

Editorial

The Mediterranean Diet and Plasma Lipid Profile



Dieta mediterránea y perfil lipídico plasmático

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Cardiovascular disease (CVD) continues to be the main cause of morbidity and mortality in the 21st century. As it is almost always more cost-effective to invest in prevention than to cover the treatment costs of most diseases, many governments and institutions consider the prevention of cardiovascular disease to be a main priority of public healthcare systems. This prevention strategy is based on promoting a healthy lifestyle, including healthier diet patterns, more physical activity, body weight control, and cessation of toxic habits like smoking, excessive alcohol consumption, etc.

The relationship between diet (nutrition) and CVD has been one of the most active areas of research in nutritional epidemiology over the last 50 years. Many studies have analyzed the effects of the consumption of certain foods and nutrients on different vascular risk factors. Currently, however, the study of the effects of different eating patterns on health is considered a better approach because it assesses the synergic interaction of different foods and nutrients that make up diet.¹

Several studies, including the most recent meta-analyses, indicate that the traditional Mediterranean diet, defined as the dietary pattern of the peoples that lived around the Mediterranean Sea during the 1960s, seems to be the most effective eating pattern for preventing numerous chronic diseases, including CVD. In other words, there is growing scientific evidence to confirm that what is known as the “Mediterranean paradox” (meaning lower absolute risk of ischemic heart disease for the same level of exposure to a risk factor) is due to a protective effect of the diet and lifestyle followed by the inhabitants of the Mediterranean countries. This dietary pattern, known as the Mediterranean diet, is characterized by: an abundant use of olive oil; high consumption of plant-based foods (fruit, vegetables, legumes, grains, nuts, seeds); frequent but moderate wine consumption (especially red) at meals; moderate consumption of fish, seafood, fermented dairy products (yogurt, cheese), poultry, eggs; and limited consumption of red meat, processed meat products, and also sweets. The diet is rich in key nutrients, such as monounsaturated fatty acids (olive oil), polyunsaturated fatty acids (fish, nuts), dietary fiber (grains, vegetables, fruit, legumes), polyphenols (wine, extra virgin olive

oil, fruit, vegetables), vitamins (vitamins A, D, E, folic acid, riboflavin, vitamin B₁₂), and minerals (potassium, calcium, phosphorus, magnesium), which could explain the cardiovascular benefits associated with this type of diet.^{2–6}

Several epidemiologic and clinical studies have evaluated the effects of this diet on intermediate markers of cardiovascular disease, such as blood pressure, glycemia, plasma cholesterol concentrations and subfractions, plasma inflammatory biomarkers, or other biological markers. While useful, this focus has certain limitations. For instance, there are possibly multiple pathways by which an inappropriate diet could lead to the development of CVD; on the other hand, different dietary components also require varying induction periods for them to take effect, and they could likewise affect different pathways. Furthermore, the results of several epidemiologic studies indicate that global dietary patterns can promote or prevent CVD to a greater degree than the consumption of isolated foods or nutrients. Thus, it is currently believed that the best way to evaluate the influence of the diet on CVD is the analysis of important clinical objectives for morbidity and mortality, which are also known as *hard endpoints*.

Operating on these premises, the PREDIMED study⁷ clearly demonstrated the beneficial effect of the Mediterranean diet for the primary prevention of CVD. This study included subjects at high cardiovascular risk but no previous CVD, who had been randomized to receive either a Mediterranean diet supplemented with either extra virgin olive oil or nuts versus a low-fat diet. The primary endpoint of the study was the appearance of the main clinical manifestations of CVD, such as cardiovascular death, nonfatal myocardial infarction, or stroke. Secondary endpoints included total mortality, type 2 diabetes mellitus, metabolic syndrome, peripheral artery disease, atrial fibrillation, neurodegenerative disease, and the main types of cancer. A total of 7447 participants were randomized to 1 of the 3 mentioned intervention groups. Said groups presented similar baseline clinical characteristics and medical treatments. During follow-up, the participants included in the 2 Mediterranean diet groups quickly and significantly improved their adherence to the traditional Mediterranean diet, and this compliance remained high during the entire trial.

After 4.8 years of follow-up, 288 major cardiovascular events were diagnosed: 96 in the Mediterranean diet and olive oil group (3.8%), 83 in the Mediterranean diet and nut group (3.4%), and 109 in the control group (4.5%). These data represent a

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reduction of 30% in the incidence of events in both Mediterranean diet groups compared with the control group. The multivariate analysis showed a similar degree of protection for both Mediterranean diet groups compared with the control diet group after adjusting for sex, age, anthropometric parameters and vascular risk factors. Thus, this study demonstrates, with the highest degree of scientific evidence, that the Mediterranean diet supplemented with extra virgin olive oil or nuts is effective in the primary prevention of major CVD complications. It is interesting to observe that these beneficial effects also extend to other relevant cardiovascular conditions, such as peripheral artery disease (with a reduction of relative risk > 50%), atrial fibrillation,⁸ and cognitive deterioration.⁹

When the effects on the main cardiovascular risk factors are analyzed, the data clearly show their benefits. It has also been observed that a greater adherence to the traditional Mediterranean diet is accompanied by better glucose metabolism and a lower incidence of type 2 diabetes mellitus in non-diabetic subjects,¹⁰ in addition to a reduction in blood pressure measured at office visits as well as ambulatory blood pressure monitoring when compared with a low-fat diet.¹¹

Nevertheless, the effects of the Mediterranean diet on the lipid profile deserve to be considered separately. While it was known that the Mediterranean diet supplemented with certain foods, such as olive oil or nuts, effectively reduced plasma concentrations of low density lipoprotein cholesterol,¹² the data from the PREDIMED study have also demonstrated that the Mediterranean diet supplemented with nuts can change the lipoprotein subfractions to a less atherogenic pattern.¹³ Thus, in a substudy of the PREDIMED trial, the one-year changes were analyzed in the lipoprotein subclasses measured by proton nuclear magnetic resonance spectroscopy. In those subjects who had been assigned to the Mediterranean diet supplemented with nuts, it was observed that the lipoprotein subfractions changed to a less atherogenic pattern. From a mechanistic standpoint, this helps explain the reduction of cardiovascular events observed in this intervention group.

It should be emphasized that the beneficial effects of the Mediterranean diet are detected shortly after the dietary changes are introduced. An analysis done 3 months after the start of the PREDIMED study assessed the effect of the Mediterranean diet on bodyweight, blood pressure, lipid profile, glucose concentration and inflammatory markers. After just 3 months, the subjects who were following a Mediterranean diet supplemented with extra virgin olive oil and nuts presented lower plasma glucose concentrations, lower blood pressure levels, higher high-density lipoprotein/total cholesterol ratio, and lower plasma concentrations of inflammation markers, such as C-reactive protein and interleukin-6, than the group that followed a low-fat diet.¹⁴

However, even though the results from the introduction of a supplemented Mediterranean diet in high-risk subjects are undeniably beneficial, it is important to know what happens in the real world, outside controlled clinical trials, in order to determine whether the adherence to a Mediterranean lifestyle pattern continues to have beneficial effects on cardiovascular health. In this journal issue, Peñalvo et al.¹⁵ publish the results of an interesting cross-sectional analysis of a series of 1290 participants from the *Aragon Workers Health Study*. They show how the participants in the highest quintile of adherence to the occidental diet pattern had a more deleterious lipid profile compared with those in the lowest quintile, with lower plasma high-density lipoprotein cholesterol and apolipoprotein A1. In comparison, the participants with better compliance to the Mediterranean diet pattern had higher concentrations of high-density lipoprotein cholesterol as well as a more favorable triglyceride/high-density lipoprotein cholesterol ratio. The authors conclude that following

the Mediterranean diet pattern is associated with a more favorable lipid profile compared with an occidental dietary pattern. It is likewise interesting to observe that, from a socioeconomic standpoint, the subjects with a non-Mediterranean dietary pattern had a lower level of education and income.

The data from the PREDIMED^{8–14} study as well as those from the Peñalvo et al.¹⁵ study confirm that adherence to a Mediterranean diet is highly effective for the prevention of CVD. The mechanisms by which this effect occurs are starting to be better understood. It has been observed that better compliance to the Mediterranean diet improves both classic and emerging risk factors. Available data confirm improved blood pressure control, insulin sensitivity, lipid profile and low-density lipoprotein cholesterol subfractions in subjects who follow a Mediterranean diet versus the control diet. Beyond the effects on classic and emerging risk factors, the available data also show effectiveness on the mechanisms for developing arteriosclerosis, including endothelial dysfunction, oxidative stress, and inflammation. Likewise, a reduction in the carotid intima-media thickness has also been seen. As for the nutrigenetic effects of the Mediterranean diet that would contribute to even better understanding of its beneficial effects, the published studies show that adherence to this diet mitigates the development of cardiometabolic phenotypes in subjects that are genetically susceptible to developing CVD.

Last of all, another aspect to mention from the Peñalvo et al. study¹⁵ is the existence of economic and education barriers that make it difficult to adhere to the traditional Mediterranean diet. Originally, the Mediterranean diet was characteristic of the lower socioeconomic classes. Now, the situation has changed drastically. In Spain, which is obviously a Mediterranean country, individuals with lower incomes often follow (or feel obligated to follow) less healthy, occidental-type diets. In contrast, it is those with higher education (and also those with higher income) who have a better understanding of nutrition and, as they are aware of the risk for CVD associated with the consumption of low-quality diets, usually follow healthier eating patterns, such as the Mediterranean diet. Given this current situation, government agencies and other institutions need to confront the challenge of developing a healthcare policy with sufficient resources to promote the traditional Mediterranean diet. It is also necessary to try to eliminate the economic, cultural or any other type of barriers that could endanger one of the most effective tools we have for the prevention of cardiovascular disease: the traditional Mediterranean diet that we have inherited from our parents and grandparents, which is so beneficial for our health.

CONFLICTS OF INTEREST

None declared.

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