

A Mediterranean-Style Diet and Metabolic Syndrome

Mohsen Meydani, DVM, PhD

A moderate increase in physical activity and a detailed and tailored Mediterranean-style diet reduce the prevalence of metabolic syndrome and associated cardiovascular risks through reducing systemic vascular inflammation and endothelium dysfunction, particularly in those patients who do not lose weight.

© 2005 International Life Sciences Institute

doi: 10.1301/nr.2005.sept.312–314

Cardiovascular disease (CVD) is the leading cause of morbidity and mortality in the United States and other Western countries. In addition to predisposing factors, lifestyle and diet play important roles in the development of this disease.^{1,2} Metabolic syndrome, which is characterized by a group of metabolic risk factors, is associated with the subsequent development of CVD and type 2 diabetes. The biologic mechanisms at the molecular level between insulin resistance and metabolic risk factors are complex and are not fully understood.³

According to the data from the Third National Health and Nutrition Examination Survey (NHANES III), the prevalence of metabolic syndrome in the US population increases with age, from 7% among young adults (20–29 years) to about 42% at later ages (60–70 years). It is estimated that 47 million people in the United States have concurrent disturbed glucose metabolism, increased abdominal fat, dyslipidemia, and hypertension.³ The risk of CVD and all-cause mortality increases with the development of metabolic syndrome.¹

Metabolic syndrome is characterized by the presence of a group of metabolic risk factors in an individual; its diagnosis as defined by the Adult Treatment Panel III⁴ includes five abnormalities: 1) abdominal adiposity as

defined by an abdominal circumference over 102 cm (40 inches) in men and over 88 cm (35 inches) in women; 2) serum HDL cholesterol under 40 mg/dL in men and under 50 mg/dL in women; 3) triglyceride level of 150 mg/dL or greater; 4) elevated blood pressure of 130/85 mm Hg or greater; and 5) fasting plasma glucose concentration of 110 mg/dL or greater. Individuals with three or more of these abnormalities are diagnosed with metabolic syndrome. The underlying and promoting risk factors for the development of metabolic syndrome are overweight and obesity, physical inactivity, atherogenic dietary habits, and genetic factors. Overweight and abdominal obesity have been associated with several components of metabolic syndrome. Therefore, reduction of body weight and long-term maintenance of weight loss is desirable and is best achieved through calorie reduction combined with an exercise regimen.

While the reduction of caloric intake and body weight is one of the main approaches to treating metabolic syndrome patients, improving the quality of the diet appears to be a more attractive and feasible approach to treatment. Lowering the intake of saturated fat, trans fats, cholesterol, and simple sugars, and increasing the intake of fruits, vegetables, and whole grains is the general dietary guideline recommended by the Adult Treatment Panel III⁴ for metabolic syndrome patients.

Several studies have suggested that the consumption of a Mediterranean-style diet is associated with a reduced risk of CVD and all-cause mortality.^{5,6} Esposito et al.⁷ have recently studied the effect of a Mediterranean-style diet on endothelial dysfunction and several markers of vascular inflammation in metabolic syndrome patients. They recruited 180 sedentary metabolic syndrome patients with three or more components of metabolic syndrome and randomized them into two groups of 90. One group of patients was instructed to follow a Mediterranean-style diet and the other was used as a control. Both groups of patients were advised to consume a dietary regimen consisting of 50% to 60% carbohydrate, 15% to 20% proteins, and less than 30% total fat, of which less than 10% was saturated fat. However, the patients in the intervention group received individualized, detailed nu-

Dr. Meydani is director of the Vascular Biology Laboratory, Jean Mayer USDA Human Nutrition Research Center on Aging at Tufts University, Boston, Massachusetts.

Address for correspondence: Dr. Mohsen Meydani, Vascular Biology Laboratory, Jean Mayer USDA-HNRC, 711 Washington St., Boston, MA 02111; Phone: 617-556-3126; Fax: 617-556-3224; E-mail: mohsen.meydani@tufts.edu.

tritional advice to increase their daily consumption of olive oil and to consume at least 400 g of whole grains daily, including: legumes, rice, corn, and wheat; 250 to 300 g of fruits; 125 to 150 g of vegetables; and 25 to 50 g of walnuts for 2 years. Patients' body weight and height were measured, and both groups received guidance to increase their physical activity by walking 30 minutes per day and by swimming or playing sports. The adherence of patients to their dietary plan and physical activity was determined by the patients providing weekly dietary diaries, including 3-day dietary records and daily physical activity records.

Endothelial function was assessed by measuring and scoring the changes in platelet aggregation and blood pressure following intravenous administration of L-arginine, the precursor of nitric oxide that causes vasodilation. The lipid profile was determined and estimated insulin sensitivity was measured by using homeostasis model assessment (HOMA). They also measured a battery of pro-inflammatory cytokines including interleukin-6 (IL-6), IL-7, and IL-18, and high-sensitivity C-reactive protein (hs-CRP) in serum before and after interventions.

At baseline, there was an increased level of hs-CRP and HOMA scores with an increased number of metabolic syndrome components. The severity of endothelium dysfunction was directly associated with the presence of high numbers of metabolic syndrome components, as well as with waist circumference, HOMA score, hs-CRP, and IL-6 levels. However, after 2 years of intervention with a Mediterranean-style diet, the prevalence of the number of components of metabolic syndrome in this group of patients was reduced by half, and they showed a significant improvement in endothelial function and a reduction in systemic vascular inflammation. The amount of physical activity in the intervention group was the same as that of the control group, and the investigators reported that the 2 years of dietary intervention had a modest effect on body weight loss in both groups overall. However, the levels of hsCRP and all of the measured pro-inflammatory cytokines were significantly reduced in the intervention group compared with the controls.

CRP is an acute-phase reactant and is a marker of inflammation. It has been shown that weight reduction does not affect CRP levels⁸; rather, the levels correlate significantly with insulin resistance, which is a feature of metabolic syndrome.^{9,10} The level of CRP is influenced by inflammatory cytokines such as IL-6 and may play a role in the development of atherosclerotic lesions through activating immune cells and causing dysfunction of the endothelium.¹⁰⁻¹² Therefore, altered CRP levels

link endothelial dysfunction and CVD to the metabolic syndrome.

Esposito et al.⁷ also reported that patients treated with a Mediterranean-style diet had significantly reduced waist circumference, plasma glucose, serum insulin levels, and HOMA score. In addition, the level of serum HDL was increased, while the levels of total cholesterol and triglycerides decreased. Since the results were adjusted for body weight changes, the findings from this study suggest that combined components of the Mediterranean-style diet may reduce the risk of CVD by reducing the inflammatory condition and endothelial dysfunction associated with metabolic syndrome.

The dietary intervention in the study by Esposito et al.⁷ was a whole-food approach rather than an intervention with specific components of the Mediterranean diet. This approach was based on previous studies in which the components of a Mediterranean-style diet have been investigated either individually or in combination. In a population-based study, Psaltopoulou et al.¹³ reported that fruits, vegetables, and olive oil in the Mediterranean diet were responsible for the apparent protection against hypertension (a component of metabolic syndrome), which in turn contributes to lower morbidity from hypertension-related diseases, including coronary heart disease and stroke.

While the consumption of whole grains has been suggested to be beneficial,^{14,15} the processing of whole-grain cereals (during which, for example, salt may be added) may alter their health benefits.¹⁶ Psaltopoulou et al.¹³ reported an increase in hypertension with cereal intake in the Mediterranean-style diet. The Mediterranean diet in the study by Esposito et al.⁷ included a substantial amount of whole grains, but this did not have a negative impact on the measured outcomes. Walnuts were also one of the components included in the Mediterranean-style diet in that study. In addition to containing bioactive compounds, walnuts have a high content of L-arginine¹⁷ and α -linolenic acid.¹⁸ L-arginine is a precursor amino acid for the production of endogenous nitric oxide, and α -linolenic acid is a vegetable n-3 fatty acid; both contribute to the anti-hypertensive and anti-atherogenic properties of walnuts. The substitution of walnuts for monounsaturated fat in a Mediterranean-style diet has been shown to improve endothelium-dependent vasodilation in hypercholesterolemic subjects.¹⁹

The amount of physical activity was the same in both the intervention and control groups in the Esposito et al. study.⁷ However, compared with the control patients, the intervention patients received more detailed and tailored dietary advice to adopt a Mediterranean-style diet. It appears that the Mediterranean diet signifi-

cantly and favorably changed all of the components of metabolic syndrome along with parameters associated with CVD and inflammation. The diet's high contents of fiber, n-3 fatty acids, and antioxidants, as well as phytochemicals from olive oil, legumes, whole grains, fruits, and vegetables, might be responsible for its beneficial effect on the health of metabolic syndrome patients. This may occur through the reduction of systemic vascular inflammation and endothelium dysfunction without having a drastic effect on body weight. Although caloric restriction and body weight reduction remain a primary approach for treating metabolic syndrome patients, intervention with a Mediterranean-style diet combined with moderate exercise might be a strategy to treat those patients who do not lose weight.

REFERENCES

- Lakka HM, Laaksonen DE, Lakka TA, et al. The metabolic syndrome and total and cardiovascular disease mortality in middle-aged men. *JAMA*. 2002;288:2709–2716.
- Isomaa B, Almgren P, Tuomi T, et al. Cardiovascular morbidity and mortality associated with the metabolic syndrome. *Diabetes Care*. 2001;24:683–689.
- Ford ES, Giles WH, Dietz WH. Prevalence of the metabolic syndrome among US adults: findings from the third National Health and Nutrition Examination Survey. *JAMA*. 2002;287:356–359.
- Expert Panel on Detection, Evaluation, and Treatment of High Blood Cholesterol In Adults. *Executive Summary of The Third Report of The National Cholesterol Education Program (NCEP) Expert Panel on Detection, Evaluation, and Treatment of High Blood Cholesterol In Adults (Adult Treatment Panel III)*. *JAMA*. 2001;285:2486–2497.
- Trichopoulou A, Costacou T, Bamia C, Trichopoulos D. Adherence to a Mediterranean diet and survival in a Greek population. *N Engl J Med*. 2003;348:2599–2608.
- Hu FB. The Mediterranean diet and mortality—olive oil and beyond. *N Engl J Med*. 2003;348:2595–2596.
- Esposito K, Marfella R, Ciotola M, et al. Effect of a Mediterranean-style diet on endothelial dysfunction and markers of vascular inflammation in the metabolic syndrome: a randomized trial. *JAMA*. 2004;292:1440–1446.
- McLaughlin T, Abbasi F, Lamendola C, et al. Differentiation between obesity and insulin resistance in the association with C-reactive protein. *Circulation*. 2002;106:2908–2912.
- Festa A, D'Agostino R Jr, Howard G, Mykkanen L, Tracy RP, Haffner SM. Chronic subclinical inflammation as part of the insulin resistance syndrome: the Insulin Resistance Atherosclerosis Study (IRAS). *Circulation*. 2000;102:42–47.
- Yudkin JS, Stehouwer CD, Emeis JJ, Coppack SW. C-reactive protein in healthy subjects: associations with obesity, insulin resistance, and endothelial dysfunction: a potential role for cytokines originating from adipose tissue? *Arterioscler Thromb Vasc Biol*. 1999;19:972–978.
- Pasceri V, Willerson JT, Yeh ET. Direct proinflammatory effect of C-reactive protein on human endothelial cells. *Circulation*. 2000;102:2165–2168.
- Yeh ET, Anderson HV, Pasceri V, Willerson JT. C-reactive protein: linking inflammation to cardiovascular complications. *Circulation*. 2001;104:974–975.
- Psaltopoulou T, Naska A, Orfanos P, Trichopoulos D, Mountokalakis T, Trichopoulou A. Olive oil, the Mediterranean diet, and arterial blood pressure: the Greek European Prospective Investigation into Cancer and Nutrition (EPIC) study. *Am J Clin Nutr*. 2004;80:1012–1018.
- Anderson JW. Whole grains protect against atherosclerotic cardiovascular disease. *Proc Nutr Soc*. 2003;62:135–142.
- Jensen MK, Koh-Banerjee P, Hu FB, et al. Intakes of whole grains, bran, and germ and the risk of coronary heart disease in men. *Am J Clin Nutr*. 2004;80:1492–1499.
- Hu FB, Willett WC. Optimal diets for prevention of coronary heart disease. *JAMA*. 2002;288:2569–2578.
- Feldman EB. The scientific evidence for a beneficial health relationship between walnuts and coronary heart disease. *J Nutr*. 2002;132:1062S–1101S.
- Lavedrine F, Zmirou D, Ravel A, Balducci F, Alary J. Blood cholesterol and walnut consumption: a cross-sectional survey in France. *Prev Med*. 1999;28:333–339.
- Ros E, Nunez I, Perez-Heras A, et al. A walnut diet improves endothelial function in hypercholesterolemic subjects: a randomized crossover trial. *Circulation*. 2004;109:1609–1614.

Copyright of Nutrition Reviews is the property of International Life Sciences Institute. The copyright in an individual article may be maintained by the author in certain cases. Content may not be copied or emailed to multiple sites or posted to a listserv without the copyright holder's express written permission. However, users may print, download, or email articles for individual use.