REVIEW

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The Mediterranean Diet, its Components, and Cardiovascular Disease

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ABSTRACT

One of the best-studied diets for cardiovascular health is the Mediterranean diet. This consists of fish, monounsaturated fats from olive oil, fruits, vegetables, whole grains, legumes/nuts, and moderate alcohol consumption. The Mediterranean diet has been shown to reduce the burden, or even prevent the development, of cardiovascular disease, breast cancer, depression, colorectal cancer, diabetes, obesity, asthma, erectile dysfunction, and cognitive decline. This diet is also known to improve surrogates of cardiovascular disease, such as waist-to-hip ratio, lipids, and markers of inflammation, as well as primary cardiovascular disease outcomes such as death and events in both observational and randomized controlled trial data. These enhancements easily rival those seen with more established tools used to fight cardiovascular disease such as aspirin, beta-blockers, angiotensin-converting enzyme inhibitors, and exercise. However, it is unclear if the Mediterranean diet offers cardiovascular disease benefit from its individual constituents or in aggregate. Furthermore, the potential benefit of the Mediterranean diet or its components is not yet validated by concrete cardiovascular disease endpoints in randomized trials or observational studies. This review will focus on the effects of the whole and parts of the Mediterranean diet with regard to both population-based and experimental data highlighting cardiovascular disease morbidity or mortality and cardiovascular disease surrogates when hard outcomes are not available. Our synthesis will highlight the potential for the Mediterranean diet to act as a key player in cardiovascular disease prevention, and attempt to identify certain aspects of the diet that are particularly beneficial for cardioprotection.

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Cardiovascular disease is the leading cause of morbidity and mortality in the world regardless of race, ethnicity, or sex, and costs related to cardiovascular disease in the United States are expected to surpass $300 billion in 2010.[1] Optimistically, simple and cost-effective steps such as a proper diet should be able to alleviate the obesity epidemic and the resultant cardiovascular disease burden, as it is estimated that lifestyle choices can account for up to 40% of premature cardiovascular disease deaths.[2] Consistently, the Mediterranean diet—consisting of fish, unsaturated fats, whole grains, fruits and vegetables, nuts and legumes—has consistently been shown to reduce cardiovascular morbidity and mortality as well as surrogate markers in meta-analyses, cohort studies, and randomized control trials (RCTs). These improvements match reductions in cardiovascular disease burden demonstrated by highly proven and advertised interventions, and approach measures such as physical activity and smoking cessation (**Figure 1**).[3-16] This historical and narrative review examines current professional society guidelines, RCTs, observational studies, and meta-analyses throughout the literature pertaining to the Mediterranean diet—and the components thereof—dating back to the inception of such a concept with the Seven Countries Study[17] in the 1980s in an effort to critically examine the

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role of the Mediterranean diet and its components in ameliorating the burden of cardiovascular disease.

THE MEDITERRANEAN DIET, IN TOTO

The authors of the Seven Countries Study[17] note that in contrast to the rest of the developed world, the farmers of Crete consumed some of the largest amounts of fat, yet had the lowest cardiovascular mortality rate. The diet does not single out specific food items or limit calories, but rather emphasizes an abundance of plant foods, olive oil as the principal source of fat, limited dairy products, consumption of moderate amounts of fish, poultry, and wine, low amounts of red meat, and fresh fruit daily—consistent with current American Heart Association (AHA) and European Society of Cardiology (ESC) recommendations for dietary caloric distribution.[18,19]

CLINICAL SIGNIFICANCE

- The Mediterranean Diet has been proven by randomized controlled trials, observational studies, and meta-analyses to be beneficial for both primary and secondary prevention of cardiovascular disease.
- No specific component of the Mediterranean diet has been shown to be as beneficial as the whole.
- Calorically mindful portions of each individual component should be recommended to patients for cardiovascular prevention. Further study is required to understand the contribution of the constituents of the Mediterranean diet.

Principal in the data favoring the Mediterranean diet is the Lyon Heart Study, which showed in an RCT that composite endpoints of cardiovascular disease events and death were reduced for up to 4 years after an initial event in those randomized to the Mediterannean diet, thus establishing it as a staple in secondary prevention.[20] Recently, the PREvencion con DIeta MEDiterannea (PREDIMED) investigators completed an RCT comparing a low-fat diet to the Mediterranean diet supplemented with either olive oil or nuts.[21] This trial was, in fact, halted early after a significant reduction in cardiovascular disease events was overwhelmingly evident in the Mediterranean diet arms of the trial, and distinctly marked almost immediately after randomization. This flagship study is one of the largest randomized trials focusing on primary cardiovascular disease prevention, and clearly places the Mediterranean diet at the forefront of preventative cardiovascular medicine. More copious, yet congruent, observational and RCT data exist, with one RCT evaluating surrogate markers of cardiovascular disease prevention showing that the Mediterranean diet reduces the risk of repeat cardiovascular events.[22] Further RCT evidence supports the use of a Mediterranean diet to reduce genetic predisposition for risk factors, not cardiovascular disease morbidity or mortality and their complications, in a high-risk population.[23] This trial (a sub-study of the multicenter PREDIMED study)[24,25] shows that patients on the Mediterranean diet had fewer monocytes, inflammatory markers, and beneficial modulation of gene expression involved in low-density lipoprotein (LDL) oxidation. The Mediterranean diet seems to show beneficial effects regarding the metabolic syndrome[26] and diabetes[25] compared with low-fat diets, especially when enriched with either nuts or olive oil.[26]

Observational and ecological studies such as the original Seven Countries Study have shown positive benefits of the Mediterranean diet in terms of cardioprotection, surrogate markers for cardiovascular disease, as well as overall morbidity and mortality.[27,28] Subsequently, a large meta-analysis of over 50,000 patients showed that the Mediterranean diet significantly reduced the risk of metabolic syndrome and protected against risk factors such as waist circumference, lipids, glucose, and blood pressure[29] in primary prevention (**Figure 2**). Another meta-analysis of 2650 patients showed that the Mediterranean diet provided a more robust reduction in cardiovascular disease risk factors and inflammatory markers.[30]

In fact, the Mediterranean diet is comparable with other interventions such as aspirin, statins, physical activity, and even antihypertensives such as angiotensin-converting enzyme inhibitors or beta-blockers in terms of reducing the risk of cardiovascular disease morbidity, mortality, and events (**Figure 1**). These estimates, of course, are rough due to the vast heterogeneity in the types and varieties of studies and their sizes, subjects, styles, and primary/secondary endpoints. Consequently, the data about the Mediterranean diet for cardiovascular disease morbidity and mortality reduction is robust, and recently cemented by a primary prevention RCT showing overwhelming benefit.

The remainder of this review will examine the foods that comprise the Mediterranean diet in an effort to review the observational vs RCT data of the individual components of the diet, which may offer insights into which foods within the diet might offer a reduction in cardiovascular disease morbidity and mortality.

OMEGA-3 POLYUNSATURATED FATS, SUCH AS FISH

The marine omega-3 fatty acids are polyunsaturated fatty acids and widely studied in the Mediterranean diet. Per recommendations made by the AHA/American College of Cardiology (ACC), fish should be consumed twice per week in cases of known cardiovascular disease.[31] European guidelines endorse the isocaloric consumption of fish for primary and secondary cardiovascular disease and possibly dysrhythmia protection.[32]

A multitude of meta-analyses have shown a potential cardiovascular disease morbidity and mortality benefit for