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## MEDITERRANEAN DIET AND CARDIOVASCULAR DISEASES

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**Summary:** Treating a person that has a cardiovascular disease diagnosis (CVD) is very complex and it has to be individualized. However treatment always includes a dietary change. The reason for this approach lies in the large number of risk factors behind CVDs. The most emphasized are the following: hypertension, hyperlipidemias, smoking, overweight and obesity, lack of physical activity and unfavorable dietary habits. Dietary approach, mostly, includes hypocaloric diet on DASH (Dietary Approaches to Stop Hypertension) principle or Mediterranean diet. Mediterranean diet is one of the most intensively researched dietary principles, which is not true only for Mediterranean countries. Large prospective studies have shown this diet's relation to prevention of CVDs, including smaller incidence of mortality and morbidity due to CVDs. Every other person in Croatia, Serbia and Montenegro dies of CVDs. It is estimated that till the year 2030 more than 23 million people worldwide will die of CVDs annually. Large public health significance of CVDs conveys the need of adequate and effective preventive action. This is where the Mediterranean diet has positioned itself. Its distinctiveness lies in the unique combination of foods, which despite variations between Mediterranean countries, has the same basics that incorporates high intake of fresh fruits and vegetables, milk and fermented dairy products, fish and whole-grain, olive oil and red wine. Moreover, it includes a psychosocial aspect, which presents an important feature of this, not only a diet principle, but a way of life. Besides the positive impact on CVDs, this diet has also been correlated with lower incidence of carcinomas, preterm death, dementia, depression and Alzheimer's disease. Despite a decreasing trend in mortality due to CVDs in the last few years, morbidity is still high. The percentage of older citizens (geriatric population) is on the rise; therefore, the quality of life is becoming a priority. Mediterranean diet may be the solution.

**Keywords:** Mediterranean diet, cardiovascular diseases, risk factors, mortality, characteristic foods, research

### *Epidemiology of Cardiovascular Diseases*

Cardiovascular diseases present the number one cause of death worldwide. WHO estimates that 17.3 million people die from CVDs and predicted mortality rate by 2030 is more than 23 million people. It is estimated that 30% of all deaths are due to CVDs. Despite the trend of lower mortality rate due to CVDs last years, they are still the main cause of mortality. Burden of CVDs is even more pronounced in low- and middle-income countries, which account for 80% of all CVD caused deaths world-wide [1].

Every other person in Croatia, Montenegro and Serbia die from CVDs; countries are in the group of countries having high risk of CVD mortality [2, 3, 5]. In Croatia, 48.7% of deaths were due to CVDs in 2011 [2], in Montenegro 56.8% of deaths were due to CVDs in 2006 [3], while in the Republic of Serbia 56.0% of deaths were due to CVDs in 2007 [4].

National health survey conducted in Montenegro in 2008 showed that 42.8% of adults were diagnosed with chronic disease and the leading diagnoses were the following: hypertension, hyper-

lipidemias, and chronic heart disease [3]. Data from Serbian 2006 study titled „Health of population in Serbia” shows improvement compared to 2000; however, RFs for CVDs are still highly abundant. Those data shows that 33.6% of adults smoke, 46.5% of adults has hypertension, 18.3% of adults are obese, and 74.3% of the population is physical inactive [4].

### *Cardiovascular Diseases Risk Factors*

Individual and complex approach to each patient with CVD is necessary due to the multiple risk factors (RFs) behind CVDs. Frequently mentioned CVD RFs are listed in the Table 1. RFs like gender, age, physical build or race cannot be changed. However, the list of those that can be modified is longer, and through their modification a direct impact can be made on the development and, more importantly, prevention of CVDs.

CVD risk assessment is simplified with a wide range of different risk calculators shown graphically in form of charts that have been developed to ease up the use by healthcare professionals and individuals [6, 8]. One of the most known and

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frequently used is the chart developed by the World Health Organization (WHO) and the International Society for Hypertension (ISH) [6]. This tool signals 10 year risk for fatal or non-fatal outcome by including the following RFs: gender, age, smoking, and cholesterol. In addition, this prediction is specially adapted for patients with type 2 diabetes; one of the most important systemic disorders linked to CVDs [9]. On the other hand, some of the newly accepted RFs like endothelial inflammation, blood clotting, change in lipid profile after meal, oxidative stress or endothelial function are still not included in these CVD risk assessment tools.

Table 1. CVDs Risk Factors [6, 7]

RISK FACTORS THAT CANNOT BE MODIFIED	Gender Age Genetic predisposition Physical build Race
RISK FACTORS THAT CAN BE MODIFIED	Smoking (passive smoking) Low physical activity Alcohol consumption Diet Obesity Hypertension, diabetes, hyperlipidemia Stress

It is believed that physical inactivity contributes to CVD etiology with 37%. Regular physical activity reduces heart and coronary disease risk, lowers blood pressure, contributes to body mass maintenance, has beneficial effect on the psychological and physical condition of a patient and helps to overcome stress [6, 7, 10]. Thus, importance of physical activity is multifold and in many ways helps cardiovascular system, for example, increased oxygen transport to heart muscle increases functionality and electrical stability of the heart. In addition, physical activity has positive effect on lipid metabolism, increases HDL cholesterol and decreases LDL cholesterol, lowers blood pressure, reduces the occurrence of type 2 diabetes, increases insulin sensitivity and reduces thrombocyte aggregation [10, 11]. Studies have shown that minimum an hour of jogging per week can reduce the risk of heart disease by 42%, while 30 minutes of brisk walking a day can reduce the risk of heart disease by about 18% and the risk of stroke by about 11% [12]. Furthermore, 30 minute walking per day is enlisted in the official preventive guidelines for CVDs [6, 7].

Increased body mass is linked to increased blood lipids, susceptibility to diabetes and increased blood pressure. Increased body mass is frequently linked with low physical activity [10]. It is believed that obesity contributes to CVD etiology with 6%. In addition, waste circumference over 88 cm for females or over 102 cm for males is an additional CVD RF [6, 7].

Hypertension (blood pressure >140/90 mmHg) contributes to the development of CVD by 13%. Currently, 15-37% of the adult population worldwide has high blood pressure, while at 60 years of age this prevalence increases to 50% of population. WHO estimates show that 45% of CVD caused deaths are associated with hypertension [13]. Moreover, WHO estimates demonstrate that 6 million people annually die from the effects of smoking. From that number 600,000 deaths are due to the effects of passive smoking [14]. The contribution of smoking is 19%.

In addition, chronic emotional conditions such as stress, anxiety, hostility, insecurity and depression are taking an increasing toll on human health. It is believed that the risk from psychological and social factors for developing CVD is as high as the risk from common CVD RFs like obesity, smoking and high blood pressure [6, 10]. Studies have shown that men have a higher risk of developing CVD than women during their child-bearing age. This effect is attributed to protecting effect of hormones. After menopause, the incidence of coronary heart disease in men and women gradually equalizes. After 60 years of age, this ratio is 1:1. According to statistics, women have fewer CVDs diagnosed, but if they are diagnosed with any of CVDs they die more often [6, 7, 15]. This trend was confirmed for Croatia [2]. However, it is important to stress that both men and premenopausal women respond positively in lipid profile and blood pressure after introduction of the diet for people with cardiovascular risk [16].

Furthermore, with aging human body gets more exposed to the environment, which results in more frequent complications; heart and blood vessels are no exception. Risk for coronary heart disease is higher in men over age 40 and for women over age 50, especially if they are exposed to two or more RFs [7, 10].

Some studies indicate that the tendency towards CVDs is inherited. It is not a classical hereditary transmission of the disease; it is more a clear correlation between the disease in parents and manifestation in children [10].

### ***Nutritional Treatment of Patients Diagnosed with Cardiovascular Disease or Risk Factors***

Treating a patient with cardiovascular disease (CVD) diagnosis is very complex and it has to be individualized, and treatment always includes change of their diet [17, 18]. Frequently, these patients are prescribed a hypocaloric diet. If the first stage did not result in significant change of blood parameters (usually total cholesterol and LDL cholesterol), statins are introduced. Statins have proven their beneficial effect in lowering LDL cholesterol and consequently reducing cardiovascular events incidence [19].

### ***Dietary Guidelines***

It should be pointed out that the need for change in diet in terms of preventing chronic non-communicable diseases was acknowledge and listed as one of the ten main goals of the Croatian nutritional policy in 1999 [22]. Montenegro's Ministry of Health in 2009 published „Action plan for nutrition and food safety in Montenegro 2010 – 2014“ [19], and the Republic of Serbia in 2010 published National program for prevention [4]. As noted by Gurinović et al. development of the national program in Serbia was necessary because several studies on quality of nutrition in Serbia together with the statistical data on mortality and morbidity rates due to CVDs showed the need for more intensive preventive action [23].

WHO defined dietary goals for the prevention of CVDs that should be met by all countries. European Heart Network [20] published nutritional guidelines for the prevention of CVDs on the European level. Dietary guidelines include regular physical activity (60 to 80 minutes of moderate or 30 minutes of intensive physical activity per day), decrease in body mass index (BMI) (goal is BMI of 23 kg/m<sup>2</sup>), while mainly focusing on intake of fat, fresh fruits and vegetables, dietary fibers and salt [21].

While planning a diet for a patient with CVD or a person at high risk of CVDs the highest importance has fat intake, and more importantly sources of that fat [21]. Plant based fats (oils) should be a main fat source while planning their diet because animal fats present significant source of saturated fatty acids (FA) [18, 24]. Earlier guidelines were focused on lower intake of cholesterol, but today the shift has been made towards saturated FA intake [25]. Intake of saturated FA should be restricted to less than 10% of the total energy derived from fats (overall intake of fats should be less than 30% of the total energy intake) [21]. Also, intake of trans-FA should be less than 2% of the

total energy intake from fats [21]. Substitution of saturated FA from animal sources with mono and polyunsaturated FA from plant sources should lead to reduction of blood cholesterol level [18, 26]. Official reports show that the intake of trans-FA is far beyond the recommended with the United Kingdom and the United States of America having the highest intakes [6]. Another important aspect is marketing and television advertising of sweets and fast food, which are the two food groups that represent the main source of trans FA in daily diet. Advertising of these products is considered a direct predictor of trans FA intake [27].

The INTERSALT study correlates the surplus intake of salt to the higher arterial blood pressure and increased risk of CVDs [28]. Moreover, large number of studies has shown that even slight decrease in dietary intake of salt leads to decreased arterial blood pressure [29]. A prospective study conducted in Finland on 2436 men and women aged 25-64 years showed clear correlation between increased intake of salt and increased risk of CVDs. This study shows that salt intake over 6g/day shows 56% increased risk of coronary disease, 36% increased risk of CVD death, and 22% increased risk of all cause mortality [30]. Therefore, accomplishing intake of up to 6g/day of salt is considered as an effective preventive measure from CVDs [18, 31]. This goal for salt intake is the main objective of the Croatian initiative CRASH [25, 32], and the Strategic plan for prevention and control of non-communicable diseases in the Republic of Serbia [33]. Despite large number of national programs targeting lower intake of salt, salt intake remains elevated around the world. The highest intake of salt was found in Hungary of 17 g/day/person, with excessive 12 g [6].

Alcohol consumption in high amounts is correlated to increased death rate, especially due to CVDs [6]. Still, results are inconsistent. Large number of studies showed relatively small risk of CVDs for moderate alcohol consumption [18, 34-36]. However, alcohol also shows some positive effects like increases level of HDL cholesterol and lowers thrombocyte activity [34, 35], which directly reduces the risk of thrombosis that lies behind the etiology of CVDs.

Developing a diet plan for a patient with CVD usually includes consideration of one of the two approaches. The first one is the Dietary Approaches to Stop Hypertension, or so called the DASH diet [37]. This approach is based on a low intake of saturated fats and sodium with increased intake of fruits and vegetables combined with low fat dairy products [37]. The other approach is the

Mediterranean diet, which was confirmed by the Lyon Diet Heart Study and the PREDIMED study to have direct correlation to lower mortality rate, especially due to CVDs [18, 38, 39].

### **Mediterranean Diet – The Definition**

Keys presented the first Mediterranean diet (MD) definition. He proved, for the first time, health benefits of the MD in a research encompassing more than 12 700 people from seven Mediterranean countries [40]. In Croatia, several studies dealing with the dietary habits of inhabitants on isolated island have been conducted [41]. All showed that even though the diet of islanders is (eg. Vis, Mljet) fundamentally Mediterranean, there is a shift that can be noticed. This shift is seen in increased consumption of industrial products, sugar and red meat, which coincides with lower consumption of fish, fruits and vegetables [41]. Although in their diets there is some traditional MD present many islanders show unfavorable shift in

their dietary patterns [42]. These findings are in accordance with the increased problems related to CVDs among researched islanders [41].

Even though there is no such thing as one MD, some characteristics are shared. These are: a) high intake of fats (more than 40% of total energy intake), mostly from olive oil; b) high intake of wholegrain, fruits, vegetables, legumes and nuts; c) moderate to high consumption of fish; d) moderate to low consumption of white meat (poultry or rabbit meat) and dairy products, mostly yoghurt or fresh cheese; e) low consumption of red meat and meat products; f) moderate consumption of red wine with meal [43, 44]. The last MD pyramid (Picture 2) includes two main changes related to consumption of cereals and dairy products. By and large, these relate to intake of wholegrain and low fat dairy products. In addition, physical activity, socialization and psychosocial aspects related to dining with friends and family have been added to the pyramid [43].

Picture 2 The Mediterranean diet pyramid [43]



### **Mediterranean Diet's Characteristics**

Discussions on the MD usually imply that the MD is a diet rich in fats. However, there are different types of the MD. Some are high in fats (Greece) and other are quite low in fats (South Italy, South France) [40, 45]. For example, the Lyon study researched a low fat content [10, 40]

with the main fat source being canola oil margarine not olive oil [45].

Beneficial effect on cardiovascular health olive oil owns to its FA profile. Mono and polyunsaturated FA reduce blood cholesterol level and risk of heart diseases when they substitute one portion of saturated FA in the diet. The most common FA from the family of monounsaturated FA is oleic

acid, the main FA of olive oil [47]. Due to its high content in olive oil and other antioxidants, consumption of olive oil reduces LDL cholesterol simultaneously affecting HDL cholesterol. Additionally, this composition of olive oil prevents oxidation of LDL cholesterol [47, 48]. Also, olive oil contains other components out of which plant sterols, and beta-sitosterols are the most important in reduction of cholesterol levels [25, 47]. Therefore, olive oil has several protective mechanisms on atherosclerosis.

Fish is a food group with almost ideal nutritional profile. They are rich in essential FA, omega-3 FA and proteins [24, 43]. Two main omega-3 FA in fish are eicosapentaenic (EPA) and docosahexaenoic acids (DHA). It has been proved that supplementation of 2 to 4 g of omega-3 FA/day in patients with increased triglycerides will reduce their triglycerides by 25 to 30%. Additionally, 1 g/day of omega-3 FA given to patients after recovered myocardial infarction significantly reduces overall mortality and risk of sudden death due to arrhythmia [46].

Studies have shown that the MD long-term leads to weight loss, change in BMI, systolic and diastolic blood pressure, fasting blood glucose level, total cholesterol and endothelial inflammation indicator and high-sensitivity C-reactive protein (hs-CRP) [45, 49]. The largest hospital in Croatia, University Hospital Centre Zagreb provides its patients with hypolipemic MD since 2011 [50].

One of the main additional characteristics of the MD is moderate consumption of red wine [43]. Phenols from red wine, especially resveratrol (also present in red grapes), decrease oxidation of LDL cholesterol, causatively affecting atherogenicity, act as an anti-aggregation, and anti-inflammatory agents, and diminish thrombocyte aggregation, contributing to possible anti atherosclerotic effects. Significant part of wine's protective effects can be attributed to HDL cholesterol increase [25, 35, 51].

#### ***Mediterranean Diet and Health Benefits***

After publication of the results of the Lyon Diet Heart Study (Lyon) [40], number of studies reported on various health benefits of the MD. In 2003 Trichopoulou et al. published the first modern epidemiological study that examined impact of the MD on different health aspect [52]. This prospective follow-up study encompassed 22 043 adult Greeks, and was observing their diet with so called Mediterranean score. Study found that the higher the score was, the lower mortality rate from CVDs was. Final data showed that mortality rate from

CVDs and cancers was inversely correlated to higher MD compliance [52], and the study confirmed earlier findings from the Lyon study [10, 40]. Higher compliance to the MD correlates to the lower prevalence of obesity [53], which was also confirmed by Croatian studies [41, 42]. Meta-analysis published in 2010 summed-up the whole inverse relation between the MD, CVDs and overall mortality [39]. Additionally, meta-analysis published in 2011 showed that the MD has higher protective effect on health than a low fat diet [49].

The last large prospective study conducted in Spain, the PREDIMED study, have shown that adoption of the MD leads to 30% reduction in complications due to hearth diseases, and 40% lower risk of heart attack, which was based on a 5 year follow-up [54]. In addition, this study confirmed earlier findings; the importance in primary prevention from the Lyon study [10, 40], epidemiologic significance from the aspects of morbidity and mortality [39, 52] from CVDs, as well as from cancers, dementia, and the risk of Alzheimer's disease [55-57]. Furthermore, Skarupski et al. [58] showed that dietary pattern that is more in accordance to the MD (based on MedDietScore principle) shows potential in reducing depression among people of 65 years and older.

Recently, more emphasis is put on possibilities to modify the MD for non-Mediterranean populations, seeing it as a possible solution for non-communicable diseases [59]. This is due to a large number of prospective studies performed in the non-Mediterranean countries that, besides already determined effect of the MD, show MD's potential to protect from premature death [60-64], and cerebrovascular diseases [65].

#### **CONCLUSION**

For years, Mediterranean diet is on the top of scientific interest. The reason lies in proven correlation with CVDs prevention, and causatively lower mortality and morbidity due to CVDs. Moreover, this effect was found for other non-communicable chronic diseases, from cancers to dementia. The Mediterranean diet is not just a specific dietary regime; it represents a way of life. Characteristic combinations of foods, with some specifics between Mediterranean countries make it plain and complicated at the same time. Undoubtedly, the Mediterranean diet will keep on positioning itself as one of the possible solutions to global issues related to CVDs.

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