

Translational Section

The Mediterranean Diet

Guest Editorial

Can a Mediterranean Diet Pattern Slow Aging?

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To identify potential secrets for longevity, we interviewed some of the long-term survivors of the Cardiovascular Health Study. One woman, 93 years of age, told us that her secret was her vegan diet. Surprised to hear of a 93-year old vegan, we asked, “How long have you been on this diet?” She replied, “Well, it has been over a year, and I never felt better in my life!” Obviously this could not be the secret to her longevity, but we appreciated her intent to live as well as possible.

While everyone agrees that diet is important to health, an ideal dietary pattern is seldom adhered to. Increasingly, the Mediterranean Diet has become a healthy eating standard. Ancel Keyes first noted the association between dietary patterns in Mediterranean regions and lower rates of heart disease the Seven Countries Study in 1958 (1). Subsequently, research focused on specific macronutrients, especially dietary fats, to determine which were most important for health (2). These studies, and the resulting emphasis on low-fat diets, led to a shift in dietary patterns that replaced fats with predominantly refined carbohydrates (3). More recently, emphasis has been placed on examining the role of diet in health as a composite of multiple nutrients and foods. We eat foods, not nutrients, and the combination of foods may be more synergistically powerful for health than any specific food or nutrient (4,5).

Recent evidence suggests that the patterns of diet that may be most healthful are plant-based food patterns, where vegetables, whole grains and legumes are the dietary staples, with less meat—but not less total fat—than is typically consumed in developed countries (2,6). In 2013, the *Prevención con Dieta Mediterránea* -PREDIMED trial reported that a Mediterranean diet enriched with olive oil or nuts reduced cardiovascular morbidity and mortality by 30% compared with a low-fat diet (7). Based on subsequent PREDIMED analyses and from observational studies, a Mediterranean diet pattern, which is rich in healthy fats, whole grains, and multiple beneficial

micronutrients, appears to prevent all kinds of age-related maladies, including stroke, atrial fibrillation, breast cancer and Alzheimer’s disease (8). The impact of this pattern does not appear to be due to promoting weight loss, though adherents tend to gain less weight over time (9). In basic aging research, rodent models of caloric restriction have long been known to promote longevity. However, specific critical nutrients or dietary patterns are less well studied for longevity and other aging outcomes. Given the protective association of a Mediterranean diet with so many chronic health conditions, should we promote this pattern specifically for healthy aging and longevity?

In this issue of the Journals of Gerontology Biological Science and Medical Science, we feature a translational section that explores potential mechanisms by which a Mediterranean diet may impact health aging and population studies that assess healthy aging outcomes. The review by Drs. Tosti, Bertozzi and Fontana (10) provides an outstanding summary of five important adaptations induced by the Mediterranean diet that could modify health span. These include lipid lowering, protection from oxidative stress and inflammation, modification of growth factors that can promote cancer, inhibition of nutrient sensing pathways by amino acid restriction, and gut microbiota-mediated production of metabolites. Many of these pathways are thought to be underlying mechanisms of aging biology. The review provides support for the idea that the biological processes important in aging can be targeted for multiple health outcomes.

Many studies of the Mediterranean diet have focused on one or a few of these pathways. Further advancing the evidence of effects on these aging-related metabolic pathways, Gomez-Delgado et al. (11) report a potential interaction between genetic variants and diet on inflammatory status. In an analysis of the Coronary Diet Intervention With Olive Oil and Cardiovascular Prevention (CORDIOPREV) study, single-nucleotide polymorphisms of telomere RNA component (TERC), known to be associated with telomere length, were assessed in groups

randomized to a low fat vs. Mediterranean diet. Both were compared to usual diet in patients of mean age 60 with coronary artery disease. The TERC SNP *rs12696304* interacted with plasma levels of monounsaturated fatty acid (MUFA) levels in association with telomere length and C reactive protein (high sensitivity, hsCRP) levels. Participants with the CC genotype and high plasma MUFA at baseline had the longest telomere lengths. While the Mediterranean diet intervention led to declines in hsCRP in both groups, individuals with the CC genotype had a greater decrease in hsCRP compared to G-allele carriers. Findings were not adjusted for multiple testing, so are exploratory, but illustrate the potential for more personalized dietary prescription.

Advanced glycation end products, which are hypothesized to be influenced by dietary composition, may be another pathway that promotes inflammation and age-related disease (12). Building on their previous studies that suggest a Mediterranean diet can decrease advanced glycation end (AGE) products, Lopez-Moreno et al. (13) tested coenzyme Q as a dietary supplement, hypothesizing that when added to a Mediterranean diet, it would further lower levels of circulating AGEs and the expression of genes related to AGEs metabolism. Twenty older participants were randomly assigned to three different isocaloric diets including Mediterranean diet with or without coenzyme Q or a western high saturated fat diet. Coenzyme Q is thought to play a key role in mitochondrial metabolism for its antioxidant capacity. It is reduced in aging, poor diet, and stress. The Mediterranean diet lowered AGE levels and increased AGER-1 and *glox1* mRNA levels compared with a western diet; this was accentuated with co-enzyme Q. Although the study is quite small it suggests that there is a signature of benefit for coenzyme Q that can be assessed in larger trials.

Along with insights on how the Mediterranean diet may influence key mechanisms involved in age-related disorders, there is a need for research directly linking this dietary pattern to healthy aging. Struijk et al. add to a limited body of evidence suggesting that the Mediterranean diet may contribute to improved physical functioning in older adults (14). In a prospective analysis of 1,630 Spanish adults, higher scores on a Mediterranean diet index that quantifies adherence based on achieving intake targets for 14 food components were associated with fewer limitations in agility, mobility, and overall physical functioning. Achieving targets for fruits, fish and nuts were associated with better outcomes. In contrast, associations were weak and largely nonsignificant with an alternative Mediterranean diet index based simply on achieving intake above the sample median for nine food components. These contrasting results highlight the challenging nature of dietary data, and the need for expertise to better develop, adapt, and interpret dietary patterns applied in aging research (15).

Similarly, Assman et al. (16) reported that a quantitative Mediterranean diet score with nine predefined intake targets was associated with a greater likelihood of healthy aging, defined as a multidimensional construct that included the absence of major chronic disease, independence in daily living, and no depressive symptoms, among others. Among 3,012 French adults with more than 10 years of follow-up, the highest tertile of both the quantitative target-based score and a relative intake score based on intake tertiles rather than the median, were associated with greater odds of healthy aging more than 3,000 French adults. Associations with the traditional score based on median intakes were weaker and nonsignificant. These intriguing results add to a growing body of evidence suggesting that adherence to food-based dietary patterns such as the Mediterranean diet, which may be characterized by high intakes of healthy fatty acids, can help to reduce morbidity and mortality (7,17).

Findings from these studies point to potential mechanisms involving the chronic inflammation increasingly thought to be a

hallmark of accelerated aging. However, the divergent findings for different Mediterranean diet indices reported in the observational studies also highlight the need for careful approaches to the use of dietary data in order to gain deeper insights on the potential benefits of this dietary pattern. Greater clarity on how this diet is defined, in both interventions and observational studies, will be critical in the aim of achieving a consensus on how to optimally apply this dietary pattern towards maximizing healthy aging.

In the meantime, a dietary pattern that emphasizes plant-based foods, as favored by our research participant has much to recommend it.

Conflict of Interest

None reported.

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