne jest wdrożenie prawid-łowego postępowania dietetycznego, programu treningu fizycznego oraz leczenia farmakologicznego. Leczenie ZM należy rozpocząć od redukcji masy ciała, która wpływa na występowanie otyłości brzusznej i zwiększenia aktywności fizycznej, prowadzącej do zwiększenia wrażliwości tkanek na insulinę. Zalecane jest wprowadzenie diety niskoenergetycznej, indy-widualnie zbilansowanej, która doprowadzi do redukcji masy ciała o 7-10% w ciągu 6-12 miesięcy. Pacjentom zaleca się również zaprzestania palenia papierosów oraz ograniczenia spożywania soli i alkoholu.

Słowa kluczowe: *zespól metaboliczny, dieta, interwencja żywieniowa, otyłość,*

INTRODUCTION

Metabolic syndrome (MetS) is a concept which refers to a simultaneous occurrence of clinically significant cardiovascular disease (CVD) risk factors that increase the risk of atherosclerosis and type 2 diabetes as well as their vascular complications. Epidemiological data indicate a significant and growing spread of MetS in the United States and Europe, including Poland. At 30-40%, incidence of MetS is particularly high among the middle-aged and elderly population [21, 38]. It should be emphasised that the incidence of MetS is dependent on the applied criteria of diagnosis, according to the established definitions of MetS and the characteristics of the study group, especially in terms of age [17].

It is estimated that MetS occurs in 15-30% of adult inhabitants in developed countries. In the United

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States, MetS is believed to affect approximately 50 million Americans, which constitutes 38% of adult females and males [13]. In Europe, it is believed to occur in 25% of the adult population [11]. Based on various epidemiological studies, MetS in Poland has been estimated to occur in approximately 20-25% of the adult population. The risk of developing MetS increases with age, especially in women. Moreover, MetS increases the risk of death due to CVD by 2.2 times in men and 2.7 times in women [27].

DEFINITIONS OF THE METABOLIC SYNDROME

Several definitions MetS along with diagnostic criteria have been proposed in the last decade. In 1998, the World Health Organization (WHO) announced a definition of MetS according to which a proper diagnosis required evidence of carbohydrate metabolism disorders [19, 28].

According to the NCEP-ATP III (The National Cholesterol Education Program Adult Treatment Panel III) definition from 2005, it was necessary to identify at least three disorders in order to diagnose MetS. In turn, the definition created by IDF (International Diabetes Federation) recognizes that the basic components of MetS consist of abdominal obesity, assessed on the basis of waist circumference measurements, and any two MetS criteria which evaluate lipid parameters, carbohydrate parameters and arterial blood pressure. The currently applied criteria for MetS diagnosis are the ones defined by IDF as well as the modified NCEP ATP III and AHA/NHLBI (American Heart Association and the National Heart, Lung, and. Blood Institute) criteria from 2009 [11, 19, 28].

MetS COMPONENTS CONTRIBUTING TO THE DEVELOPMENT OF METABOLIC CHANGES

MetS occurs due to a combination of genetic and environmental factors. Studies have shown that the basic components of MetS, such as insulin resistance with hyperinsulinaemia, obesity, arterial hypertension, atherogenic dyslipidemia, hyperglycaemia and diabetes, are often accompanied by other disorders. These include: hyperuricemia, microalbuminuria, endothelial dysfunction, prothrombotic and proinflammatory states. Each of MetS components is a well-known risk factor of atherosclerosis [11, 17].

The most important aetiological factors of MetS include: abdominal obesity and insulin resistance, which are closely related to each other and constitute the core of MetS, thus increasing cardiometabolic risk in patients. Their occurrence, and the resulting occurrence of MetS, is driven by: genetic predispositions, incorrect lifestyle comprising a high-calorie and atherogenic diet as well as low physical activity [17].

Abdominal obesity is not a mere derivative of the BMI (Body Mass Index), therefore a measurement of waist circumference better reflects the amount of adipose tissue in the abdominal cavity [15]. Excess fat located in the abdominal cavity is particularly dangerous in terms of potential MetS development. High accumulation of intraperitoneal fat is associated with increased levels of hormones secreted by this tissue in addition to proinflammatory factors - adipocytes (interleukin 6, C-reactive protein, leptin, resistin, tumor necrosis factor alpha, plasminogen activator inhibitor-1) and reduced levels of the adiponectin hormone which prevents the development of MetS [11].

The occurrence of abdominal obesity and excessive visceral fat also leads to the activation of neurohormonal systems, especially the sympathetic nervous system and the renin–angiotensin–aldosterone system. The role of adipose tissue in the postprandial period as a lipid buffer which drains the fatty acids originating mainly from TG (triglycerides)- and VLDL (very low density lipoprotein) -rich lipoproteins, is also emphasised. Their high concentration in the blood serum, and the variations of lipase and lipid transfer proteins which accompany obesity and insulin resistance, modulate the metabolism of plasma lipoprotein, leading to the formation of highly atherogenic lipoproteins [7].

MetS is often associated with cardiovascular complications. Vascular endothelial dysfunction, which is one of the earliest disorders leading to premature atherosclerosis, develops as a result of both hyperglycaemia and insulin resistance. Insulin resistance is considered a key pathogenetic mechanism of MetS. In a study conducted by *Rodriguez et al.* [32], 579 people, aged 66 years on average, who were not affected by cardiovascular diseases, were examined in terms of their health. Elevated fasting blood glucose levels were found in approximately 16% of the patients. *Thomas et. al.* [35] found that along with elevated fasting glycemia levels, the intima- media thickness (IMT), considered a subclinical marker of carotid artery atherosclerosis, also increases. Apart from obesity, hypertension and age, hyperglycaemia was the most important factor determining the dysfunction of endothelial functions in both studies. Investigating the changes in vascular reactivity in patients at risk of type 2 diabetes, other authors [5] determined that both the people with a burdened family history and those with elevated levels of fasting glycemia showed clear signs of vascular endothelial dysfunction.

One of the mechanisms explaining the influence of insulin resistance on the endothelial function lies

in the reduction of vasodilatation and the associated impaired distribution of glucose to insulin-sensitive tissues. In addition, insulin resistance leads to increased release of free fatty acids from the tissues, resulting in increased production of free oxygen radicals [29].

Lifestyle and stress have the most significant impact on rapid development of insulin resistance. Excessive consumption of food products combined with insufficient physical activity creates favourable conditions for the development of overweight and obesity, which consequently induces a decreased peripheral tissue sensitivity to insulin and impairs the endothelial function, leading to hyperglycaemia.
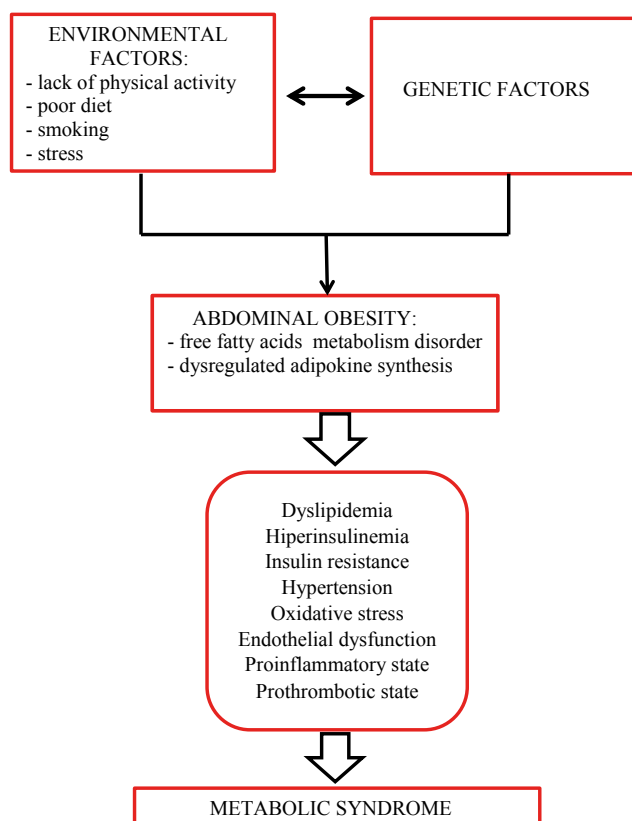

Figure 1. Causes and consequences of the metabolic syndrome (MetS) [11, 15, 17].

In the view of both the IDF and the NCEP ATP II definitions, two criteria for diagnosing MetS are associated with lipid disorders. A characteristic lipid disorder in MetS is atherogenic dyslipidemia (AD), defined as an increased level of triglycerides (TG) and a low level of HDL cholesterol in the blood serum. According to the WOBASZ study, elevated levels of TG occur in 32% men and 20% women, while decreased levels of HDL cholesterol can be observed in 20% men and 26% women [29].

Low HDL cholesterol constitutes a risk factor for CVD. The beneficial effect of HDL cholesterol involves it capturing free cholesterol from the artery wall macrophages and transporting it to the liver.

Apart from enterohepatic transport by HDL particles, it also shows has antioxidant, anti-inflammatory and anti-atherosclerotic effects [20].

European studies confirmed the concurrence of lipid and carbohydrate disorders with hypertension. Data obtained from the NATPOL PLUS 2002 study show that hypertension is the most frequent component of MetS. An important part in its development is played by increased activity of the sympathetic nervous system as well as: stimulation of the renin-angiotensin-aldosterone system, increased sodium reabsorbtion in the renal tubules and endothelial dysfunction, all mainly associated with obesity and insulin resistance [40].

In the NHANES III study, it was found that the most commonly observed disease connected to overweight and obesity was hypertension, the incidence of which increased with age and depended on the type of obesity [26]. Visceral tissue adipocytes are extremely active metabolically and release to the blood a number of substances which increase insulin resistance and create favourable conditions for chronic inflammatory and prothrombotic states, at the same time taking part in pathogenesis of hypertension [31, 33].

There are several key mechanism which link obesity with hypertension, one of which is increased activity of the sympathetic nervous system. Reasons for hyperactivity of the sympathetic nervous systems in obesity include: hyperleptinemia, frequent occurrences of obstructive sleep apnea (OSA), hyperinsulinaeamia and insulin resistance, hyperactivity of the renin-angiotensin-aldosterone system (RAAS), increased inflammation and hipoadiponektynaemia. Fat tissue reduction significantly reduces the activity of the sympathetic nervous system in hypertension pathogenesis [12, 18, 39].

Authors of numerous epidemiological studies have shown that hypertension occurs from 1.5 to 7 times more often in patients suffering from obesity as compared to people with correct body mass [25, 36]. In addition, NT is much more common in patients with abdominal obesity. Increasing the waist circumference by 2.5 cm in women and 4.5 cm in men leads to a systolic blood pressure (SBP) increase of 1 mmHg [9]. Moreover, increasing the body weight by 10% increases the risk of hypertension by 70% [14].

The basic strategy of hypertension treatment in obese patients is to reduce the fat body mass and maintain a healthy body mass. In the TOPH I and II study [6], low-calorie diet and properly selected physical activity were introduced in patients with BMI= 33 kg/m^2 and prehypertension. Only 13% of those studied managed to maintain a 4.5 kg lower body mass for 3 years. In those patients who achieved the goal, blood pressure values decreased and the risk of hypertension fell by 65%.

DIETARY INTERVENTIONS AND CHANGING THE LIFESTYLE

Such modifications to the lifestyle as increasing physical activity, introducing a well-balanced diet and reducing the body mass are associated with reduced occurrence of MetS and its individual components.

Authors of the Greek ATTICA study [30] noted that the application of the Mediterranean diet is associated with a 20% reduction of MetS risk. The Mediterranean diet is considered one of the healthiest dietary patterns. It has been shown that its use is beneficial to patients with cardiovascular diseases as well as for the prevention and treatment of: diabetes, hypertension and metabolic syndrome.

In the PREDIMED study [4], the Mediterranean diet was recommended to patients with a high risk of CVD or MetS. It was found that the use of this diet had a positive effect on reducing the occurrence of MetS, abdominal obesity, hyperglycemia and type 2 diabetes. In addition to monounsaturated fatty acids, the Mediterranean diet also consists of nutrients which reduce inflammation, oxidative stress, insuline resistance and production of pathogenic factors which lead to obesity, type 2 diabetes and MetS.

Giuliano et al. [16] pointed out that probably none of the individual nutrients found in a diet seems to be responsible for the association between diet and the occurence of MetS. However, there might be a correlation between multiple components of the diet or its overall quality and the occurrence of MetS. The authors suggest that lower incidence of MetS is observed in patients whose diet is rich in fruit and vegetables, wholegrain products, low-fat dairy products and unsaturated fats.

Patients diagnosed with hypertriglyceridemia should avoid excessive use of alcohol or stop its consumption altogether due to increased synthesis of TG in the liver caused by alcohol consumption. In these patients, additional supplementation of polyunsaturated *omega*-3 acids at a dose of 2-4 g/day may be considered.

Reduction of carbohydrate consumption in the treatment of MetS, especially in relation to those carbohydrates which are easily absorbed and have a high glycemic index (GI), is dictated by their hyperinsulinemia- and hypertriglyceridemia-inducing effects as well as glucose intolerance. Excessive amounts of carbohydrates in the diet also contribute to the reduction of HDL cholesterol levels in the blood serum. Decreasing the intake of carbohydrates in the treatment of MetS leads to a fats intake increase to the point of 35% of the energy from DFI while maintaining an appropriate food energy level in the diet.

A special role in MetS and CVD prevention is attributed to the essential unsaturated fatty acids belonging to the polyunsaturated *omega*-6 and *omega*-3 groups. Deficiencies of these fatty acids in the diet lead to irregularities in the lipid profile of the blood serum. Oily sea fish caught in cold waters are the main source of omega-3 fatty acids. Their effect is a result of beneficial interaction with metabolic processes, and in particular the systems which regulate biochemical transformations in cells and tissues [8].

Saturated fatty acids (SFA) on the other hand, are associated with hypercholesterolemic and prothrombotic effects. It is therefore beneficial to replace them with food products which are source of monounsaturated fatty acids (MUFA) in the diet [22].

The main lifestyle changes in patients with MetS where hypertension is one of the components include: giving up on smoking, reduction of excessive body weight, limited consumption of alcohol, increased physical activity, limited consumption of salt, increased consumption of fruit and vegetables, reduced consumption of fats in general as well as food product which are the source of omega-6 polyunsaturated fatty acids.

The DASH (Dietary Approaches to Stop Hypertension) study [1] constituted a significant contribution to the formulation of comprehensive dietary recommendations for patients with hypertension. The study was conducted among patients with prehypertension and patients with hypertension who did not use pharmacological treatment. Over a period of 11 weeks, 3 groups of participants received diets of different compositions. Patients from the first group consumed a typical American diet of low calcium, potassium and magnesium. The second group received a similar diet, however it added fruit and vegetables. The DASH diet was used in the third group of patients. The main ingredients of this diet are fruit and vegetables, low-fat dairy products, wholegrain cereals, poultry, fish and nuts. All participants consumed a similar amount of sodium (≈3g/d) and limited their alcohol consumption. The authors of the study noted a decrease in blood pressure by 5.5/2.7 mmHg in patients with prehypertension as well as those with hypertension. The anti-hypertensive effect of the DASH diet was significantly higher (11.4/5.5 mmHg) in patients with hypertension compared with other study groups.

The DASH-Sodium study additionally assessed the influence of excessive sodium consumption on blood pressure [34]. The best anti-hypertensive effect was observed in patients who used the DASH diet in combination with low sodium consumption (50 mmol/d). Apart from the anti-hypertensive effect of the DASH diet, the authors also observed its beneficial contribution to lowering the level of cholesterol in the blood serum and weight loss [3].

The DEW-IT study [23] went on to confirm the beneficial impact of the DASH diet on blood pressure. In the studied persons, a non-pharmacological intervention was introduced in addition to pharmacological treatment. The intervention involved the use of the DASH diet combined with reduced consumption of calories and sodium (100 mmol/d) and introduction of daily physical activity. As a result of dietary modification, a significant decrease of 9.5/5.3 mmHg was achieved in the arterial blood pressure.

Azadbakht et al. [2] evaluated the effects of a DASH-based nutritional plan on the development of risk factors for cardiovascular diseases in patients suffering from type 2 diabetes. For 8 weeks, patients received the DASH diet, while the control group received a typical diet comprising 50-60% of energy (E) from carbohydrates, 15-20% of E from proteins and <30% of E from fats, while simple sugars accounted for <5% of E from DFI. It was noted that the DASH-based plan had a positive effect on the improvement of cardiometabolic parameters in patients affected by type II diabetes in comparison with the control group.

Recommendations regarding the amounts of individual nutrients and portions of different food groups in the DASH diet are presented in Table 1.

The type of dietary intervention applied according to the occurring MetS components is an important element of nutritional therapy. *Esposito et al.* [10] applied the Mediterranean diet in MetS patients. After two years of research, it was found that the application of the Mediterranean diet was associated with MetS subsidence in 56% of the patients. Lipid profiles of these patients improved significantly. In another study, the authors used the DASH diet for MetS therapy in the patients. After 6 months of observation, the incidence of MetS decreased by 35% in comparison with the control group.

Table 1. Nutritional recommendations in the DASH diet [24, 37]

Amount of nutrients in the DASH diet	27% of E from fats in DFI 6% of E from unsaturated fatty acids in DFI 18% of E from protein in DFI 55% of E from carbohydrates in DFI *Dietary cholesterol 150 mg/d *Sodium 1500 - 2300 mg/d *Potassium 4700 mg/d *Calcium 1250 mg/d *Magnesium 500 mg/d *Dietary fiber 30 g/d		
Number of individual food product portions per day or week in the DASH diet according to calorie supply			
Food groups	1600 kcal	2100 kcal	3100 kcal
Grain products	6 p/d	7-8 p/d	12-13 p/d
Vegetables	3-4 p/d	4-5 p/d	6 p/d
Fruit	4 p/d	4-5 p/d	6 p/d
Low-fat dairy products	2-3 p/d	2-3 p/d	3-4 p/d
Lean meat, poultry and fish	1-2 p/d	2 p/d	2-3 p/d
Nuts, seeds, legume seeds	3 p/week	4-5 p/week	1 p/d
Fats and oils	2 p/d	2-3 p/d	4 p/d
Sweets	0	5 p/week	2 p/d

DASH- Dietary Approaches to Stop Hypertension; E- energy; DFI- daily food intake; *Nutrient content in a 2100 kcal; p/d - portions per day; p/week - portions per week

SUMMARY

The prevalence of MS depends on the criteria used to diagnose the disease, in accordance with the definitions of MS and the characteristics of the study group, especially its age.

The most important etiological factors of MS are abdominal obesity and insulin resistance, which are closely related and constitute the central link of MS, increasing the cardiometabolic risk of the patient.

Excess fat located inside the abdominal cavity is particularly dangerous for the development of MS in the future. A large accumulation of intraperitoneal fat is associated with an increase in hormone levels secreted by this tissue and proinflammatory factors - adipocytes and lowering of the hormone adiponectin, protecting against the development of MS.

Insulin resistance is considered to be the key pathogenetic mechanism of MS. One of the mechanisms explaining the effect of insulin resistance on endothelial function is the reduction of vasodilatation and the associated disruption of glucose distribution to tissues susceptible to insulin. In addition, insulin resistance leads to increased release of free fatty acids from the tissues, resulting in increased production of free oxygen radicals.

Metabolic syndrome is a complex disorder, therefore its treatment should be multifactorial and intense. It is necessary to implement proper dietary management, physical training program and

pharmacological treatment. Treatment with MS should begin with weight reduction, which affects the occurrence of abdominal obesity and increase physical activity, leading to increased sensitivity of tissues to insulin.

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