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REVIEW ARTICLE

What is the best diet for cardiovascular wellness? A comparison of different nutritional models

Silvia Migliaccio[1] · Caterina Brasacchio[2] · Francesca Pivari[2] · Ciro Salzano[3] · Luigi Barrea[3] · Giovanna Muscogiuri[3] · Silvia Savastano[3] · Annamaria Colao[3] · on behalf of Obesity Programs of nutrition, Education, Research and Assessment (OPERA) Group

Abstract

Cardiovascular diseases (CVD) represent to date the leading cause of mortality in both genders in the developed countries. In this context, a strong need for CVD prevention is emerging through lifestyle modification and nutrition. In fact, several studies linked CVD with unhealthy nutrition, alcohol consumption, stress, and smoking, together with a low level of physical activity. Thus, the primary aim is to prevent and reduce CVD risk factors, such as impaired lipid and glycemic profiles, high blood pressure and obesity. Different types of diet have been, therefore, established to optimize the approach regarding this issue such as the Mediterranean diet, Dietary Approaches to Stop Hypertension diet (DASH), vegetarian diet, ketogenic diet, and Japanese diet. Depending on the diet type, recommendations generally emphasize subjects to increase vegetables, fruits, whole grains, and pulses consumption, but discourage or recommend eliminating red meat, sweets, and sugar-sweetened beverages, along with processed foods that are high in sugar, salt, fat, or low in dietary fiber. In particular, we evaluated and compared the peculiar aspects of these well-known dietary patterns and, thus, this review evaluates the critical factors that increase CVD risk and the potential application and benefits of nutritional protocols to ameliorate dietary and lifestyle patterns for CVD prevention.

Introduction

Cardiovascular diseases (CVD) are the consequence of several different disorders such as excessive abdominal adipose tissue, hypertension, dyslipidemia, and glucose intolerance [1], which increase the risk of developing cardiovascular events such as stroke and heart attack. Certainly, CVD often overlaps with several of the above-mentioned comorbidities, which represent the greatest risk factors for all-cause mortality worldwide [2] and, indeed, CVD is still the first cause of mortality in both genders in industrialized countries worldwide [3]. Furthermore, the increasing incidence of CVD over the last 3 decades has become a burning health and socioeconomic priority, as well as the need for prevention of CVD and CV events through modifications of lifestyle [4]. The development of CVD is linked to unhealthy nutrition patterns (i.e., excessive intake of sodium and refined foods; added sugars; unhealthy fats; low intake of fruit and vegetables, whole grains, fiber, pulses, fish, and nuts), alcohol consumption, stress, and smoking, together with a sedentary lifestyle [5, 6].

Thus, a large body of scientific evidence has described how dietary intervention, and physical activity, might be the most important factors for prevention of CVD and could reduce heart disease. As the number of older individuals continues to increase, it is important to understand the pathophysiological mechanisms of metabolic changes in order to develop interventions that can be easily implemented to prevent noncommunicable diseases, such as CVD, which significantly alter quality of life, increase morbidity and mortality and, also, socioeconomic costs.

✉ Silvia Migliaccio
silvia.migliaccio@uniroma4.it

[1] Department of Movement, Human and Health Sciences, Health Sciences Section, University "Foro Italico", Rome, Italy

[2] Department of Health Sciences, University of Milan, Milan, Italy

[3] Dipartimento di Medicina Clinica e Chirurgia, Unit of Endocrinology, Federico II University Medical School of Naples, Via Sergio Pansini 5, 80131 Naples, Italy

Thus, this review will evaluate and highlight the potential nutritional factors predisposing to the increase of CVD risk and the potential of nutritional protocols to prevent CVD.

Search strategies

Articles were individually retrieved by each author up until August 2019, by search in PubMed (MEDLINE) using the following search terms: "Cardiovascular Diseases", "Obesity", "Diet", "nutrition", "glucose metabolism", Mediterranean diet (MeDi), ketogenic diet (KD), Japanese diet, vegetarian diet (Veg diet), Dietary Approaches to Stop Hypertension (DASH) diet. The reference lists of relevant articles and reviews were also searched manually. Eight hundred papers were identified, of which 136 were selected and included in the paper.

Nutritional factors

Energy excess

It is well known that diets characterized by energy excess, which leads to obesity, increase cardiovascular risk. Published data indicate how a 20–50% reduction in energy intake, in the absence of malnutrition, delays the onset of metabolic diseases, such as obesity and type 2 diabetes, in experimental animal models such as rats and mice [7]. Indeed, published clinical studies confirm that energy restriction reduces cardiovascular risk.

Interestingly, a small pilot study involving 24 subjects demonstrated how a 10-week energy restriction (80% of habitual) significantly reduced both systolic and diastolic blood pressure levels [8], which is known to be a CVD risk factor. In addition, a significant reduction of glucose levels was observed after a similar 10-week energy restriction diet [9], which implies an improvement of metabolic pattern, which is an additional risk factor for cardiometabolic disorders.

Furthermore, several studies indicate how a long-term reduced energy nutritional pattern improves cardiovascular risk demonstrating that a 2-year energy restriction diet could improve serum lipid profile, fasting glycaemia, and blood pressure levels [10–12].

More recently, the Comprehensive Assessment of the Long-term Effect of Reducing Intake of Energy trial evaluated the effect of long-term energy restriction on cardiovascular health. This multicenter randomized trial, which involved 218 subjects, was conducted as follows: two groups of subjects of which one had for 2 years a diet of 25% energy reduction and the other followed 2 years of habitual energy intake. The results indicated that already after 6 months of low-energy diet there was a significant reduction of body weight, and an improvement of lipid profile and blood pressure levels [13], both related to high CVD risk.

Saturated fat intake

High intake of saturated fat is linked to an increased CVD risk, primarily due to an increased concentration of low-density lipoprotein (LDL) cholesterol. Even more important, diets rich in saturated fat lead, in particular, to atherosclerosis [14] and insulin resistance, independently of adiposity status due to the increase they can induce in the level of atherogenic lipoproteins, LDL and very-low-density lipoprotein (VLDL), and the reduction of high density lipoproteins (HDL) [15]. Furthermore, diets rich in saturated fat lead to a low-grade inflammation status, considered a cardiovascular risk and a cause of insulin resistance. Further, intake of saturated fat promotes lipopolysaccharide uptake in the gut which can cause inflammation [16, 17] by its binding to TLR-4, which further explains the increased CVD risk. Activation of TLR-2, ceramide production and formation of lipid rafts also appear involved in the inflammatory process due to saturated fat [18–20]. The Seven Countries Study was one of the first trials evaluating CVD risk linked to saturated fat intake. This study evaluated cardiovascular mortality in 11,579 men who were observed for 15 years and the results demonstrated a positive correlation between cardiovascular deaths and saturated fat intake [21]. In the following years, a study investigated Japanese men living in Japan and Western countries indicating an increased prevalence of cardiovascular mortality in the Western country group, likely correlated to a diet with high-saturated fat intake, strongly suggesting that an imbalance of nutrients intake can alter homeostasis leading to an increase in CVD risk [14, 22].

Free sugars and refined starches' intake

Published data describe how people with overweight or obesity significantly eat more sweet products as compared with people with a healthy body weight and the risk of obesity or overweight increases of about 14% with each additional spoon of sugar (5 g) eaten every day [23]. Moreover, diets with high intake of free sugars and refined starches' are linked to elevated fasting triglycerides, a recognized CVD risk factor, while data on the effects on LDL-cholesterol levels are conflicting. In particular, the American Heart Association Scientific Statement recommended to significantly decrease the amount of free sugars intake and, further, to avoid fructose, instead of sucrose, often used for preventing hypertriglyceridemia, since fructose intake has been linked to increased metabolic alterations [24–27].

Diets with high amount of free sugars support de novo lipogenesis and liver fat and, in particular, the conversion of free sugars and refined starches to fat generates saturated fat, which is a well-known CVD factor risk. Fructose is the main sugar implicated in de novo lipogenesis due to its hepatic metabolism, in contrast to glucose that is predominantly metabolized in extrahepatic tissues, such as muscle tissue [28]. Also, fructose appears implicated in insulin resistance [29].

Further, conflicting data are present in the literature about the role of free sugars on blood pressure. Nevertheless, a recent meta-analysis confirmed that the use of free sugars within an isoenergetic diet does not have negative effects on blood pressure [30].

Dietary fiber intake

Dietary fibers can be defined as the portions of plant foods that are edible but cannot be completely broken down by digestive enzymes. It has been largely described that low dietary fiber intake is linked to increased risk of CVD while, in contrast, diets rich in fruits, vegetables, and whole grains have high-fiber contents. [31]. The positive effects of fiber on cardiovascular health are due to several factors such as increase in bile acids excretion, lowering cholesterol levels [32], reduction in fatty acid synthesis in the liver through the production of short-chain fatty acids resulting from fermentation [33], increase of insulin sensitivity [34] and increase in satiety, due to the space occupying food mass by fiber, leading also to a decrease in food intake, which then leads to a lower energy density diet [35].

Data in the literature report an inverse correlation between dietary fiber intake and CVD and total mortality. In particular, a recent study has demonstrated that people following a diet with low-fiber intake (~15.0 g/day) have a 23% higher total mortality as compared with people with a high fiber intake (~26.9 g/day), and this association appeared to be uninfluenced by either sex or race [36]. Moreover, a recent meta-analysis evaluated 15 prospective cohort studies with 1,409,014 subjects and confirmed the inverse association between dietary fiber intake and mortality for CVD [37]. In particular, similarly to what was demonstrated previously, an intake of ~29.6 g/day, comparable with the recommended doses of 30 g/day, was associated to a 23% reduced CV mortality compared with a low intake of ~14.0 g/day.

Fruit and vegetable intake

A low fruit and vegetable intake is considered one of the main causes of premature death worldwide, being responsible for 25.5 million deaths in 2013 [38]. Beneficial effects of fruit and vegetable are due to dietary fiber (as discussed later), vitamins, minerals, antioxidants content that reduce chronic diseases, total mortality and have a beneficial effect on gut microbiota [39, 40]. Furthermore, published data provide evidence of a positive effect of dietary fiber, fruit, and vegetable intake on serum cholesterol levels, blood pressure levels, inflammation, and platelet aggregation [41]. A recent meta-analysis, evaluating 95 unique cohort studies, showed that for each daily increase of 200 g of fruit, vegetables, and combined intake of fruit and vegetables there was an 8–16% reduction in the relative risk of coronary heart disease, 13–18% reduction in the relative risk of stroke, 8–13% reduction in the relative risk of CVD [42]. Overall, people with high fruit and vegetable intake (~500 g/day) have a 22% reduction of cardiovascular risk compared with people with low intake (0–40 g/day).

Dietary fiber

Several studies have highlighted the benefits of dietary fiber on cardiovascular health by improving the lipid profile and decreasing blood pressure; whereas a low dietary fiber intake is linked to higher CVD risk [43]. Moreover, high dietary fiber intake is associated with lower all-cause mortality [44]. Although the specific functions and mechanisms of action are not fully understood, the proposed mechanisms are that dietary fiber decreases cholesterol, glucose absorption and downregulates the expression of oxidative stress-related cytokines or the inflammatory response mediated by gut microbiota [45, 46].

Furthermore, the protective role of dietary fiber seems to be influenced not only by the amount of fiber but also by the specific type and source [47]. In fact, different types or sources of dietary fiber may be responsible for different physiological effects: soluble fibers are responsible for the cholesterol-lowering effect, whereas insoluble fibers influence the intestinal absorption of foods and the glycemic response [33, 48].

Interestingly, a recent study, in an experimental animal model of hypertensive mice, demonstrated that fibers and acetate led to the downregulation of the transcription factor Egr1, considered a master regulator in homeostasis in many systems, since it modulates the expression of a wide range of genes and pathways implicated in CVD processes, such as cardiac hypertrophy, renal fibrosis, and inflammation [49].

Moreover, regarding the lipid-lowering effect, soluble fibers found in whole grains, pulses, seeds, and nuts play a crucial role [50]. In particular, many studies have highlighted the potential benefits of beta-glucan, a water-soluble fiber mostly found in oat and barley. Beta-glucan consumption has been associated with lower triglycerides and LDL-cholesterol levels ~5–10% [51–53].

In this regard, a meta-analysis by Whitehead et al. highlighted that diets containing ~3 g/day of oat beta-

glucan decreased triglycerides and LDL-cholesterol levels, but without significant effect on HDL-cholesterol levels, even with a high beta-glucan intake (up to 12.4 g/day). Interestingly, a higher LDL-cholesterol-lowering effect was observed in subjects with type 2 diabetes and subjects with higher baseline LDL-cholesterol levels [54], suggesting a better efficacy in those with a worse metabolic profile.

Mirmiran et al. performed a prospective cohort study on 2295 healthy subjects followed for 4.7-year demonstrating that dietary fiber intake, especially from pulses, fruit, vegetable, and nut sources, had protective effect against the development of CVD events. Beneficial effects of vegetable fibers in reducing CVD risk appeared related to decreased triglycerides and triglycerides to HDL-cholesterol ratio during the study follow-up [55]. Finally, another recent study highlighted the link between dietary fiber, gut microbiota, and reduction of CVD risk, suggesting a potential role of microbiota in the modulation of CVD risk [56].

Polyunsaturated fatty acids (PUFA): omega-3

There is a growing evidence showing that omega-3 PUFAs have a variety of cardioprotective properties, such as reduction of plasma triglycerides, regulation of blood pressure, reduction of arrhythmias and inflammation, and improvement of endothelial dysfunction [57].

Omega-3, in particular eicosapentaenoic acid and docosahexaenoic acid, have been topics of experimental studies that have demonstrated several different mechanisms by which circulating and incorporated omega-3 PUFAs might act at cellular and molecular levels, including genetic and epigenetic modulations [58].

Nonesterified omega-3 PUFA or their acyl-CoA thioesters can bind and directly modulate activities of nuclear receptors and transcription factors that regulate gene expression in multiple tissues [59].

These receptors are central regulators of several cellular functions related to CVD, including lipid metabolism, glucose-insulin homeostasis, and inflammation [60]. Interestingly, effects of omega-3 PUFA on these pathways likely contribute to triglyceride-lowering [61] and increased production of "beneficial adipokines, batokines" known to improve metabolic homeostasis [62]. Moreover, omega-3 PUFA can reduce translocation of nuclear factor-kappa B to the nucleus, decreasing inflammatory cytokines production [63].

The anti-arrhythmic effects of omega-3 PUFAs appear mediated through mechanisms that include direct and indirect modulation of ion channel properties, membrane composition and fluidity, as well as anti-inflammatory and anti-fibrotic effects [64].

Interestingly, long-term omega-3 PUFA supplementation in humans induces prolonged atrial refractoriness and reduced vulnerability to inducible atrial fibrillation [65], which could explain their anti-arrhythmic effects. PUFA consumption can also affect resting heart rate and both systolic and diastolic blood pressure [66]. In short-term trials, omega-3 PUFA intake increased nitric oxide production, mitigated vasoconstrictive responses to norepinephrine and angiotensin II, enhanced vasodilatory response and improved arterial compliance [67–70]. Such effects could contribute to decrease systemic vascular resistance and blood pressure.

Monounsaturated fatty acids (MUFA)

More controversial are the available data on MUFA and cardiovascular protection, due to the small number of published studies. The most common MUFA in food are oleic acid, palmitoleic acid, and vaccenic acid.

The results of a recent meta-analysis indicate an overall reduction of risk of all-cause mortality (11%), cardiovascular mortality (12%), cardiovascular events (9%), and stroke (17%) when comparing the top versus bottom third of MUFA, olive oil, oleic acid, and MUFA: small fatty acids ratio [71]. In particular, only olive oil seems to be associated with reduced CVD risk. In fact, several other studies indicate that extra virgin olive oil (EVOO) seems to be the relevant factor in lowering the incidence of cardiovascular events, including myocardial infarction and stroke [72, 73]. Even if the molecular mechanisms exerted by EVOO are not fully understood, the healthy role of EVOO might be referred to its high level of MUFA and several biologically active phenolic compounds known to play important roles in cardiovascular protection [74].

Anthocyanins

Anthocyanins are polyphenolic compounds responsible for red, violet, and blue colors of fruit and vegetables, present also in red wine.

Several epidemiological revisions support the preventive effect of both anthocyanins and polyphenols towards the onset of CVD [75, 76], due to their antioxidant and anti-atherosclerotic activity [77, 78]. Moreover, preclinical studies, both in experimental animal models and in vitro cellular systems, support their potential role in influencing lipid profile, a commonly used biomarker of CVD risk. Anthocyanins can slow or inhibit the absorption of lipids and glucose in the gut and inhibit cholesterol synthesis, which results in a decrease in serum triglyceride, total cholesterol, and non-HDL cholesterol and in an increase in serum HDL [78, 79].

Phenolic compounds have a very low bioavailability: only 10% is absorbed in the small intestine, whereas about 90% is excreted or metabolized by the intestinal microbiota [80].

Therefore, the primary protective effect of anthocyanins cannot be due to the antioxidant properties, which will be active only at the intestinal level (where the concentration is high), but to their action as secondary intracellular mediators in different signaling pathways.

Other studies highlighted the cardioprotective and anti-inflammatory effect of anthocyanins. Specifically, anthocyanins intake promotes nitric oxide production that improves blood circulation and, on the other hand, can inhibit Nfk-B transcription, decreasing pro-inflammatory molecules production [81].

Zhu et al. highlighted the anti-inflammatory effect of anthocyanins in a randomized controlled clinical trial (RCT) [82]. In this study, a total of 150 subjects with hypercholesterolemia consumed a purified anthocyanins mixture (320 mg/day) or a placebo twice a day for 24 weeks. Anthocyanins consumption significantly reduced the levels of serum C-reactive protein (−21.6% vs. −2.5%), soluble vascular cell adhesion molecule-1 (−12.3% vs. 0.4%) and plasma IL-1β (−12.8% vs. −1.3%) compared with the placebo. They also found a significant difference in the LDL-cholesterol (−10.4% vs. 0.3%) and HDL-cholesterol level changes (14.0% vs. −0.9%) between the two groups.

If micronutrients play an important role in modulating CVD risk, it is also well known that maintaining normal body weight is a protective factor for CVD.

Bertoia et al. performed three prospective cohort studies on 124,086 men and women to assess whether dietary intake of specific flavonoid subclasses was associated with body weight change over time. Interestingly, increased consumption of most flavonoid subclasses, including anthocyanins, was inversely associated with body weight change over a 4-year time interval. The greatest magnitude of association was observed for anthocyanins, flavonoid polymers, and flavonols [83]. Thus, in this context, choosing high flavonoid fruits and vegetables, such as apples, pears, berries, and peppers, might help with weight control and CVD prevention.

Vitamins

Several studies indicate that vitamins E, C, and other antioxidants can reduce CVD by trapping organic free radicals and deactivating excited oxygen molecules to prevent tissue damage [84]. Antioxidants may have the ability to slow or prevent atherosclerotic plaque formation, likely, by inhibiting LDL-cholesterol oxidation [85].

However, data regarding the role of vitamin C and E in CVD prevention in human studies are still controversial.

In a pooled analysis of nine cohorts, vitamin C supplement usage, exceeding 700 mg/day, was significantly associated with a 25% reduction in coronary heart disease risk [86].

Sesso et al. performed a RCT on 4641 US middle-age men to evaluate whether long-term vitamin E or vitamin C supplementation decreases the risk of major cardiovascular events demonstrating, with an 8-year follow-up, that neither vitamin E nor vitamin C supplementation could reduce the risk of major cardiovascular events [87].

A RCT conducted by Ellulu et al. in 64 people with obesity and hypertension and/or diabetes, reported the potential anti-inflammatory effect of 500 mg of vitamin C, twice daily. Vitamin C might act by inducing a decline in CRP, IL-6, and fasting blood glucose after 8 weeks of treatment [88].

Regarding dietary vitamins intake (not supplemented), few studies were, to date, performed. A huge study by Zhao et al. examined the association of total carotene, vitamin C, and vitamin E from diet and the risk of mortality from all causes, cancer, and CVD in over 130,000 Chinese adults [89]. The results indicated an inverse association of total carotene and vitamin C with all-cause mortality in men. Compared with the lowest quintiles, the corresponding risk reductions in the highest quintile were 17% for both carotene and vitamin C. Although these associations were weaker in women than in men, the results were interesting and statistically significant.

Another study evaluated the intake of antioxidant vitamins (vitamin E, C, and A) from food and supplements in over 3000 postmenopausal women with no CVD for a period of 7-years follow-up, demonstrating that the intake of vitamin E from food was inversely associated with the risk of death from coronary heart disease without using vitamin supplements. Instead, the intake of vitamins A and C was not associated with lower risks of CVD death [90].

Age-related changes in body composition, metabolic factors, and hormonal levels, accompanied by a decline in physical activity, might all provide mechanisms for the tendency to lose muscle mass, gain fat mass and, also, increase subclinical inflammatory status which has been described as one of the mechanisms involved in atherogenesis and in CVD [1, 2].

In particular, obesity, which is due to an imbalance between energy intake and energy expenditure over a prolonged period, has always been known and recognized as a risk factor for metabolic diseases and CVD [91, 92]

Sedentary behavior

It is well known that lifestyle can strongly influence the development of metabolic chronic diseases, including CVD [93, 94]. In particular, physical activity and exercise can improve health and decrease CVD Risk [95]. However, few studies have evaluated whether patterns of sedentary time are linked with higher risk for CVD and data on sedentary time and higher risk for CVD are based mainly on self-

report. Interestingly, a recent published study, performed on over 5000 older women, demonstrated that high sedentary time, and long mean bout durations, were associated in a dose-response manner with higher CVD risk [96]. Another interesting recent study was performed with the aim of examining the association of sitting and moderate to vigorous physical activity (MVPA) with CVD and all-cause mortality, and of estimating the theoretical effect of replacing sitting time with physical activity. Interestingly, among the 149,077 subjects evaluated over an 8.9-year (median) follow-up a total of 8689 deaths, of which 1644 were due to CVD, occurred, demonstrating a statistically significant interaction between sitting and MVPA for all-cause mortality [97].

Different type of diets

Several types of diet have been proposed to prevent and reduce risk factors for CVD. Interestingly, in ancient Greek medicine, the word diet meant a set of rules of life to maintain the state of health and wellness of the subject, including nutrition and physical activity. However, the modern meaning refers to diet as what people eat. However, the word diet should include nutritional indications, in qualitative and quantitative terms, aimed to maintain good health and wellness in healthy individuals and, thus, intended to correct potential dietary mistakes, but, also, nutritional indications to subjects affected by certain pathological conditions for therapeutic, preventive, or experimental purposes. Different types of diets have, somehow, been characterized and/or developed to approach these specific issues. MeDi, DASH diet, Veg diet, KD, and Japanese appear to play a role in maintaining health and/or prevent metabolic chronic diseases in different subject categories.

Depending on the type of diet, recommendations emphasize increasing consumption of vegetables, fruits, whole grains, and pulses but discourage or even recommend eliminating red meat, sweets, and sugar-sweetened beverages, along with processed foods that are high in sugar, salt, or fat or low in fiber [98, 99].

Mediterranean diet (MeDi)

The MeDi diet is characterized by high consumption of fruits, nuts, vegetables, whole-cereal products, fish, and seafood; in particular, the consumption of whole-grain cereal products high in dietary fiber and the consumption of fruit and vegetables, have been reported to contribute to the reduced risk of obesity, type 2 diabetes and CVD. Moreover, this dietary regimen strongly suggests limitation of red meat, refined sugars, and saturated fatty acids [100]. MeDi has a large body of evidence in regard to its correlation with significant reduction in the incidence of mortality caused by CVD [101, 102]. Indeed, MeDi has been proven, by RCTs, observational studies, and meta-analyses to be beneficial for both primary and secondary prevention of CVD. One of the most prominent aspects of the MeDi is the high concentration of unsaturated fats, the significant sources of fiber and protein, coupled with a paucity of saturated fats. Both the American Heart Association/American College of Cardiology (AHA/ACC) and the European Society of Cardiology guidelines strongly endorse substituting mono- and polyunsaturated fats in place of saturated and trans-fatty acids for both primary and secondary prevention [103]. Data indicating the positive effects of MeDi have been produced in the RCT Lyon Heart Study, which showed that composite endpoints of CVD events and death were reduced for up to 4 years after an initial event in those subjects who were randomized to the MeDi group, thus establishing it as a staple also for secondary prevention [104, 105]. Recently, the PREvenciòn con Dieta MEDiterànnea investigators shows that subjects following the MeDi had fewer monocytes, inflammatory markers, and beneficial modulation of gene expression involved in LDL oxidation, [106]. Mechanisms underlying the beneficial effects of unsaturated fats content in olive oil, fish oil, and nuts on cardiovascular disease include improved lipid profiles and reduced blood pressure likely through reduced inflammation, oxidation, and coagulation [107]. Moreover, the increased fruit and vegetable intake in MeDi has also been linked to a lower body mass index and reactive oxygen species level. Thus, MeDi has been recognized by UNESCO as “intangible cultural heritage of humanity” for the well-demonstrated health benefits.

Dietary Approaches to Stop Hypertension (DASH) diet

The DASH diet was born in the USA with the aim to reduce blood pressure and, also, to prevent CVD [103]. This diet recommends a reduction of salt intake, a main factor for hypertension and it emphasizes the intake of fruits, vegetables, vegetable proteins, whole grain, low-fat dairy foods, and reduced saturated and total fat, being quite similar to the MeDi recommendations. The benefits of the DASH dietary pattern have been recognized by general dietary guidelines from the US-based National Heart, Lung, and Blood Institute (NHLBI) and the United States Department of Agriculture (USDA). International diabetes and cardiovascular clinical practice guidelines have also recommended the DASH dietary pattern for cardiovascular risk reduction [108].

In fact, RCT studies of the DASH dietary pattern demonstrated a decrease in LDL-cholesterol among other cardiometabolic risk factors and it also appeared, in prospective cohort studies, that the DASH diet was associated with a reduction in diabetes and cardiovascular mortality [109].

Vegetarian diet (Veg diet)

Veg diets are characterized by reduced or abolished consumption of animal products typically emphasizing vegetables, fruits, grains, pulses, and nuts intake. Though lacking a standardized definition, "vegetarian" generally describes a lacto-ovo vegetarian dietary pattern (here in, referred to as vegetarian), which is free of meat, poultry, and fish; however, "vegetarian" is occasionally used interchangeably to describe more restrictive dietary patterns such as vegan (eliminates eggs and dairy), semi-vegetarian (varying definitions), and fish-vegetarian (consumes fish but not meat). Abolishing meat, an attribute of Veg diets, is commonly presumed to contribute to the improved CVD health outcomes [110]. The AHA/ACC issued nutrition recommendations which include Veg diets among the dietary patterns that help to accomplish the AHA/ACC guidelines, together with the Mediterranean and the DASH diets. Populations following traditional plant-based diets, such as in rural Africa or in Asia, have low prevalence of CVD. The first major study to look at the vegetarian dietary patterns in the USA was conducted among Seventh-day Adventists and described a clear dose-response relationship between meat consumption and CVD risk [111]. The EPIC-Oxford study showed a 32% lower risk of CVD in vegetarians as compared with nonvegetarians (HR 0.68; 95% CI 0.58–0.81). In particular, a Veg diet is rich in phytonutrients such as carotenoids, lycopene, flavonoids, anthocyanins, and others, which work synergistically to reduce inflammation and oxidative stress, leading to CVD protection [112]. However, the Veg diet is characterized by lower bioavailability and absorption of vegetable proteins and of iron, zinc, and calcium, which are minerals important to maintain health status and wellness. In fact, these vegetal foods contain high levels of antinutritional factors, which may be naturally occurring (e.g., digestive enzyme inhibitors, tannins, phytate, glucosinolates, and isothiocyanates), formed during processing (e.g., D-amino acids, lysinoalanine), or due to genetic modification (e.g., lectins). Pulses, cereals, potatoes, and tomatoes contain inhibitors of digestive proteolytic enzymes. Soybeans are the most concentrated source of trypsin inhibitors, whereas peas and processed soybean products contain considerably lower levels [113–115].

Ketogenic diet (KD)

The KD was developed in the 1920s to control seizures in epilepsy. It implies a high-fat (60–80%) and protein (10–20%) content and very low-carbohydrate amount (5–10%). It could reproduce some of the effects of fasting, with the beneficial effects mostly ascribed to the production of ketones, such as β-hydroxybutyrate, acetoacetate, and acetone in the liver [116]. The clinical use of KD received increased attention in the 1990s, and KD is now an established non-pharmacological therapy for difficult-to-treat epilepsies in addition to a wider use in a variety of neurological disorders. Recently, KD has also been used as therapy for treatment of obesity and prevention of CVD [117]. Studies regarding KD and prevention of CVD risk factors are still controversial [118]. A study by Sharman and colleagues, conducted in adult men, indicated that adaptation to this diet resulted in significant reductions in fasting plasma triacylglycerols (TAG) (−33%), postprandial lipemia after a fat-rich meal (−29%), and fasting insulin concentrations (−34%). Also, there was a significant increase in LDL particle size with no change in oxidative LDL concentrations.

Interestingly, the authors described a significant increase in HDL cholesterol after 3 weeks of KD. Collectively, the responses in serum lipids, insulin, and lipid subclasses to the KD were favorable in terms of overall CVD risk profile. In addition, KD seems to have a benefit on weight loss, notably by increasing energy expenditure in animals and decreasing food intake in humans, leading to loss of both fat and lean mass. Weight loss is probably due to a greater energy deficit, but the mechanisms have not been fully described as yet, and no relationship between weight loss and ketosis was found at any time during the diet period. Long-term studies are nevertheless needed to fully depict the evolution of weight loss and better characterize the mechanisms involved. On the contrary, liver fat content was shown to be increased during an isoenergetic high-fat low-carbohydrate diet. This event suggests that high-fat intake in KD might increase the risk of nonalcoholic fatty liver disease (NAFLD), even if other studies, in which high-carbohydrate ("standard") hypoenergetic diet and hypoenergetic low-carbohydrate diet (KD) were compared, demonstrated that liver fat content was significantly reduced during KD [119–121]. This effect appeared limited in time, with no significant difference after 11 weeks. KD have also been associated with a stronger decrease in liver volume compared with a standard hypocaloric diet, probably due to the depletion of liver glycogen. Finally, the response to KD may be influenced by genetic predisposition to NAFLD, as shown by two studies with a better response to KD for patients with variants of the PNPLA3 gene [122]. Indeed, subjects with PNPLA3 variants had a lower liver fat content than controls when fed with KD [123]. However, no data are available to date regarding the low-fiber intake with KD, thus further longitudinal studies are needed to fully characterize all the issues regarding this type of nutritional pattern in long-term studies.

Japanese diet

The Japanese diet includes a wide variety of foods as beans and bean products, fresh fish, vegetables, Japanese pickles,

fungi, seaweeds, and fruits [124]. Even though the food is different from diets in Western countries, the Japanese diet has characteristics similar to MeDi. Previous published studies showed that intake of individual food groups such as fruits, vegetables, beans, and fish were inversely associated with both all-cause and/or CVD mortality in Japan [125, 126]. The Japanese diet has been characterized by high-sodium intake and a low-potassium intake contributing to a high sodium-to-potassium (Na–K) ratio, which may be a strong indicator for risk of CVD mortality [127]. In particular, studies show that Na–K ratio was positively associated with hemorrhagic stroke, but was borderline significant for ischemic stroke. In addition, this diet is rich in acidogenic foods, such as fish, and cheese, but low in alkaline foods, such as fruit and vegetables, which can induce endogenous acid production [128]. High dietary acid load has been linked to an unfavorable profile of cardiometabolic risk factors, including insulin resistance [129], high blood pressure or hypertension [130, 131], large waist circumference, high triglycerides and LDL cholesterol, and type 2 diabetes [132, 133]. In contrast, recent studies have indeed shown how this type of nutritional pattern can reduce mortality for both cancer and CVD disease [134, 135], suggesting a potential nutritional alternative pattern for CV health.

Conclusion

CVD is a multifactorial disease and is linked to unhealthy nutrition patterns. In particular, several studies suggest that an excessive intake of sodium and refined foods; added sugars; unhealthy fats; low intake of fruit and vegetables, whole grains, fiber, pulses, fish, and nuts; alcohol consumption, stress, smoking together with a deficiency of physical activity promote the risk of CVD.

Among the different types of diets analyzed in this review, MeDi appears the diet with the best nutritional pattern since it includes whole grains, pulses, fibers, PUFAs without completely excluding food of animal origin such as meat, fish, dairy products, eggs, and limiting alcohol consumption. Moreover, the MeDi style takes into consideration not only foods, but also conviviality and physical activity, which means a specific lifestyle not limited to food. Indeed, several studies demonstrate that subjects who are adherent to MeDi have lower risk of obesity, type 2 diabetes, inflammatory markers, and beneficial modulation of gene expression involved in LDL oxidation [106] and all causes of CVD event risk. On the contrary, despite the scientific evidence we discussed, the other diets analyzed do not seem to have enough data to be considered better diets than MeDi in the prevention of CVD, since the nutrition patterns proposed limit or exclude some food in favor of others based on limiting risk without considering nutrition as a lifestyle.

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