Circulation
JOURNAL OF THE AMERICAN HEART ASSOCIATION

Lyon Diet Heart Study : Benefits of a Mediterranean-Style, National Cholesterol Education Program/American Heart Association Step I Dietary Pattern on Cardiovascular Disease

Penny Kris-Etherton, Robert H. Eckel, Barbara V. Howard, Sachiko St. Jeor and Terry L. Bazzarre

Circulation. 2001;103:1823-1825
doi: 10.1161/01.CIR.103.13.1823
Circulation is published by the American Heart Association, 7272 Greenville Avenue, Dallas, TX 75231

Print ISSN: 0009-7322. Online ISSN: 1524-4539

Lyon Diet Heart Study

Benefits of a Mediterranean-Style, National Cholesterol Education Program/American Heart Association Step I Dietary Pattern on Cardiovascular Disease

Penny Kris-Etherton, PhD, RD; Robert H. Eckel, MD; Barbara V. Howard, PhD; Sachiko St. Jeor, PhD, RD; Terry L. Bazzarre, PhD; for the Nutrition Committee, Population Science Committee, and Clinical Science Committee of the American Heart Association

Diet is a cornerstone of cardiovascular disease (CVD) prevention and treatment efforts. Step I and Step II diets are widely recommended as the first line of CVD intervention.[1] At the core of this dietary guidance are the recommendations to decrease saturated fat and cholesterol and to consume more fruits, vegetables, and whole grain products. Information from an extensive database, especially regarding saturated fat, indicates that these diets significantly lower blood cholesterol levels, a major risk factor for CVD. Consequently, it is beyond debate that these diets reduce CVD risk. Since the advent of Step I and Step II diets, nutritionists have sought to develop effective implementation strategies, including identifying dietary patterns that augment the beneficial effects of these diets. Recent findings indicate that we are making impressive progress in attaining these goals. There is provocative evidence from the Lyon Diet Heart Study[2] suggesting that a Mediterranean-style, Step I diet (emphasizing more bread, more root vegetables and green vegetables, more fish, less beef, lamb and pork replaced with poultry, no day without fruit, and butter and cream replaced with margarine high in α-linolenic acid) has effects that may be superior to those observed for the usual Step I diet. These findings raise the interesting, but not yet corroborated, question of whether a modified Step I diet (ie, a Mediterranean-style Step I diet) that features a dietary pattern consistent with the new American Heart Association (AHA) Dietary Guidelines may augment the Step I or Step II diets that are presently implemented in clinical practice.

Defining a Mediterranean-style diet is challenging given the broad geographical region, including at least 16 countries, that borders the Mediterranean Sea. As would be expected, there are cultural, ethnic, religious, economic, and agricultural production differences that result in different dietary practices in these areas and that preclude a single definition of a Mediterranean-style diet. Nonetheless, there is a dietary pattern that is characteristic of Mediterranean-style diets. This pattern emphasizes a diet that is high in fruits, vegetables, bread, other forms of cereals, potatoes, beans, nuts, and seeds. It includes olive oil as an important fat source and dairy products, fish, and poultry consumed in low to moderate amounts; eggs consumed zero to 4 times weekly; and little red meat. In addition, wine is consumed in low to moderate amounts. This dietary pattern is based on food patterns typical of many regions in Greece and southern Italy in the early 1960s. The Mediterranean-style Step I diet used in the Lyon Diet Heart Study was comparable to this pattern but uniquely different in that it was high in α-linolenic acid.

The Lyon Diet Heart Study, a randomized, controlled trial with free-living subjects, tested the effectiveness of a Mediterranean-type diet (consistent with the new AHA Dietary Guidelines) on composite measures of the coronary recurrence rate after a first myocardial infarction. Subjects in the experimental group were instructed by the research cardiologist and dietitian to adopt a Mediterranean-type diet that contained more bread, more root vegetables and green vegetables, more fish, fruit at least once daily, less red meat (replaced with poultry), and margarine supplied by the study to replace butter and cream. The saturated fatty acid (15% kcal) and oleic acid (48% kcal but 5.4% kcal 18:1 trans) contents in the margarine were comparable to those in olive oil, with the exception that the margarine was higher in linoleic acid (16.4% versus 8.6% kcal) and more so in α-linolenic acid (4.8% versus 0.6% kcal). Exclusive use of rapeseed oil and olive oil was recommended for salads and food preparation. Use of olive oil exclusively was not recommended because it was not acceptable as the only oil source in the diet. Wine in moderation was allowed with meals. Subjects in the experimental group participated in a 1-hour counseling session. In contrast, control subjects received no specific dietary advice apart from that generally provided by hospital dietitians or attending physicians.

The diet of the control group did not meet the AHA Step I diet guidelines (<30% of calories from fat, 8% to 10% from saturated fat, and <300 mg/d cholesterol; Table). The AHA recommends a Step II diet for individuals who have heart disease or who have not met the LDL cholesterol treatment

This statement was approved by the American Heart Association Science Advisory and Coordinating Committee in July 2000. A single reprint is available by calling 800-242-8721 (US only) or writing the American Heart Association, Public Information, 7272 Greenville Ave, Dallas, TX 75231-4596. Ask for reprint No. 71-0202.

(*Circulation*. **2001;103:1823-1825.**)

Nutrient Profile of the Mediterranean-Style Step I Diet in the Lyon Diet Heart Study and the NCEP/AHA Step I and Step II Diets

	Lyon Diet Heart Study	Step I Diet	Step II Diet
Total calories	1947	To achieve and maintain desirable weight	
Percent of total calories			
Fat	30.4	≤30	≤30
Saturated fat	8.0	8–10	<7
Polyunsaturated fat	4.6	up to 10	
18:1 (n-9) (oleic acid)	12.9	up to 15 MUFA	
18:2 (n-6) (linoleic acid)	3.6		
18:3 (n-3) (linolenic acid)	0.84		
Alcohol	5.8		
Protein, %	16.2	≈15	
Fiber, g	18.6	20–30*	
Cholesterol, mg/d	203	<300	<200

MUFA indicates monounsaturated fat.
*A recommended total dietary fiber intake by many authorities.

goals of <160 mg/dL (in individuals without coronary heart disease and with <2 risk factors) or <130 mg/dL (in individuals without coronary heart disease and with ≥2 risk factors) after having followed a Step I diet. The Step II diet allows <30% of calories from fat, <7% of calories from saturated fat, and <200 mg/d cholesterol (Table). Subjects in the control group consumed a diet that included ≈34% of calories from fat, 12% from saturated fat, 11% from monounsaturated fat, 6% from polyunsaturated fat, and 312 mg/d of cholesterol. This diet is comparable to that presently consumed in the United States. In contrast, subjects on the Mediterranean-style diet averaged 30% of calories from fat, 8% from saturated fat, 13% from monounsaturated fat, 5% from polyunsaturated fat, and 203 mg/d of cholesterol (Table). Moreover, these subjects consumed less linoleic acid (3.6% versus 5.3% kcal) and more oleic acid (12.9% versus 10.8% kcal), α-linolenic acid (0.84% versus 0.29% kcal), and dietary fiber. Plasma fatty acid analysis conducted after 52 weeks of follow-up confirmed the dietary fatty acid data. The experimental group had higher plasma levels of oleic acid, linolenic acid, and eicosapentaenoic acid and lower levels of stearic acid, linoleic acid, and arachidonic acid. Thus, the experimental group modified dietary fat and cholesterol, consistent with the National Cholesterol Education Program/AHA Step I diet, and implemented a Mediterranean-style dietary pattern.

After 46 months of follow-up, 204 control and 219 experimental subjects (93% of the original cohort) participated in the final examination. A total of 302 experimental and 303 control group subjects were randomized into the study; however, the study was stopped early because of significant beneficial effects noted in the original cohort. Despite a similar coronary risk factor profile (plasma lipids and lipoproteins, systolic and diastolic blood pressure, body mass index, and smoking status), subjects following the Mediterranean-style diet had a 50% to 70% lower risk of recurrent heart disease, as measured by 3 different combinations of outcome measures including (1) cardiac death and nonfatal heart attacks; (2) the preceding plus unstable angina, stroke, heart failure, and pulmonary or peripheral embolism; and (3) all of these measures plus events that required hospitalization.

Although these results are quite impressive, there are methodological limitations that raise questions about the true impact of this diet on the risk of recurrent heart disease and related measures. Specifically, the baseline diet was only assessed in the experimental group at the beginning of the study, and the diet of the control group at baseline was presumed to be comparable. Moreover, nutrient intake in the control group was only assessed at the conclusion of the study so the dietary behavior of these subjects would not be influenced. Thus, it is not clear whether any dietary changes were made by the control group. In addition, dietary data are reported for only 83 (of 303 randomized into the study) and 144 (of 302 randomized into the study) subjects in the control and experimental groups, respectively. With only 30% of the total control cohort and <50% of the total experimental group providing dietary data at the conclusion of the study, the diet of the other subjects who completed the study is not known. This raises questions about the role of diet in accounting for the results reported for recurrent coronary events.

The findings from the Lyon Diet Heart Study illustrate the potential importance of a dietary pattern that emphasizes fruits, vegetables, breads and cereals, and fish, as well as α-linolenic acid within the context of a Step I diet. The clinical findings from the Lyon Diet Heart Study implicate risk factors beyond lipids and lipoproteins, which have historically been our primary targets of intervention. The fact that omega-3 fatty acids exert cardioprotective effects via multiple mechanisms (ie, prevent arrhythmia, have anti-inflammatory properties, decrease synthesis of cytokines and mitogens, stimulate endothelial-derived nitric oxide, are antithrombotic, are prostaglandin and leukotriene precursors, and inhibit atherosclerosis) suggest that they could have accounted for the cardioprotective effect observed. The unprecedented reduction in coronary recurrence rates, despite the fact that lipid/lipoprotein risk factors were comparable, clearly points to other important risk factor modifications as major influences in the development of CVD. There is a pressing need to identify these risk factor(s) and effective intervention strategies. Moreover, had this dietary pattern been prescribed with a Step II diet, as is presently recommended for individuals with CVD, the beneficial effects of the diet intervention could have been even more remarkable. Irrespective of this, a Mediterranean-style Step I diet can be followed by free-living people, although this diet plan has not yet been evaluated in a long-term primary prevention model.

It would be short-sighted to not recognize the enormous public health benefit that this diet could confer with adoption by the population-at-large if the findings are confirmed. Thus, the task at hand is to corroborate the results of the Lyon Diet Heart Study in both primary and secondary prevention models as expediently as possible and verify, as would be expected, that this dietary pattern is safe. In the meantime, we should take advantage of the possible opportunity to dramatically lower CVD risk in the population by widely recommending a Step I diet that features a dietary pattern that includes fruits, root vegetables (ie, carrots, turnips, potatoes, onions, radishes), leafy green vegetables, breads and cereals, fish, and foods high in α-linolenic acid such as vegetable oils (ie, flaxseed, canola), vegetable oil products (ie, salad dressing and margarine made with nonhydrogenated oils high in α-linolenic acid), and nuts and seeds (walnuts and flaxseed).

In conclusion, the AHA and its partners should take advantage of the remarkable opportunity to dramatically lower CVD risk in the population by funding further nutrition-based research. Research is needed to resolve what dietary constituents confer the cardioprotective effect seen in the Lyon Diet Heart Study. Although the authors propose that α-linolenic acid plays an independent role in lowering CVD risk, other dietary differences between the experimental and control groups could account for the observed effects. Studies are also needed to clarify whether additional effects can be attained when α-linolenic acid is included in a Step I and Step II diet. It will also be important to ascertain the specific effects of an increased intake of fruits and vegetables. These studies will provide important information about the effects of a unique dietary pattern that emphasizes fruits, vegetables, breads and cereals, fish, and α-linolenic acid in a Step I or Step II diet. Funding is needed to address these questions and move us closer to our long-sought goal of developing and implementing dietary strategies that have a major beneficial impact on CVD risk. The public health benefits that now seem to be achievable by dietary intervention, using emerging evidence, clearly warrant an investment of significant research funding by the AHA and its partners.

References

1. National Cholesterol Education Program. *Second Report of the Expert Panel on Detection, Evaluation, and Treatment of High Blood Cholesterol in Adults (Adult Treatment Panel II).* Bethesda, Md: National Institutes of Health, National Heart, Lung and Blood Institute; 1993. NIH Publication No. 93-3095.
2. de Lorgeril M, Salen P, Martin JL, et al. Mediterranean diet, traditional risk factors, and the rate of cardiovascular complications after myocardial infarction: final report of the Lyon Diet Heart Study. *Circulation*. 1999; 99:779–785.

KEY WORDS: AHA Science Advisory ■ diet ■ cardiovascular diseases