

Mediterranean diet, hypertension and cardiovascular disease

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Hypertension (HT) remains the main risk factor for developing coronary artery disease, congestive heart failure, stroke and kidney disease [1]. Its prevalence continues to increase exponentially due to better detection and an increase in other associated factors such as obesity, physical inactivity and diabetes mellitus. Recently published data from the National Health and Nutritional Examination Survey (NHANES) between 2007 and 2010 show that HT affects 33% (77.9 million) of people aged ≥ 20 years in the United States [2] and this prevalence is estimated to increase to 37.3% by 2030 [3]. The prevalence of hypertension increases with age, with the estimated lifetime risk for elderly subjects reaching 90%. The magnitude of this burden underscores the need for increased awareness, treatment, control, and, primarily, prevention.

The north-south gradient with respect to CVD has been confirmed in several epidemiological studies, as evidenced by data from the MONICA Project (multinational monitoring of trends and determinants in cardiovascular disease) [4], in which Spain, the South of France and Italy showed a lower

incidence of and mortality due to coronary heart disease (in both men and women) than Northern European countries and the United States. In light of this evidence, numerous studies have been made showing the benefits of adherence to a "healthy diet" in reducing CVD. Data from the CARDIA study (Coronary Artery Risk Development in Young Adults), published by Liu et al. [5] and conducted in 3154 participants aged 18-30 years, underline the importance of maintaining a healthy lifestyle over a 20-year follow-up. In this study, adherence to a "healthy diet" increased the maintenance of a low cardiovascular risk profile (28.3% for a healthy diet vs. 22.4% for an unhealthy diet; $P < 0.01$) upon reaching adulthood, thus reducing the likelihood of future CVD. Therefore, all cardiovascular prevention guidelines placed diets and lifestyles as the cornerstone for reducing and preventing the development of HT and CVD [6].

The lifestyle changes that have shown benefit in reducing BP values include weight reduction, reduced sodium intake, increased potassium intake, promotion of a reduction in excessive alcohol intake, and the so-called DASH diet (Dietary Approaches to Stop Hypertension) [7, 8]. Initially, this diet potentiated increased consumption of fruits, vegetables and fat dairy products with a relatively low intake of total and saturated fat [9], although restrictions in sodium intake were later added in order to achieve greater reductions in BP values [10].

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In recent decades, the vasculoprotective potential of diet and its various nutrients has been increasingly recognized, although in recent years more solid evidence on the benefits of the Mediterranean Diet (MD), a food pattern based on high consumption of fruits, vegetables and monounsaturated fats, with olive oil being the main source of fat, has emerged. Since the 1990s, evidence on the benefits of the MD in the prevention of CVD and the reduction of BP and cholesterol levels and/or diabetes, has become stronger, although the level of evidence remains very heterogeneous. As stated, the MD is characterized by a diet rich in fruits, vegetables and cereals, with a high intake of mono- and polyunsaturated fats, and with olive oil being the main source of fat. Likewise, the MD encourages moderate fish and poultry consumption and a low consumption of dairy products, red meat, prepared meats and sweets and pastries. The MD also promotes moderate consumption of wine, preferably red, during meals [11].

The strongest evidence on the benefits of the MD comes from the multicentre, randomized PREDIMED study of 4,774 patients at high cardiovascular risk in primary prevention. Patients were assigned to one of three arms of a dietary intervention: MD supplemented with virgin olive oil (VOO), MD supplemented with nuts, or a control low fat diet. The study was halted prematurely at 4.8 years of follow up in accordance with data obtained in an interim analysis. The PREDIMED [12] study is the first randomized trial in primary prevention, and showed that a MD supplemented with in VOO or nuts significantly reduces the incidence of major cardiovascular events, with a HR of 0.70 (95% CI, 0.54 - 0.92) and 0.72 (95% CI, 0.54-0.96), respectively.

Prior studies of the effects of the MD on BP have relied on clinic (office) BP measurements, an approach that is limited by poor reproducibility, the white-coat effect, and observer and patient variability. It is important to remember that 24-hour ambulatory BP (ABP) monitoring is considered the gold standard for the assessment of the effects of interventions on BP, as repeated measurements more accurately reflect usual BP than isolated office measurements. The latest evidence of the beneficial effect of the MD on BP comes from a recent substudy of the PREDIMED study by Domenech et al. [13], which included 235 subjects (56.5% female; mean age, 66.5 years) at high cardiovascular risk (85.4% with hypertension). The results showed that the MD supplemented with either extra-virgin olive oil or nuts resulted in significant reductions in 24-hour ABP compared with a control diet in individuals at high risk of CVD. The net differences between the MD supplemented with extra-virgin olive oil and nuts and the control diet were -4.0 for

mean systolic BP, -4.3 mm Hg for mean diastolic ABP, and -1.9 mm Hg for both MD after adjustment for between-diet imbalances in baseline BP and for trial changes in antihypertensive medication. The impact of such BP changes, even if their magnitude seems small, could be remarkable at the population level if we consider the lack of BP control rates in spite of pharmacological treatment. Similar effects were also seen in studies of the MD in Italy, where significantly lower BP was observed [14, 15]. In comparison to randomized controlled trials, observational studies do not have control over dietary patterns, so not surprisingly, results from observational studies show more conflicting results for the MD.

Finally, a recent meta-analysis that includes 17 randomized controlled trials reinforces the evidence on the effect of dietary patterns on BP in adults. In this study a significant reduction of 4.26 mm Hg in SBP and 2.38 mm Hg in DBP was observed [18] and reductions of 4.25 and 2.27 mmHg respectively in those in which weight loss, increased exercise or sodium restrictions were not achieved. Certainly, these results should have public health implications because the MD, a vegetable-based and high-unsaturated fat dietary pattern, seems to be a useful adjunct to established dietary and pharmacological approaches for improving hypertension control while incurring no expense for the health system.

The interface between the adoption of healthy diets and other behavioral lifestyle changes cannot be ignored, taking into account that co-interventions such as sodium restriction, physical exercise, and weight loss also led to significant BP reductions. We shouldn't forget that a wide range of combinations of these interventions may be more effective for the management of BP, and further research on relative efficacy would be desirable.

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