

Mediterr J Nutr Metab (2012) 5:187–193
DOI 10.1007/s12349-012-0097-8

REVIEW

Dietary strategy for prevention and management of dyslipidemia: international guidelines

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Received: 15 February 2012 / Accepted: 5 March 2012 / Published online: 23 March 2012
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Abstract Primary prevention of cardiovascular disease should begin with a detailed metabolic study of our patients who must follow a nutritional therapy. Recently, new guidelines ESC/EAS 2011 on the treatment of dyslipidemia have been drawn up, according to which it is possible to arrive at desirable values of cholesterol and triglycerides with a synergy between drug treatment and adequate diet therapy. At this time, Mediterranean diet has been undergoing a radical transformation: there is hyperalimentation of the Mediterranean diet in all its components. The effectiveness of the Mediterranean diet on the reduction of lipids has been demonstrated, and the problem is how to implement this diet in the general population and dyslipidemic patients. Certainly, awareness, education of their nutritional status, suitable food and portions can increase adherence to diet.

Keywords Diet · Dyslipidemia · Prevention · Guidelines · Education

Introduction

The significant results that have been recorded on the improvement of the lipid profile in dyslipidemic patients

are due to the increase of a therapeutic strategy in their diet alongside of drug therapy. In June 2011, new guidelines on the management of dyslipidemia were drawn up by the European Society of Cardiology (ESC)/European Society for Atherosclerosis (EAS) 2011, which stated that the synergy among an adequate diet, therapy and drug treatment might be appropriate to achieve desirable levels of cholesterol and triglycerides. In Italy, patients with different forms of dyslipidemia make up 20 % of the population. The same statistical reality applies to people affected by metabolic syndrome, who make up 30 % of Italy's population and consist mainly of people who live in the southern regions, mostly females.

Studies conducted on patients in North America have shown that while the standard pharmacological intervention reduces total cholesterol by 5–7 %, those who were on a low-cholesterol diet saw a reduction in total cholesterol by 10–12 % [1]. The data from the “Seven Countries Study”, which later expanded to 18 various countries, showed that saturated fat, the introduction of dietary cholesterol, and CHD mortality were directly related to each other. Later, the data from the Oslo Study was added, showing that a decreased intake of saturated fat and the increased consumption of polyunsaturated fats reduced mortality and/or morbidity of cardiovascular diseases (Oslo Study) [2].

In countries such as Finland, the USA, New Zealand and Australia, extensive campaigns were carried out on topics such as fighting against smoking and hypertension, which were supported by central governments, leading to a significant and steady reduction in cholesterol levels and mortality resulting from coronary heart disease.

Spreading awareness about the risks that increase the chance of cardiovascular disease, with regard to average heart problems, can motivate people to implement positive

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changes in their diet. However, asking a population to adopt nutritional habits and putting into practice the advice provided by the dietary recommendations and made by the international scientific community seem to be a significant challenge. Although health education campaigns are growing steadily throughout the world, we have yet to define the most effective strategies that can lead to better results in the actual prevention of cardiovascular disease along with the reduction of morbidity and mortality.

Pediatricians should play a key role in initiating a correct and continuous nutritional education from early childhood, so as to then influence the future behavior of the child. This is something that requires the involvement of the parents or guardians, who are responsible for making those “alimentary decisions” for their child’s future [3]. Concerning the dietary recommendations addressed to the population, they should adopt and implement these strategies to facilitate a healthy lifestyle. This can be achieved in many ways with help from government facilities, schools, food industries and restaurants. Strategies should focus on education, production, composition and distribution in order to induce the consumption of such foods recommended by the American Heart Association of 2006 [4] (Table 1) that are appropriate for the general population worldwide, which includes adults and children above 2 years of age.

New guidelines: ESC/EAS 2011 for the management of dyslipidemia

Recently, the guidelines of the ESC and EAS on lipid disorders have been published in the European Heart Journal of Atherosclerosis. This is a long-awaited document from the European medical community that marks an important update for clinical practice regarding the management of cardiovascular risk in primary and secondary

prevention. According to the guidelines, the estimated cardiovascular risk remains a key factor in the framing of the patient’s diet and subsequent management. It recommends the SCORE model, which defines high-risk subjects as those who have an odds of fatal events $>0.5\%$ for the year and over the next 10 years [5]. Approximately, the conversion factor between the SCORE and probability of fatal and non-fatal events is 3, so a score of 0.5 SCORE is the probability of having 1.5 % of cardiovascular events for a year. Also, this score includes the calculation of risk values of HDL cholesterol which can significantly change the condition of risk for the same SCORE. Most important is the calculation of risk in young and old people. The overall risk seems to be low because of young age, even in those who suffer very high risk factors. In this case, the assessment of relative risk—the relationship between perceived risk and the risk of individuals of the same age but with no risk factors—may indicate a risk, however, much higher than expected and, therefore, recommend the implementation of those lifestyles that can reduce the odds of events by keeping under control over the following decades. Similarly, in old persons, because of the burden of age, the overall risks are generally higher and, therefore, the aggressiveness of the interventions should consider this issue more seriously, contextualizing each case in accordance with the characteristics of old patients.

As for the new recommendations on the assessment of lipid parameters, all men over 40 years and women over 50 years should be screened for lipids, which should be anticipated in individuals with family history of premature ischemic heart disease and in the presence of other risk factors such as hypertension, diabetes, obesity, dyslipidemia, familial autoimmune disease or chronic renal failure. Lipid screening should include the following parameters: total cholesterol, triglycerides, HDL and LDL, according to the Friedewald formula (if triglycerides are <400 mg/dl). Therefore, the guidelines recommend other

Table 1 Recommendations for diet and lifestyle for the reduction of cardiovascular risk of American Heart Association (AHA) in 2006

Balanced calorie intake and physical activity to achieve or maintain a healthy body weight
Rich in carbohydrates and fruit diet
Choose whole grains and fiber-rich foods
Consume fish, especially oily fish at least twice a week
Limit your intake of saturated fatty acids $<7\%$ energy intake, trans fatty acids to $<1\%$ and cholesterol <300 mg per day by assuming:
Lean meats and vegetable alternatives
Milk and dairy products skimmed or 1 % fat or low fat
Minimize partially hydrogenated fat intake
Minimize your intake of foods and beverages with added sugar
Choose foods and cook with little or no salt
Moderate use of alcohol, if allowed
For meals eaten outside, follow the same recommendations

indicators only in special cases, although have being recognized their validity such as the determination of ApoB or relationship ApoB/ApoA1 or lipoprotein a. The dosage of triglycerides should be made after at least 12 h, and it is not influenced by the meal for the other parameters. These recommendations have been reached as a result of the undisputed evidence of the ongoing relationship between LDL reduction and reduction of mortality and morbidity.

The LDL are the therapeutic targets and their levels should be <70 mg/dL in those patients with a very high risk. Particularly, all subjects with documented cardiovascular disease, diabetes, chronic renal failure or SCORE >1 % per year (the category of very high risk) should reach the target <70 mg/dl. In subjects with high risk (score between 0.5 and 1 %), the recommended target is 100 mg/dl, also obtained with pharmacological therapy in primary prevention, in addition to lifestyle interventions.

The guidelines have focused attention on a number of populations usually not studied in large clinical trials, namely children, women and old persons. In children, except in special cases, drug treatment should be conducted over the age of 18 years [6], whereas in women and old people, although poorly represented in large studies, there is no reason to differentiate the therapeutic strategy in both primary and secondary prevention than in men. Finally, the therapeutic strategy in patients with acute coronary syndrome (ACS) has been widely discussed; in particular, it is recommended that therapy with high doses of statins start between 1 and 4 days of the SCA as recommended by current guidelines on acute coronary syndromes, although the importance of caution in old patients with renal or hepatic impairment is emphasized. But the real novelty lies in the recommendation to re-evaluate LDL levels after 4–6 weeks, and to adjust the dose for the target to maintain [7]. Therefore, the guidelines should answer the usual question on how long to maintain the high doses of statins, and properly draw attention to the target rather than the dosage.

Diet therapy and behavioral changes

Although considerable progress has been made in the treatment and prevention of cardiovascular disease with drug therapy, diet therapy and lifestyle remain the foundation of clinical intervention. Unfortunately, there is a wide gap between the existing dietary guidelines on how to feed the population. The nutritional approach of the various types of diets is often substantially different from each other. Those used the most are as follows:

- low carbohydrate diet;
- low-fat diet;
- Mediterranean diet;
- diet recommended by scientific American societies such as: National Cholesterol Education Program (NCEP), ATP III (step 1 and step 2), Therapeutic Lifestyle Changes (TLC) and American Heart Association (AHA).

Each of these give different results for lipids and only the low-fat diet (like dietary guidelines) and the Mediterranean diet have documented a reduction in cardiovascular events (Table 2).

The National Cholesterol Education Program (NCEP) Adult Treatment Panel (ATP) III has affirmed the validity of the changes in lifestyle as a therapy of choice for primary prevention. The priority is to reduce the risk of cardiovascular disease [5]. Therefore, strategies to prevent cardiovascular disease are based on improving the changes in lifestyle of the population. A key role is played by proper diet, in the context of more focused goals such as an ideal body weight, recommended levels of LDL cholesterol, HDL and triglycerides, a normal blood pressure and blood glucose, physical activity and avoidance of use and exposure to tobacco smoke.

From a behavioral point of view, sugary drinks are strictly prohibited because they provide empty calories in the form of simple sugars that have a rapid impact on metabolism, insulin secretion and triglyceride synthesis. It seems to be significant to moderate the intake of foods

Table 2 Diets compared

Diet	Nutritional features	LDL	HDL	Triglycerides	Risk of CHD	Level of evidence
Mediterranean	Olive oil 35–40 g, walnuts <20 g, fruit, vegetables at will (Table 4)	Reduced	Increased	Reduced	Reduced	A
Low sugar	Carbohydrates 20 g at the beginning, then till 120 g limitation of vegetables and fruit	Reduced	Increased	Reduced	No data	B
Low fat	Lipids <10 %, rich in carbohydrates	Reduced	Reduced	Increased	Reduced	B
TLC (therapeutic lifestyle changes)	Lipids <30 % saturated fat <7 %, cholesterol <300 mg	Reduced	Unchanged	Unchanged	No data	A

containing sugar or fructose, and limit the consumption of fruit to two servings per day (150 g net per meal). Pastry consumption must be reduced and preferably placed in the context of a mixed meal and an appropriate count of simple sugars. It is best to avoid the preparation of industrial sweet as well as simple sugars containing eggs, cocoa, butter, lard or other fat pastries such as palm oil and coconut. It should be therefore preferable to always have moderately sweet dishes prepared at home [6].

The high consumption of simple sugars causes an increase in plasma triglycerides that occurs using complex carbohydrates with suitable water-soluble fiber content. The introduction of fiber foods has been linked to reduced risk for chronic degenerative diseases, tumors such as colorectal cancer, diabetes and cardiovascular disease, due to a reduction in the levels of plasma lipids. The main recommendation is: the optimal choice for an adult seems to be a global consumption of 20–30 g of dietary fiber [8].

The total fat intake can be maintained in most cases at about 30 % of the total calories by providing a 7–6 % reduction in saturated and monounsaturated fatty acids and replacing them with foods mostly derived from olive oil. Therefore, the lipid-lowering cholesterol, LDL and triglycerides may be controlled, as well as the palatability of the diet and the feeling of satiety may be maintained [9, 10].

The low blood levels of triglycerides and cholesterol and reduced mortality from cardiovascular disease in populations with high consumption of fish have focused on fatty acids of the ω -3 series that are able to reduce the levels of blood pressure, platelet adhesiveness, production of thromboxane A₂, levels of fibrinogen and blood viscosity, and adhesion and migration of monocytes [11]. But their action is primarily exerted on lipid's/lipidic metabolism and triglyceride levels significantly through a reduction in

their hepatic synthesis, by reducing the synthesis of APO B, with a positive effect on post-prandial levels. The preference of ω -6 is, rather than improving the lipid profile, to positively affect insulin sensitivity [12]. In the study by reviewing the literature published by Harris, the effect of ω -3 fatty acids is given as a reduction in triglycerides, which is particularly important in patients with isolated hypertriglyceridemia or in cases where it is associated with an increase in LDL cholesterol [13]. The report is made more interesting with some cases of patients with severe hypertriglyceridemia, associated with recurrent episodes of acute pancreatitis. The treatment in those patients with ω -3 fatty acids resulted in a significant reduction in serum triglycerides and a reduction of recurrent pancreatitis. There is no doubt from convincing epidemiological demonstration that a regular consumption of fish of three servings per week is very beneficial for the treatment of hypertriglyceridemia (Table 3).

The messages from the media, from nutritionists and even physicians, concerning alcohol consumption and mortality from cardiovascular disease are absolutely conflicting. It seems therefore appropriate to cite the evidence from literature, such as observational and epidemiological studies conducted in countries around the world that have demonstrated an inverse correlation, with a high coefficient ($r = 0.58$), between liters of wine/person/year introduced and mortality due to cardiovascular disease [14]. It is quite logical that other food components play a role, but the data obtained on large cohorts of the population has an indisputable value. From the point of view of lipoproteins, the main beneficial effect of alcohol is to increase HDL. A careful study of the pathophysiology has established that “on average” 1 g of ethanol increases plasma HDL-C by 0.133 mg/dl (so, 30 g per day taken continuously increases the HDL-C of 4 mg/dl); this amount of ethanol corresponds

Table 3 Effect and recommendations for foods associated with cholesterol-lowering effect

Food	Source	Effects	Recommendation
Phytosterols	Vegetable oils (e.g., corn), nuts, yogurt, milk, margarine and other additional products	↓10 % LDL	2–2.5 g/die
Soy	Dry soy, soy milk, tofu, etc.	↓LDL	25 g of soy protein
Soluble fiber	Legumes, fruit, vegetables	↓LDL,	30–35 g/die
CHOCOLATE	Dark chocolate, cocoa	↓Total cholesterol ↓10–12 % LDL ↑4–13 % HDL	50–75 g (dose in the works)
Alcohol	Red wine	↓Oxidation of LDL ↑HDL	1–2 glasses per day
Nuts	Nuts	↓Oxidation of LDL ↓Platelet aggregation Anti-inflammatory activity ↓LDL	5–7 nuts, <20 g

to an average of one-quarter of a liter of wine per day or 700–1,000 ml of beer [15]. The other side of the coin is that 30 g of ethanol increases triglycerides by about 6 mg/dl, so individuals with various forms of hypertriglyceridemia should be against the use of wine, beer, aperitifs and super-alcoholic drinks. Apart from the effects of alcohol, red wine can have, instead, a salutary effect in reducing cardiovascular risk. In particular, the red wine is a very rich source of antioxidant flavonoids, whose principal is resveratrol, a phenolic compound responsible for many of its taste and sensory properties and its aging [16]. Resveratrol is also present in red grape juice, and this could be an alternative for those who cannot or do not wish to have alcohol, although the amount contained in it is approximately nine times less than that contained in red wine. The recommended amount of red wine is one or two glasses of wine a day [17, 18].

The new guidelines for the management of dyslipidemia ESC/EAS 2011 carefully considers how to reduce LDL cholesterol with non-pharmacological and pharmacological therapy. In particular, the guidelines highlight the roles of physical activity and modest weight reduction (reduction of about 8 mg/dl for every 10 kg of weight lost) on the levels of LDL, while the role of favorable levels of HDL, triglycerides and insulin sensitivity is of considerable importance. But the real novelty of the document will examine the so-called “nutraceuticals”, or the principals contained in natural foods or commercial products that can be used in addition to drugs to reduce cholesterol. In these guidelines, one chapter is dedicated to functional food: the nutraceuticals. This can be used either as alternatives or in addition to lipid-lowering drugs. Several functional foods have been found to improve health and reduce risk, including lowering of LDL-C [19]. FDA has recognized LDL-lowering health claims for plant sterols (5 %), viscous fiber (4 %), nuts and soy proteins with a combination of all four decreasing LDL-C by 13–14 % (1). Phytosterols compete with cholesterol for intestinal absorption, thus modulating cholesterol levels [20]. Daily consumption of 2 g of phytosterols per day can lower LDL-C by 5–10 % [21]. Phytosterols and ezetimibe can be used together without adverse interaction and their fundamental effects on whole-body cholesterol metabolism complement one another. The principal phytosterols are sitosterol, campesterol and stigmasterol. They occur naturally in oils and in smaller amounts in vegetables, fresh fruits, chestnuts, grains and legumes. The dietary intake of plant sterols ranges between an average of 250 mg/d in northern Europe to 500 mg/d in Mediterranean countries. Phytosterols have been added to spreads and vegetable oils (functional margarine, butter and cooking oils) as well as yogurt and other foods without losing their cholesterol-lowering efficacy. These are usually given as sterol-enriched margarine [22]. Soy protein

(in the form of soy milk, soy meat analog or tofu) has modest LDL-C lowering effect (3–5 %) and can be used as a substitute for animal proteins [23, 24]; both soy and milk protein also lower blood pressure (2 mm Hg). Thus, partially replacing carbohydrate with soy or milk protein might be an important component of nutrition intervention strategies for the prevention and treatment of hypertension [25]. Dietary fiber, especially soluble fiber from oat bran, barley, beta-glucan and psyllium, is recommended for LDL-C lowering at a daily dose of 5–15 g/d [26, 27]. This can also be used as foods enriched with these fibers. Epidemiological studies have consistently associated nut consumption with reduced risk for coronary heart disease. Nut consumption improves blood lipid levels in a dose-related manner, particularly among subjects with higher LDL-C or with lower BMI. The effects of nut consumption are e dose related, and different types of nuts had similar effects on blood lipid levels. With a mean daily consumption of 67 g of nuts, the following estimated mean reductions were achieved: LDL-C 10 mg/dL and ratio of total cholesterol concentration to HDL-C (0.24). Triglyceride levels were reduced by 21 mg/dL in subjects with blood triglyceride levels of at least 150 mg/dL [28]. Omega-3 unsaturated fatty acids from marine sources (DHA and EPA) can lower triglyceride levels 25–30 % at a dose of 3 g per day in people with high triglycerides, but may increase the LDL by 5 %. Plant sources of omega-3, such as alpha-linolenic acid present in chestnuts, some vegetables and seed oils, are less effective in lowering triglycerides. Policosanol is a natural mixture of long chain aliphatic alcohols extracted primarily from sugarcane wax. Contrary to common belief, policosanol from sugarcane,

Table 4 Genes able to modify the individual response to nutrients

Gene	Function
5HTT (SLC6A4)	Adapting to stress
ACE	Sensitivity to salt
ADH1C	Sensitivity to alcohol
APOC3	Olive oil (use)
CYP1A2*1F	Sensitivity to caffeine and meat
GSTM1	Crucifers (use)
IL6	General inflammation
LPL	Sensitivity to saturated fat
MTHFR	Metabolism vitamin B
PPARG	Sensitivity to sugars and refined carbohydrates
SOD2	Oxidative stress
TNF	Sensitivity to nickel
VDR	Metabolism of vitamin B
LCT	Sensitivity to lactose
DQ2/8 (6 GENI)	Sensitivity to gluten (Celiac disease)

rice or wheat germ has no beneficial effect on lipids [29]. Red rice yeast (RYY) is a source of fermented pigment used in China as a food colorant and flavor enhancer for centuries. It can lower LDL-C by a statin-like mechanism, but the various preparations have markedly different content of biologically active ingredients, predisposing to serious toxicity to the liver, kidneys and muscles. Other herbal and natural agents that have been considered to lower cholesterol remain controversial. These include policosanol, flaxseed, eggplant extract, garlic, guggulipid and chromium. Finally, after diet therapy an evaluation must be made after 6 months, before starting drug treatment. This will allow maintaining the normalization of plasma levels with the lowest possible dose of the drug, and avoiding the collateral effects inherent in most of the molecules with lipid-lowering action [30].

Conclusions

Many studies demonstrated the effectiveness of good diet on the reduction of lipid, but the problem is how to implement the grip in the total sense in the general population and dyslipidemic patients.

In recent years, many studies have been conducted to evaluate the interactions between genes and diet. Research in the field of nutrition will be guided through the nutrient–gene interactions, the elucidation of the biochemical mechanisms of control and characterization of the individual response to dietary manipulations. This new possibility that genetics applied to nutrition makes available to us has given birth to a new branch of medicine: nutrigenetics (see Table 4) [31]. The final approach could lead to the concept of gene–diet interaction in addition to the metabolic unit in the real world. Scientific research of nutrigenetics has just begun, but the potential of specific dietary recommendations based on genotype. It should increase the basis of further correlations between polymorphisms and cardiovascular disease [32].

Actually, awareness of the population's nutritional status, knowledge of foods and suitable portions might increase their adherence to diet, but a healthy future also needs to adopt other necessary measures including government facilities, schools, food manufacturers, restaurants and strategies that relate to education, production, composition and distribution of food [33]. In recent years, various types of diets have been implemented on patients such as low-fat diet, low carbohydrate and the Mediterranean diets. Even better results on lipids have been shown from these diets, in addition to diets based on the recommendations of the NCEP guidelines, TLC and AHA. However, for low carbohydrate diet like Atkins, the studies

are not associated with corresponding data on morbidity, mortality or quality of life. In addition, carbohydrate diet is not clear yet about whether the positive effects of HDL and triglycerides are offset by the negative one, on total cholesterol and LDL, and therefore could not currently be recommended for the prevention of cardiovascular disease. The greater adherence to Mediterranean diet by the general population, which is also in trial for diseases, is associated with significant improvement in people's health, with a reduction of incidence and mortality due to cardiovascular disease and cancer. Therefore, at present, given the results of the meta-analysis and recent trials, the demonstration of efficacy in reducing cardiovascular mortality, including the reduction of cardiovascular risk factors (e.g., high blood pressure) and inflammatory markers (e.g., protein C-reactive), has made Mediterranean diet to be considered as a long-term application, and also as optimal nutrition for healthy subjects, especially for patients with hypercholesterolemia or at risk of ischemic coronary events. [34]. The dietary recommendations should be associated with information (or advice) for a healthy lifestyle, aimed at both primary and secondary prevention, in which even physical exercise plays an equally important role. International guidelines suggest targets for LDL cholesterol levels to be reached, which may require values reduced by more than 50 % in some patients. This level of reduction is difficult to achieve with medical treatment or dietary intervention alone. The effectiveness of a dietary treatment associated with the Mediterranean diet and statin drug therapy has shown excellent results, reducing by 43 % the risk of coronary artery disease, and significantly increasing the advantage conferred by statin therapy alone [35].

Following the guidelines of the management of dyslipidemia ESC/EAS 2011, drug treatment is necessary. It reaffirms the central and irreplaceable role of statins, and represents the drug of choice for blood the control of cholesterol. [36–38] The guidelines clearly state that the benefits trials are independent from the type of statin and, therefore, the choice of the latter must be considered in relation to the entity of the reduction required in the individual patient, as well as the efficacy and tolerability to the molecule.

The statin seems to be most effective under maximum tolerated doses. If the desired target could not be reached, alternative strategies or combination can be considered. In this regard, statins may be associated with various other drugs that lower cholesterol, in particular the combination with ezetimibe is the best for its tolerability and efficacy. Other combinations may be considered in relation to the patient's lipid profile, including omega-3 fatty acids, niacin, fibrates and phytosterols.

Conflict of interest None.

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