Review article

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DIETETIC APPROACHES IN PREVENTION AND TREATMENT OF CARDIOVASCULAR DISEASES

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Cardiovascular diseases (CVDs) are responsible for 30% of all death causes worldwide, and according to the World Health Organization predictions this negative trend will be continued further on. CVDs include diseases related to macro and microvascular system. There are numerous underlying risk factors, but the biggest emphasis is on those that can be modified and therefore lower the incidence of CVD, its complications, and causative morbidity and mortality due to CVDs. This is especially related to hypertension, hyperlipidemias, smoking, increased body mass, diagnosis of type 2 diabetes, and inadequate level of physical activity and unfavourable dietary habits. The last two are the mostly highlighted and all preventive measures and actions go in that direction. From the aspect of diet, high intake of fats in total, and especially saturated and trans fats, high intake of salt, and high intake of simple carbohydrates, i.e. refined carbohydrates present the backbone of unfavourable dietary habits responsible for rising global problem of CVDs. World's, European's as well as the national's guidelines for prevention and treatment of CVDs contain specific guidelines aiming at the abovementioned aspects. Several dietary approaches arise from these guidelines, but the Mediterranean diet positioned itself as the most optimal for its centuries-old reputation. The other thing is that the Mediterranean diet contains all of the principles set by guidelines, and has another important aspects - the aspects of cultural, sociological, and quality-of-life aspect. Mediterranean diet was and has remained the most frequently researched dietary principle, not only across the Mediterranean, but in countries with non-Mediterranean populations. All of these researches have proven its beneficial impact that goes well beyond the impact on CVDs. *Acta Medica Medianae 2014;53(1):65-72.*

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Epidemiology

Cardiovascular diseases (CVDs) are the main cause of death worldwide. According to the World Health Organization (WHO) in 2008 around the globe 17.3 million people died from CVDs, and it is estimated that by the year 2030 more than 23 million people annually will have died from CVDs (1). In other words, 30% of all death causes are from CVDs. Besides, premature death and the quality of life are significantly affected by CVDs (2). The fact that 80% of CVD-related deaths occur in undeveloped and developing countries is in line with the previous statement (1).

CVDs include myocardial infarction, heart failure, ischemic heart diseases (which are largely caused by impaired arterial flow), stroke, changes in leg vessels, arterial hypertension, and atherosclerosis (3). Despite notable trend of lower mortality rate due to CVDs for the last several years, in developed countries (2), as well as in Serbia and Croatia (4-7), CVDs still present the number one cause of death (1).

Both Serbia and Croatia are among the countries with high risk of CVD mortality (4,7). This is obvious from the fact that every other person dies from CVDs. In the Republic of Serbia, 56.0% of deaths were due to CVDs in 2007 (8). In Croatia, 48.7% of all death causes were due to CVDs in 2011 (7).

Risk factors

Some of the most commonly discussed risk factors (RF) for CVDs are shown in Table 1. One part of these cannot be modified, like gender, age, physical built or race; but the higher number of RFs can be modified. That is how the development of CVDs can be directly influenced, and more importantly prevented.

Table 1. CVDs risk factors (2)

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

To ensure simplified risk assessment, a range of different predictive charts has been developed. These charts should ensure easier risk assessment in practice, i.e. by medical doctors. One of the most known is the predictive chart developed by the WHO and the International Society for Hypertension (ISH) (2). This chart shows a 10-year risk assessment of fatal or non-fatal outcomes, and includes RFs of gender, age, smoking, blood pressure, and total cholesterol. Specific feature of this chart is in its adaptation for the type 2 diabetes, which is considered to be one of the most important systemic disorders related to CVDs (9). In addition to the above discussed predictive chart, The Mayo Clinic Risk Score for Mortality is also commonly used. This one calculates the risk of fatal outcome according to several clinical variables. By summing these variables, coefficient is determined, based on which the risk of premature death is estimated (10).

Some of the newly accepted RFs for CVDs such as inflammation, blood clothing, and change in lipid profile after meal, oxidative stress or endothelial function are still not included in CVD risk assessment tools. It is also important to assess nutrition according to geographic locations, with special insight in dietary patterns (e.g. consumption of food at home, dining out, and food consumption induced by stress), as well as the other interactions between food consumption and other behavioural indicators (11).

Data from the „Health of population in Serbia" study conducted in 2006 showed that despite improvements in CVD RFs from the 2000 data, RFs are still highly abundant. Data showed that 33.6% of population smoke, 46.5% have hypertension, 18.3% are obese, and 74.3% of the population are physically inactive (8). Stojanović et al. (12) conducted a research on a student population from the University of Niš Faculty of Medicine and showed that all of the above mentioned RFs are highly expressed in this population as well, regardless of their educational background. Authors have noted some differences between genders; besides obesity, the most significant RFs are smoking and alcohol consumption among male students, and in female students smoking and physical inactivity (12). Recently finished study (30th November 2013) entitled „Hello, how are you?" will show eventual shifts in previously determined patterns, and what steps should be taken by the Serbian public health system.

Increased body mass is for sure one of the major RFs, often linked to increased blood lipids, susceptibility to diabetes, increased blood pressure, and its frequently linked with low physical activity (13). Obesity *per se* contributes to the CVD etiology with 6%. In addition, waist circumference over 88 cm for females or over 102 cm for males is an additional CVD RF (2).

For physical inactivity contribution to the CVD etiology is estimated 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 and helps to overcome stress (2,13). The importance of physical activity is multiple, enhancing the overall cardiovascular system through increased oxygen transport to heart muscle, which reduces myocardial oxygen demand and increases functionality and electrical stability of the heart. In addition, physical activity shows 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 (13,14). Studies have shown that jogging in duration of one hour or more 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% (15). Furthermore, 30 minute walk per day is enlisted in the official preventive guidelines for CVDs (2).

Around the globe, 15-37% of adult population 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 (16). For hypertension (blood pressure >140/90 mmHg) contribution to the development of CVD is estimated to be 13%.

Smoking is considered to be responsible for 6 million people annually, according to WHO. From that number, 600.000 deaths are due to the effects of passive smoking (17). The contribution of smoking is 19%.

Increasing number of evidence suggests that chronic emotional conditions such as stress, anxiety, hostility, insecurity and depression are taking an increasing toll on human health. The risk of psychological and social factors for developing CVD is as high as from the common CVD RFs like obesity, smoking and high blood pressure (2,13).

Studies have shown that men have a higher risk of developing CVD than women in childbearing age. This effect is attributed to protective role 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 the statistics, women have fever CVDs diagnosed, but if they are diagnosed they die more often (2,18), as confirmed for Croatia (7). However, it is important to stress out that both men and premenopausal women respond positively in change of lipid profile and blood pressure after the diet for CVD RF has been introduced (19). This was achieved after the 2 month compliance to the Mediterranean diet (MD), but the significant improvement of insulin homeostasis was achieved only in men (19).

Etiology of CVDs includes inheritance. Still, it is not a classical hereditary transmission, but rather more clear correlation between disease in parents and expression in offspring (13).

With aging human body gets more exposed to the environment, resulting in larger number of complications; heart and blood vessels are no exception. Risk of CVD is higher in men over 40 years of age, and in women over 50 years of age, especially if they are presented with two or more RFs (13).

Nutrition of patients with CVDs

Nutrition is always the first stage in treatment of a patient with diagnosis of CVD (3,20). Only in case when change in a diet do not result in positive change of blood parameters (total cholesterol and LDL cholesterol), drugs are introduced. Medicament therapy includes statins that show extreme efficacy on lowering LDL cholesterol, causatively reducing the incidence of CVD events (21). In planning a diet, international, i.e. European and national guidelines should be consulted.

WHO defined dietary goals for the prevention of CVDs while accounted for all RFs, and they should be met by European countries (2). European Heart Network (EHN) published nutritional guidelines for the prevention of CVDs on the European level. These 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^2), while mainly focusing on intake of fat, fresh fruits and vegetables, dietary fibres and salt (22).

It should be noted that the need for change in diet in terms of preventing chronic non-communicable diseases was acknowledged and listed as one of the ten main goals of the Croatian nutritional policy in 1999 (23). As stated in the policy: „Modification of dietary habits will induce lower incidence of chronic non-communicable diseases that are correlated to the diet. Or in other words, modification should include lower consumption of salt, refined carbohydrates, intake of fats should be restricted by 15% (~6g) of saturated fats, while consumption of fresh fruits and vegetables, milk and dairy products, and fish should be increased" (23). Dietary guidelines by WHO and EHN have been included in the National preventive programme in the Republic of Serbia (8). As emphasized by Gurinović et al., development of the national program was a necessity since several studies on quality of nutrition in Serbia together with the statistical data on mortality and morbidity rates due to CVDs required more intensive preventive action (24).

Intake of fats has been stressed out as the most important aspect in the diet plan for both a patient with CVD, or a person with increased RF (22). The main fat source should be plant oils, because animal fats present significant source of saturated fatty acids (FA) (20,25). According to EHN guidelines, the 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) (22). Earlier guidelines were focused on lower intake of cholesterol, but today the shift has been made towards intake of saturated FA (26), and restricted intake of trans-FA of less than 2% of the total energy intake from fats (22). Substitution of saturated FA from animal sources with mono and polyunsaturated FA from plant sources reduces blood cholesterol (20,27). Intake of trans-FA is far beyond the recommended; the United Kingdom and the United States of America have the highest intakes (2). Importantly, marketing and television advertising of sweets and fast food, the two food groups that present the main sources of trans-FA in a daily diet, is considered to be a direct predictor of trans-FA intake (28).

Surplus intake of salt is correlated to the higher arterial blood pressure and increased risk of CVDs, as confirmed by the INTERSALT study (29). Moreover, a large number of studies has shown that even slight decrease in dietary intake of salt leads to decrease in arterial blood pressure (30). A prospective study conducted in Finland on 2.436 men and women aged 25-64 years showed a clear correlation between increased intake of salt and increased risk of CVDs. Salt intake of 6 g/day is correlated with 56% increase in risk of coronary disease, 36% increase in risk of CVD death, and 22% increase in risk of all cause mortality (31). Therefore, accomplishing intake of 6g of salt per day is considered to be an effective preventive measure for CVDs (20,32). This is also the main goal of the Croatian initiative CRASH (26,33). Despite a 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 17g/day/person, with excessive 12g (2).

Alcohol consumption in high amounts is correlated to increased death rate, especially due to CVDs (2). Still, studies have shown mixing results. A large number of studies showed a relatively small risk of CVDs for moderate alcohol consumption (20,34-37). Alcohol shows undoubted positive effects: increases the level of HDL cholesterol and lowers thrombocyte activity (34-

37), directly reducing the risk of thrombosis, which is underlined in the CVD etiology.

Discussing a diet for a patient with CVD usually includes two principles. These are the so-called DASH diet i.e. The Dietary Approaches to Stop Hypertension (38). This principle is based on a low intake of saturated fats and sodium with increased intake of fruits and vegetables combined with low fat dairy products (38). Second, and the most often discussed principle is the Mediterranean diet, which was confirmed by the Lyon Diet Heart Study, research done by Trichopoulou and colleagues in Greece, and more recent the PREDIMED study in Spain to have direct correlation with lower mortality rate, especially CVDs related (20,39,40).

Mediterranean diet

Mediterranean diet is not a special type of diet or diet regime; it presents a group of dietary habits traditionally followed among people from the Mediterranean area. The concept and the definition were introduced by Ancel Benjamin Keys, American physiologist and nutritionist, from the School of public health from the University of Minnesota. He spent half of his life in the Mediterranean searching for the explanation of relatively small incidence of CVDs among native Mediterranean population. For the first time scientifically was proven that the Mediterranean diet has beneficial impact on health, according to the results gained from the study that encompassed 12.700 people from the seven Mediterranean countries (41).

Fundaments of the MD are seasonal fruits and vegetables, and every day foods differ throughout the week in order to maintain diversity of the diet. Large quantities of fresh fruits and vegetables are consumed, and if otherwise consumed, thermal preparation is very short. Foods that dominate the MD are presented in the Mediterranean diet pyramid (Picture 1).

There is no such thing as the one, unique MD. Some features of the MD are shared between the Mediterranean countries. The shared features 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 (42,43). The last Mediterranean diet pyramid includes two main changes related to the consumption of cereals and dairy products. Generally, these changes refer 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 (42).

Foods characteristic for the Mediterranean diet

When discussing the MD, usually the emphasis is put on its richness in fats. However, different types of the MD differ in fat content. Some are high in fats (Greece) and others are quite low in fats (South Italy, South France) (41). For example, the Lyon study was on low fat content (13,41,44), but the main fat source was canola oil margarine, not olive oil (11).

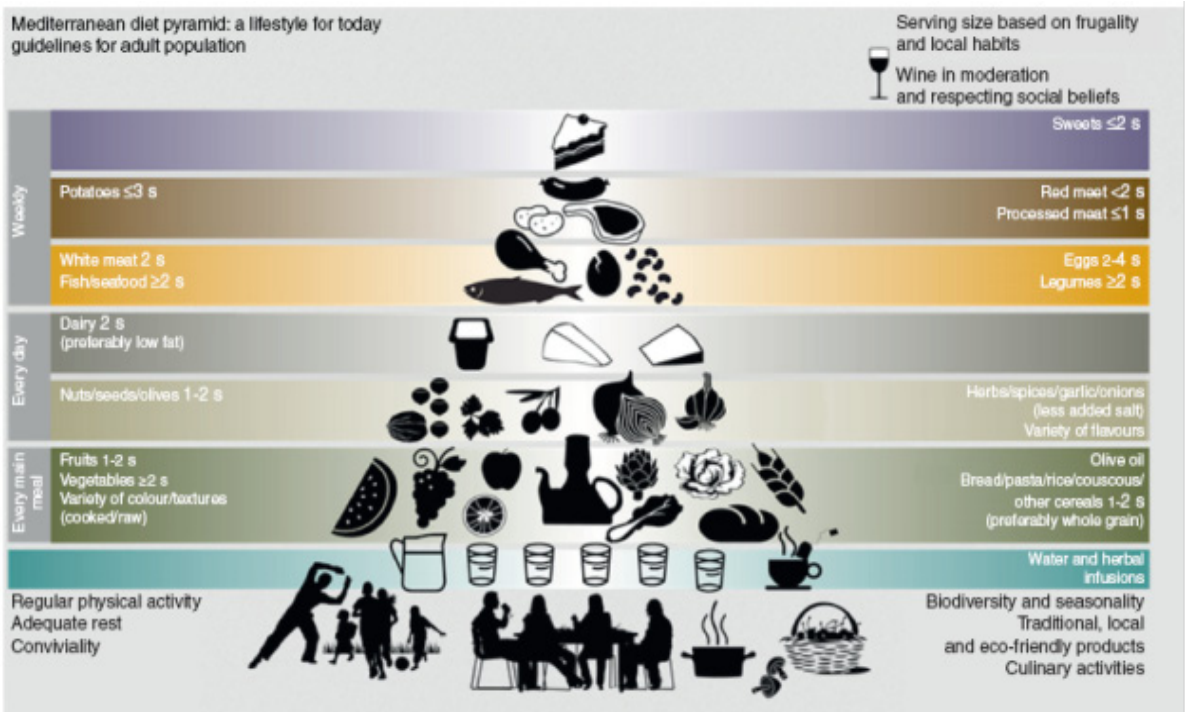

Figure 1. The Mediterranean diet pyramid (42) (source: Arós F, Estruch R. Mediterranean Diet and Cardiovascular Prevention. Rev Esp Cardiol 2013; 66(10): 771-4)

Olive oil has its beneficial effect on cardiovascular health 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 (45). Due to the high content of oleic acid and other powerful antioxidants, consumption of olive oil reduces LDL cholesterol simultaneously increasing the level of HDL cholesterol. Additionally, they are responsible for preventing oxidation of LDL cholesterol, acting as preventive mechanism on atherosclerosis. Also, olive oil contains other components out of which plant sterols, and beta-sitosterols are the most important in reduction of cholesterol levels (26,45).

Fish presents food group of almost ideal nutritional profile. They are rich in essential FA and proteins. FA from fish are unsaturated, and include essential FA necessary for the optimal health (25,42). Two main omega-3 FA in fish are eicosapentaenic (EPA) and docohexaenoic acids (DHA). In patients with increased triglycerides supplementation with 2 to 4g of omega-3 FA/day will reduce their trigliceride level by 25 to 30%. Also, supplementation with 1g of omega-3 FA per day in patients after recovered myocardial infarction significantly reduces the overall mortality and risk of sudden death due to arrhythmia (11).

Moderate consumption of red wine is an additional characteristic of the MD (42). Red wine phenols, especially resveratrol (also present in red grapes), decrease the 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 (26,37,46).

Health significance of the Mediterranean diet

After the results of the Lyon Diet Heart Study (44) have been published, a number of studies reported on various health benefits of the MD. In 2003 Trichopoulou et al. published the first modern epidemiologic study that examined the impact of the MD on different health aspect (47). This prospective follow-up study encompassed 22.043 adult Greeks, and was observing their diet with the so-called Mediterranean score: the higher the score, the lower mortality rate from CVDs was. The final analysis showed the inverse correlation between higher compliance to the MD and mortality rate from CVDs and cancers (47), confirming earlier findings from the Lyon study (13,44,48). This study showed that the MD should be observed entirely, and not its specific components (41). Meta-analysis published in 2010 summed-up complete inverse relation between the MD, CVDs and overall mortality (40).

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 five-year follow-up (49). PREDIMED study was a multicenter prospective study on 7.500 participants without CVDs. Participants were randomized in three groups: control group was on a low fat diet, while the other two groups followed the MD with an additional intake of extra virgin olive oil or nuts. This study confirmed earlier findings on importance of primary prevention from the Lyon study (13,44,48), and epidemiologic impacts on mortality and morbidity (40,47), not only related to CVDs, but also cancers, dementia and the risk of Alzheimer's disease (50-52).

The MD presents focus of interest in the non-Mediterranean populations as well. As early as 1999, Kouris-Blazos et al. (53) conducted a research in Australia, on Australians and Greeks living in Australia. They have showed that higher compliance to the traditional MD leads to lower risk of death by 17% in elderly (70 years of age and older), without difference in these populations (53). These findings have encouraged large interest on quality of nutrition in the non-Mediterranean populations comparatively to the MD, compiling a large number of prospective studies in the last few years (results published between 2011 and 2013). Besides already determined effects of the MD, studies have shown its preventive role from premature death (54-58), and lower death rate due to cerebrovascular diseases (59).

The important findings published in a meta-analysis from 2011 showed that the MD has higher protective effect than the low-fat diet (60). After a two-year follow-up the MD showed higher beneficial effect on weight loss, BMI, systolic and diastolic blood pressure, fasting blood glucose, total cholesterol and high-sensitivity C-reactive protein (h-CRP).

All of these studies continue to position the Mediterranean diet as a possible solution for the global problem of chronic non-communicable diseases (60).

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DIJETETIČKI PRISTUPI LIJEČENJU KARDIOVASKULARNIH BOLESTI

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Kardiovaskularne bolesti (KVB) su odgovorne za 30% svih smrtnih slučajeva u svijetu, a prema procjenama Svjetske zdravstvene organizacije, ovaj će se negativan trend nastaviti. U kardiovaskularne bolesti ubrajaju se stanja koja obuhvataju makro- i/ili mikrovaskularni sustav. U pozadini ovih bolesti krije se veliki broj rizičnih faktora, no najveći naglasak je upravo na onima koji se mogu modificirati i na taj način smanjiti incidenciju KVB, njezine komplikacije, te posljedično mortaliteta i morbiditeta uslijed KVB. Posebno se ističu hipertenzija, hiperlipidemija, pušenje, povećana tjelesna masa, prisutnost dijabetesa tipa 2, te niska razina fizičke aktivnosti i loše prehrambene navike. Upravo su poslednja dva najistaknutija i sve se preventivne mjere usmjeravaju upravo na te aspekte. Gledano s aspekta prehrane, visok unos masnoća, posebice zasićenih masnoća i trans masti, visok unos soli i jednostavnih ugljikohidrata, odnosno rafiniranih ugljikohidrata predstavljaju okosnicu loših prehrambenih navika, odgovornih za sve veći globalni problem KVB. Svjetske, evropske, pa tako i nacionalne smjernice za prevenciju i liječenje KVB u sebi sadrže smjernice usmjerene upravo na ove aspekte. Iz smjernica je proizišlo nekoliko prehrambenih principa, no mediteranska prehrana se pozicionirala kao najoptimalnija zbog stoljećima stare reputacije. Osim toga, mediteranska prehrana u sebi sadrži sve principe postavljene u smjernicama, a u sebi sadrži još jedan važan aspekt, a to je kulturološki, sociološki i aspekt kvaliteta života. Mediteranska prehrana bila je i ostala najintenzivnije proučavan prehrambeni princip, ne samo u zemljama Mediterana, već i u zemljama s nemediteranskom populacijom. Sva su istraživanja dokazala njezin povoljan učinak, koji seže daleko više od utjecaja na KVB. *Acta Medica Medianae 2014;53(1):65-72.*

Ključne reči: *kardiovaskularne bolesti, rizični faktori, prehrambene navike, prehrambene smjernice za kardiovaskularne bolesti, mediteranska prehrana*

