Review

Effects of the Mediterranean diet on the components of metabolic syndrome

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Keywords

Mediterranean diet • Metabolic syndrome • Effect mechanisms

Summary

Metabolic syndrome, also as known as Syndrome X or Insulin Resistance Syndrome, is a complex health problem featuring visceral obesity (the main diagnostic criterion), insulin resistance, dyslipidemia and high blood pressure. Currently, this health condition has gained a momentum globally while raising concerns among health-related communities. The World Health Organization, American Heart Association and International Diabetes Federation have formulated diagnostic criteria for metabolic syndrome. Diet and nutrition can influence this syndrome: for example, the Western diet is associated with increased risk of metabolic syndrome, whereas the Nordic and Mediterranean diets and the Dietary Approach to Stop Hypertension are potentially beneficial. The Mediterranean diet can affect the components of metabolic syndrome due to its high dietary fiber, omega 3 and 9 fatty acids, complex carbohydrates, antioxidants, minerals, vitamins and bioactive substances, such as polyphenols. These nutrients and bioactive substances can combat obesity, dyslipidemia, hypertension and diabetes mellitus. The mechanisms by which they do so are generally related to oxidative stress, inflammation (the most common risk factors for metabolic syndrome) and gastrointestinal function. The literature also shows examples of positive effects of the Mediterranean diet on the metabolic syndrome. In this review of the literature, we shed light on the effects, mechanisms and dynamic relationship between the Mediterranean diet and metabolic syndrome.

Definition of metabolic syndrome

Metabolic syndrome, also known as Syndrome X or Insulin Resistance Syndrome is a complex abnormality associated with coronary artery disease [1]. Visceral obesity (abdominal obesity/android type obesity), insulin resistance (IR), hypertension and dyslipidemia are components of this cluster of metabolic problems [2]. There are many diagnostic criteria that have been developed by different organizations (Tab. I). Visceral obesity is the basic diagnostic criterion of metabolic syndrome and is associated with generalized low-level inflammation, accompanied by elevated serum concentrations of pro-inflammatory cytokines, such as tumor necrosis factor alfa (TNF-α), which can decrease insulin sensitivity in human tissues. Pro-inflammatory cytokines are known to affect negatively blood pressure hemostasis and lipid metabolism. Besides low-grade inflammation, visceral obesity is commonly related to overnutrition. A positive energy balance has some long-term comorbidities such as IR and coronary artery disorders. This explains why visceral obesity is the main diagnostic criterion of metabolic syndrome [2-4]. Other common complications include stroke, myocardial infarction and diabetes mellitus [5].

The prevalence of metabolic syndrome differs between countries. Aguilar et al. [6] reported a 33% overall prevalence of metabolic syndrome in the United States of America (USA) in 2012. Liang et al. [7] reported a 38.3% prevalence in 2018. In 2017, prevalence was 48.8% in Qatar [8] and 42.87% in Iran [9]. Metabolic syndrome, a preventable health problem, is therefore very common all over the world. This condition is definitely related to unbalanced and Western style nutritional habits and also sedentary lifestyle behaviors which are common even in childhood. Practices such as a healthy diet and physical activity may protect against metabolic syndrome. The literature shows benefits of the Mediterranean diet in decreasing risk of metabolic syndrome [10-12].

Diagnostic criterAia of metabolic syndrome

As already mentioned, obesity is the main diagnostic criterion for metabolic syndrome. Defined as undesirable weight gain, it is a common chronic non-communicable disease of our time [13].

Obesity, especially visceral/abdominal obesity, is associated with comorbidities such as IR, high blood pressure and dyslipidemia (e.g. low high-density lipoprotein, HDL and high triacylglycerol, TAG) [14]. Insulin resistance is defined as poor tissue response to the hormone insulin and it is definitely related to visceral obesity with its associated inflammation and oxidative stress. IR may increase dyslipidemia, atherosclerosis and other coronary artery disease risk factors. It is regarded as the first stage of type II diabetes mellitus [15]. Another modifiable cause of mortality is high blood pressure, which is a risk factor for renal dysfunction, myocardial infarcts and stroke. Angiotensin-converting enzyme (ACE) system impairment and high sodium intake are related to high

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blood pressure [16]. Dyslipidemia means low plasma concentrations of HDL, high TAG and/or low-density lipoprotein (LDL). There are two types of dyslipidemia: primary and secondary. Secondary dyslipidemia is related to issues such as obesity and IR which are related in turn to overnutrition [17]. Figure 1 shows these mechanisms as a summary.

Risk factors for metabolic syndrome

There are two types of risk factors for metabolic syndrome: those that can and cannot be altered. Diet, physical activity and smoking are alterable risk factors that people can change to reduce their risk of metabolic syndrome [23]. A Western diet is more likely to induce metabolic syndrome than certain other diet models [24], because it includes a large proportion of red meat, processed red meat products, refined grains, high-fat dairy products and few fruits, vegetables, nuts or legumes [25]. Saturated, trans and omega 6 (n-6) fatty acids, simple carbohydrates, sucrose and salt are major elements of the Western diet, which is poor in complex carbohydrates, dietary fiber and n-3 fatty acids [26]. The above elements can be associated with oxidative stress, inflammation, dyslipidemia and non-communicable disorders such as obesity and its comorbidities [27]. Another risk factor for metabolic syndrome is sedentary lifestyle [28]. Regular physical activity can increase energy expenditure, lipolysis and insulin sensitivity, while decreasing blood pressure. It can improve blood lipid parameters [29]. Thus, there is a relation between sedentary lifestyle and metabolic syndrome risk [28, 29]. Smoking, one of the worst habits, is linked to accumulation of abdominal fat and visceral obesity, IR, dyslipidemia, hypertension and other abnormalities which are all linked to oxidative stress and inflammation [30]. High alcohol consumption can also increase health risks, such as visceral obesity, poor insulin sensitivity, high blood pressure and abnormal lipid profile [31].

The Mediterranean diet is the most effective nutrition model which is a potential agent to decrease noncommunicable chronic disorders via its contents. It includes many beneficial nutrients that can influence metabolic pathways adversely affected due to chronic diseases, of course, has a potential impact on metabolic syndrome (see section 2.2). Accordingly, we review the recent literature on the links between the Mediterranean diet and metabolic syndrome.

Tab. I. Diagnostic criteria for metabolic syndrome according to various health organizations.

Organization	Visceral obesity	TAG	HDL	Blood pressure (BP)	Fasting plasma glucose	Other	Reference
• World Health Organization (WHO) • Diabetes, IR or impaired glucose tolerance PLUS two or more other criteria.	Body mass index > 30 kg/m^2 Waist hip ratio *For males* > 0.9 *For females* > 0.85	≥ 150 mg/dL	*For males* < 35 mg/dL *For females* < 39 mg/dL	≥ 140/90 mmHg	Impaired glucose tolerance or diabetes and/or IR	Microalbuminuria *Urinary albumin excretion rate* ≥ 20 µg/min *Albumin creatine ratio* ≥ 30 µg/mg	WHO [18]
– International Diabetes Federation (IDF) – Visceral obesity PLUS two or more other criteria.	Waist circumference Defined with ethnic-specific values	≥ 150 mg/dL (1.7 mmol/L) or specific treatment for this abnormality	*For males* < 40 mg/dL (1.03 mmol/L) *For females* < 50 mg/dL (1.29 mmol/L) or specific treatment for this abnormality	Systolic BP ≥ 130 mmHg or Diastolic BP ≥ 85 mmHg or treatment of previously diagnosed hypertension	≥ 100 mg/dL (5.6 mmol/L) or previously diagnosed with type II diabetes	-	IDF [19]
- American Heart Association (AHA) - At least three criteria.	Waist circumference *For males* ≥ 102 cm (≥40 inches) *For females* ≥ 88 cm (≥ 35 inches)	≥ 150 mg/dL (1.7 mmol/L) or specific treatment for this abnormality	*For males* < 40 mg/dL (1.03 mmol/L) *For females* < 50 mg/dL (1.29 mmol/L) or specific treatment for this abnormality	Systolic BP ≥ 130 mm Hg or Diastolic BP ≥ 85 mmHg or treatment of previously diagnosed hypertension	≥ 100 mg/dL or specific treatment for this abnormality	-	Grundy et al. [20] Alberti et al. [21] AHA [22]

The Mediterranean diet vs common diets

Various nutrition models, such as the Dietary Approach to Stop Hypertension (DASH), the Nordic diet and the Mediterranean diet have been designed as alternatives to Western style eating habits, which have spread all over the world [32]. DASH was developed to decrease the risk of hypertension and it is often prescribed for people diagnosed with this disorder. DASH may also be effective against obesity, coronary artery disease and related non-communicable disorders [33]. The Nordic diet is a nutritional model based on the nutritional habits of the Nordic peoples [34]. The Mediterranean diet is another region-specific nutritional model based on the healthy eating habits of Mediterranean peoples [35]. These three nutrition models (DASH, Nordic and Mediterranean diet) are rich in nutrients beneficial for health [33-35]. The Western diet contains many harmful elements which may increase the risk of non-communicable diseases [36]. The United Nations Educational, Scientific and Cultural Organization (UNESCO) has listed the Mediterranean diet as an Intangible Cultural Heritage [37].
From this point, it is possible to indicate, DASH is a therapeutic nutrition model and there is no food pyramid to make it easier for adherence to this nutrition model. Nordic diet is based on the Nordic region-related nutrition habits which is so difficult to adopt by other people elsewhere. And also, some recommendations are not compatible with the optimal nutrition principles such as canola oil consumption (due to omega 6 content). In this prospect, the Mediterranean diet has a general food pyramid with easy food consumption recommendations while each recommendation is objective and compatible with the principles of optimal nutrition.

Beneficial nutrients and bioactive substances in the Mediterranean diet

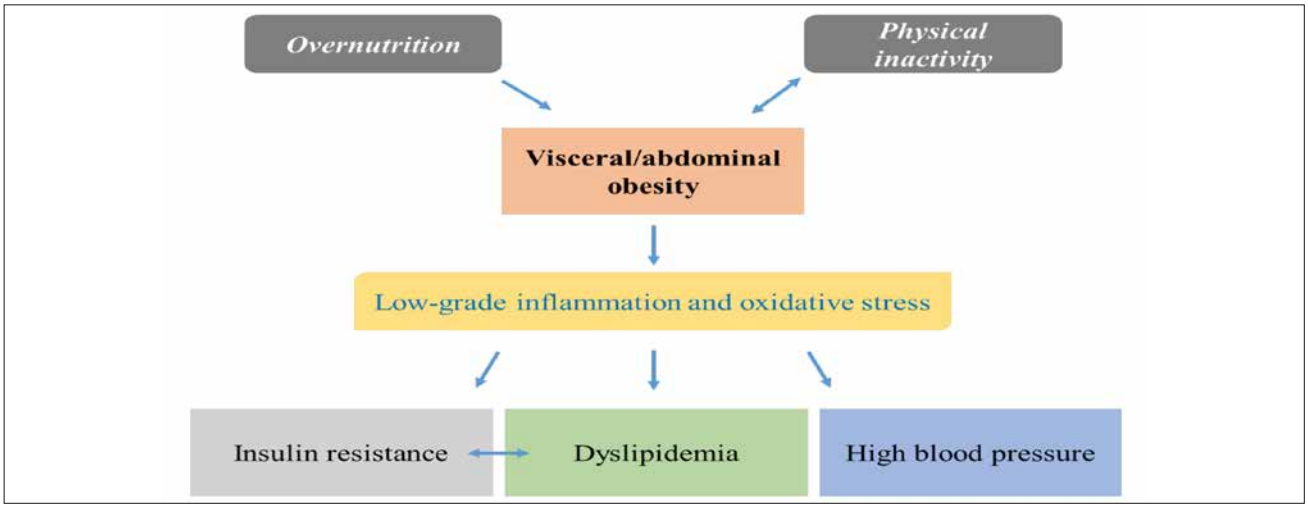
The Mediterranean diet includes items that are consumed with different frequencies, indicated in Table II as *often*, *moderate*ly and *rarely* [38, Tab. II].

Bach-Faig et al. [40] developed a Mediterranean diet pyramid with consumption frequencies and amounts. The pyramid also includes suggestions for physical and social activities. In 2020, Serra-Majem et al. [41] updated the pyramid with sustainability principles and Dayi et al. [42] replaced some items with traditional foods of Cyprus to facilitate users in that location and decrease human impact on the planet.
Certain items of the Mediterranean diet contain polyphenols such as naringenin, apigenin, kaempferol, hesperidin, ellagic acid, oleuropein, rosmarinic acid, resveratrol and quercetin, as well as dietary fiber, monounsaturated fatty acids such as omega 9 (n-9), polyunsaturated fatty acids such as omega 3 (n-3), complex carbohydrates and many vitamins (A, C and E) and minerals (calcium, potassium, magnesium etc.) which can reduce the risk of metabolic syndrome [43-46]. Figure 2 shows the nutrients and their food sources according to the basic Mediterranean diet pyramid.

Effects of dietary nutrients and bioactive substances on metabolic syndrome diagnostic criteria

Figure 3 shows the potential beneficial effects of the Mediterranean diet on the different components of metabolic syndrome. Olive oil is a typical item of the Mediterranean diet and its polyphenols can mitigate the risk of metabolic syndrome by reducing of visceral obesity, IR, blood pressure and lipid peroxidation. These polyphenols can also block signaling and expression of nuclear factor kappa B (NFKB), important risk factors for metabolic syndrome, thus decreasing secretion of proinflammatory cytokines [47, 48]. Another typical item of the Mediterranean diet is red wine. The main polyphenol in red wine, resveratrol, can exert anti-inflammatory and antioxidant effects [49, 50]. Resveratrol may also help regulate the human gut microbiota, an important component of metabolic syndrome, activate sirtuin 1, which is important for lipolysis, and activate adenosine mo-

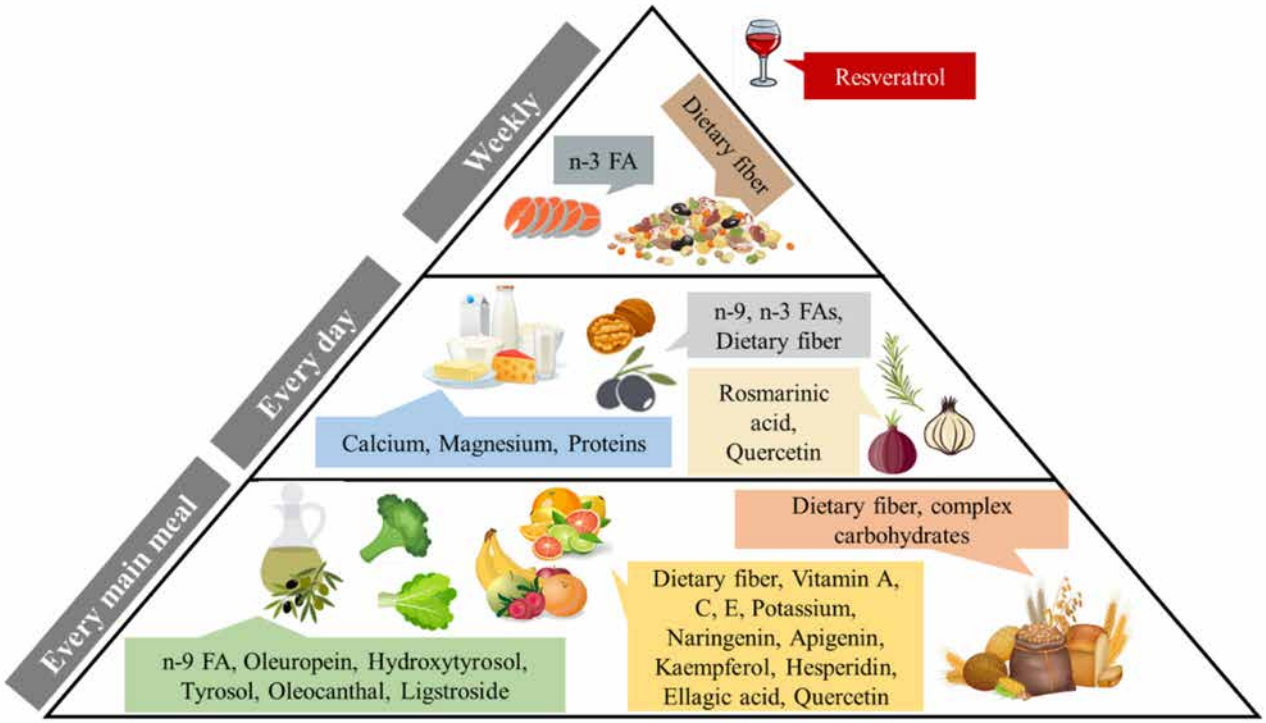
Fig. 1. Simple mechanism of development of metabolic syndrome.



Tab. II. Consumption frequencies of the various items of the Mediterranean diet [38, 39].

Consumption frequencies		
Often	Moderately	Rarely
Olive oil, vegetables, fruit, nuts, legumes, unprocessed cereals	Fish, red wine, dairy	Poultry, red meat, processed red meat products

Fig. 2. Some nutrients and polyphenols of the Mediterranean diet that may reduce the risk of developing metabolic syndrome [Prepared by authors, based on the references in section 2.1., 3rd paragraph].



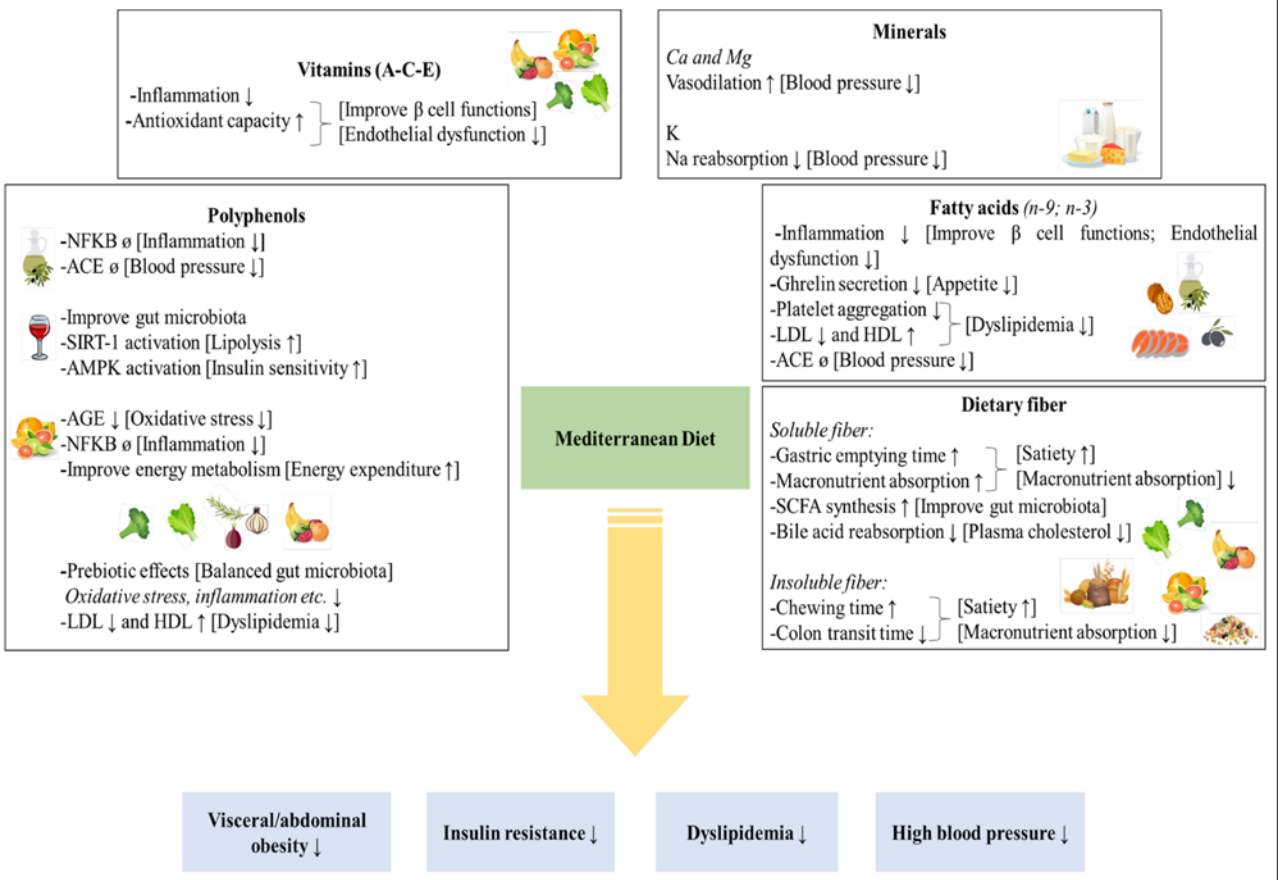
nophosphate protein kinase, which can increase insulin sensitivity [49, 50].

Citrus production and consumption are common in the Mediterranean region. Citrus polyphenols can decrease advanced glycation end products and block NFKB expression, thus decreasing oxidative stress and inflammation in the human body. A decrease in oxidative stress and inflammation biomarkers may in turn increase insulin sensitivity, improve lipid metabolism and lower blood pressure. Polyphenols such as naringenin may improve energy metabolism thus reducing visceral obesity [51]. Mediterranean vegetables, fruits and spices are good sources of polyphenols, important bioactive substances which as we have said, can block oxidative stress- and inflammation-related pathways. They therefore increase plasma concentrations of HDL and decrease those of LDL, as well as improving IR, body mass index and blood pressure [52]. Dietary polyphenols can be an effective prebiotic, potentially decreasing pathogenic and increasing beneficial microorganisms of the gut microbiota. A balanced microbiota may be related to good glucose tolerance and insulin secretion, while decreasing lipogenesis and inflammation [53]. In summary, polyphenols typical of the Mediterranean diet can decrease inflammation, oxidative stress, IR, lipid oxidation, body weight, blood pressure and endothelial dysfunction, reducing the risk factors for metabolic syndrome [54].

The Mediterranean diet includes some beneficial fatty acids such as n-9 and n-3 (due to frequent consumption of olive oil and moderate consumption of fish), while containing few saturated and trans fatty acids [39]. Omega 9 fatty acids, especially oleic acid, have antioxidant and anti-inflammatory effects and may therefore improve pancreatic beta-cell functions, insulin sensitivity and endothelial function [55]. Oleic acid can affect hypothalamic function and decrease ghrelin secretion [55]. It may inhibit platelet aggregation. It can also decrease plasma concentrations of LDL and increase those of HDL [56]. The oleic acid and polyphenols of olive oil can inhibit the ACE pathway, thus regulating blood pressure [57]. Omega 3 fatty acids can also diminish metabolic syndrome criteria [58, 59].

There are two types of dietary fiber: soluble and insoluble [60]. Soluble and insoluble fiber both have potential beneficial effects on metabolic syndrome [61]. Soluble fiber increases gastric emptying time and macronutrient absorption by increasing intraluminal viscosity. It may therefore be effective for reduction of body weight and regulation of postprandial blood glucose levels. During

Fig. 3. Potential effects of the Mediterranean diet on different components of metabolic syndrome. Each box indicates major nutrients and nutritional substances with effects marked as up or down arrows, increased or decreased effect consequently. Furthermore, potential general effects were marked with brackets. [Prepared by authors, based on the references in section 2.2.1.



↓: Reduction; ↑: Enhancement; Ø: Inhibition []: Potential general effect

fermentation, soluble fiber produces short chain fatty acids, which can decrease glucose and fatty acid production by the liver, as well as absorption of macronutrients via inhibition of enterocyte contact of these [62]. In addition, soluble fiber reduces bile acid reabsorption so the liver has to produce more bile acid. Since cholesterol is a building block of bile acid, while our body produces new bile acid, plasma concentrations of cholesterol decrease [63]. Insoluble fiber increases chewing time and decreases colon transit time, which stimulates the vagus nerve and creates a sense of satiety. These mechanisms can lead to lower food intake and nutrient absorption which are important factors against obesity and IR [62]. According to the literature, complex carbohydrates can have similar effects [64].

Vitamin A, C and E are antioxidants that can protect against oxidative stress which plays a role in many non-communicable disorders such as IR, cardiovascular disease and cancer [65, 66]. Antioxidants can reduce stress on pancreatic beta-cells and tissues. These effects may increase insulin sensitivity and secretion which are important factors against IR and for promoting weight loss [67]. These vitamins also decrease proinflammatory cytokines and reactive oxygen species, improving endothelial function. They therefore have roles in blood pressure regulation, lipid metabolism and cardiovascular health [68, 69].

Minerals such as calcium, magnesium and potassium can have antihypertensive effects [70]. Low calcium intake can stimulate the renin-angiotensin pathway, increasing blood pressure through sodium reabsorption, while calcium deficiency stimulates parathyroid hormone secretion further increasing calcium uptake by cells, which can cause peripheral vascular resistance and an increase in blood pressure [71].

The calcium antagonist magnesium decreases calcium concentrations in cells and increases certain prostaglandin E series which in turn instigate vasodilation [72]. Likewise, potassium is a sodium antagonist which decreases reabsorption of sodium, a prohypertensive mineral, by the kidneys [73].

In addition to these nutrients and bioactive substances beneficial for metabolic syndrome, the Mediterranean diet features fewer harmful items, such as saturated and trans fatty acids, linoleic acid (n-6), cholesterol, simple carbohydrates, sodium, nitrites and nitrates, and contains lower total fats [38, 39, 74].

Based on these potential effects, the Mediterranean diet carries a chance to decrease the risk of metabolic syndrome and increase life expectancy. On the other hand,

the effects of the Mediterranean diet are not only limited to metabolic syndrome. So, it can be estimated that, governments/health authorities can decrease financial expenditure on health if they develop some programs to increase adherence to the Mediterranean diet.

Relation between other patterns of the Mediterranean diet and metabolic syndrome

Social and physical activities and fun are important components of the Mediterranean lifestyle. These factors are related to physiological and psychological wellbeing [40]. Regular physical activity has positive effects on health, such as decreasing fat mass, plasma levels of LDL and TAG, inflammation, oxidative stress and blood pressure, while increasing insulin sensitivity, glucose tolerance and plasma levels of HDL [75]. Due to these beneficial effects, regular physical activity has to be a complementary behavior to the Mediterranean diet to further decrease the risk of the metabolic syndrome. And also, WHO suggests at least 150 minutes/week of moderate-intensity physical activity for adults to be healthy. Thus, all the Mediterranean diet pyramids have regular physical activity suggestions at the base [40-42].

Even more, the adherence to the MD is also embedded into the attitude of individuals for encouraging their own food production. This brings up two positive features, firstly the activity levels are increased and secondly the environmental impact becomes self-rewarding. Therefore, this circle is a very proliferative one: the more the MD is favored, the more the self-productivity is achieved resulting in a stronger life style adaptation [42].

Social activities are important for mood: depression and anxiety are linked to many diseases, higher food intake and lower physical activity, which are risk factors of metabolic syndrome [76]. Furthermore, chronic melancholy may cause inflammation and oxidative stress and so be related to metabolic syndrome [77].

Table III list various studies on the subject. For the meta-analysis, 'number of studies' shows how many original studies are included and the sample size of studies has been shown as 'n'.

Results of some current studies support the potential effect mechanisms of the Mediterranean diet on metabolic syndrome which this review article shows. According to these results, the Mediterranean diet has been shown to be effective for weight loss, regulation of blood glucose and lipids, decreasing inflammation and blood pressure (Tab. III).

In conclusion, the Mediterranean diet is an effective nutritional model against non-communicable chronic disorders anywhere in the world. This review examined one such disease, metabolic syndrome, via a literature search for related mechanisms. Future research should address local Mediterranean food consumption by country, such as Cyprus, and its effects on the components of metabolic syndrome.

Acknowledgments

None.

Conflicts of interest

There are no conflicts of interest.

Tab. III. Studies on the effects of Mediterranean diet on metabolic syndrome.

Authors	Type	Effects of Mediterranean diet
Kastoroni et al. [78]	Meta-analysis (Number of studies: 50; n: 534,906)	0.42 cm ↓ waist circumference 1.17 mg/dL ↑ HDL 6.14 mg/dL ↓ TAG 2.35 mm Hg ↓ systolic and 1.58 mm Hg ↓ diastolic BP
Huo et al. [79]	Meta-analysis (Number of studies: 9; n: 1178)	0.30% ↓ HbA1c 0.72 mmol/L ↓ FPG 0.55 μU/mL ↓ fasting insulin 0.14 mmol/L ↓ total cholesterol 0.29 mmol/L ↓ TAG 1.45 mm Hg ↓ systolic and 1.41 mm Hg ↓ diastolic BP
Richard et al. [80]	Original research (n: 26 males)	C-reactive protein (CRP) ↓ IL-6, IL-18 and TNF-α ↓ ≥8.5 cm waist circumference ↓ IL-6 and IL-18 ↓
Moosavian et al. [81]	Systematic review (Number of studies: 10; n: 856)	Improved body measurements, plasma lipid profile and glucose regulation
Mayneris-Perxachs et al. [82]	Original research (n: 424)	Incidence, reversion and prevalence of metabolic syndrome ↓
Pavić et al. [83]	Original research (n: 124)	HDL ↑ and systolic BP ↓ The Mediterranean diet was effective for the components of metabolic syndrome
Meslier et al. [84]	Original research (n: 82 healthy overweight and obese participants)	Plasma cholesterol and LDL ↓ Insulin sensitivity ↑ Systemic inflammation ↓

↓: Reduction; ↑: Enhancement

Authors' contributions

TD searched the literature and wrote the main outline of the article. MO contributed the concept of the article and revised the main outline of the manuscript.

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