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Chili Pepper Consumption and Cardiovascular Mortality

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EDITORIAL COMMENT

Chili Pepper Consumption and Cardiovascular Mortality*

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In this issue of the *Journal*, a report from an Italian population-based study indicates that intake of hot chili pepper was associated with a significant reduction of all-cause cardiovascular and cerebrovascular mortality (1). In the Moli-sani study,

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22,811 men and women were enrolled between 2005 and 2010 and were followed for 8.2 years. During that time, there were 1,236 deaths, 36% of which were cardiovascular, 39% were from cancer, and 25% were from other causes. Chili peppers were consumed >4 times/week by 23.4% of participants, whereas 33.7% of participants never or seldom consumed them. Multivariable risk estimates contrasting those 2 groups gave a hazard ratio (HR) of 0.77 (95% confidence interval [CI]: 0.66 to 0.90) for all-cause mortality, 0.66 (95% CI: 0.50 to 0.86) for cardiovascular disease, 0.56 (95% CI: 0.35 to 0.87) for ischemic heart disease, and 0.39 (95% CI: 0.20 to 0.75) for cerebrovascular death. The effect of chili pepper was independent of a number of factors. In adjusted models, chili pepper consumption was a supplement to the Mediterranean diet score (MDS) and benefit was not seen in hypertensive subjects. It did not appear to be mediated by changes in risk factors such as fasting lipids, glucose, insulin, or other biomarkers. Intake of sweet peppers also reduced mortality risk but to a lesser extent. A small benefit was also observed with intake of vitamin D.

The magnitude of the observed risk reduction was much greater than that in previous studies. In 2015, a Chinese population-based study in ~500,000 men and women (2) reported that consuming spicy food almost daily was associated with a 14% reduction of total mortality and a 22% reduction of death from ischemic heart disease. In 2017, the U.S. NHANES (National Health and Nutrition Examination Survey) trial reported a 13% risk in total mortality associated with consumption of hot chili peppers (3). Reasons why the magnitude of risk reduction with chili pepper was much greater in the Italian study are not clear, but 1 reason may be that the background diet in Italy was healthier. The U.S. diet was so bad that the American Heart Association statistical report of 2015 indicated that only 0.1% of Americans ate a healthy diet (4). On the basis of that background, it was difficult to show the harm from dietary cholesterol and egg consumption. Early studies showed harm from eggs only among participants who became diabetic (5,6). Only recently did a pooled analysis of data in 29,615 Americans followed for a median of 17.5 years report a dose-dependent increase in cardiovascular risk with both dietary cholesterol and egg consumption (7). Similarly, it may be difficult to show the benefit from any single ingredient in the U.S. diet.

In the Moli-sani study (1), a low MDS (i.e., score of 1 to 3) was observed in 30% of participants, whereas 26% had a high MDS score (score of 6 to 9). Those with a high MDS also had a significant reduction of cardiovascular risk (HR: 0.64; 95% CI: 0.42 to 0.97). The reported HRs were highly adjusted. The full model included adjustment for "age, sex and energy intake, educational level, occupational class, smoking, leisure-time physical activity, cardiovascular disease, cancer, drugs for diabetes, lipid-lowering drugs, medication for hypertension, Mediterranean diet score (deprived of sweet pepper intake), sweet pepper intake (g/day, ordered quartiles), garlic,

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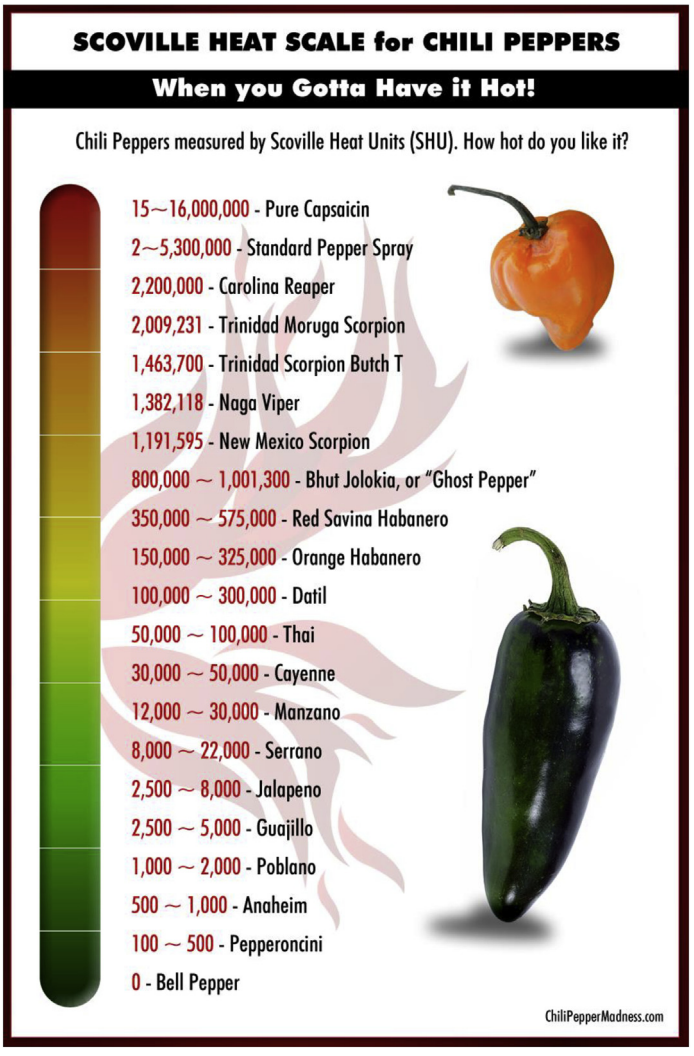
parsley, and black pepper (consumption yes/no)" (1). Over-adjustment may therefore be a reason for concern. However, risk reduction was observed with regular chili pepper consumption even without adjustment.

Biological plausibility for beneficial effects of chili peppers relates at least in part to obesity and insulin resistance. Chili peppers are the major source of naturally occurring capsaicinoids, including capsaicin, dihydrocapsaicin, nordihydrocapsaicin, homodihydrocapsaicin, and homocapsaicin. Sweet peppers are the major natural source of capsinoids, including capsiate, dihydrocapsiate, and nordihydrocapsiate (8). Capsaicin, the neurotoxin that accounts for the burning sensation of the tongue with chili peppers, reduces diet-induced obesity in rodents and humans and appears to be an activator of AMP-activated kinase and PPAR-γ (9). It increases browning of fat and reduces insulin resistance (10). Capsaicin also appears to have antiplatelet and anticoagulant activity, to reduce low-density lipoprotein oxidation, (8) and to improve endothelial function (11). **Figure 1** shows the enormous range of "heat" in varieties of chili peppers.

Should we all begin taking tablets of capsaicin and dousing our food with hot sauce? The history of food supplements suggests that we should wait for randomized trials. A recent meta-analysis of randomized trials of food supplements (vitamins and antioxidants such as vitamins C, D, E, niacin, beta carotene, selenium, and zinc) reported that only folic acid reduced cardiovascular disease and stroke risk and that vitamin B complexes that included vitamin B12 reduced the risk of stroke; no other supplement reduced cardiovascular risk (12). (Reduction of stroke with B vitamins was obscured in early trials by harm from cyanocobalamin among participants with impaired renal function [13].)

What appears to be most beneficial is the eating pattern, rather than any one food. The Mediterranean diet, which is high in whole grains, fruits, vegetables, and legumes, is high in beneficial phytochemicals. Because it is a "mainly vegetarian diet" (14), the Mediterranean diet is also low in cholesterol and saturated fat. As the fat intake is high (40% of calories from fat, mainly olive oil) (15), the diet also has a low glycemic index. In an Israeli diet study, the Mediterranean diet was clearly better than either a low-fat or low-carbohydrate diet for lowering fasting glucose and reducing insulin resistance among diabetic participants (16). In secondary prevention, the Mediterranean diet was twice as effective in the Lyon Diet Heart study (17) as was simvastatin in the contemporaneous Scandinavian Simvastatin Survival Study (18) (a reduction of >60% in coronary risk in 4 years vs. a 40% reduction in 6 years, respectively). In primary prevention, the Mediterranean diet reduced cardiovascular events by 30% over 5 years (19). (Results were confirmed in a re-analysis of the data after excluding participants who were not strictly randomized; persons in the same household were allocated to the same diet after 1 was randomized; and at 1 study site, all participants were allocated to the

FIGURE 1 A Range of "Heat" in Chili Peppers



There is an enormous range of "heat" in chili peppers, as assessed by the Scoville scale. It is probably not necessary to endure severe neurotoxicity to achieve the cardiovascular benefits of chili peppers. Reprinted with permission from Hultquist M, Hultquist P. Chili Pepper Madness. Baltimore, MD. Available at: https://www.chilipeppermadness.com/frequently-asked-questions/the-scoville-scale/. Accessed August 30, 2019.

Mediterranean diet.) Thus, adopting the Cretan Mediterranean diet would be much more likely to reduce cardiovascular risk than adding Tabasco sauce (McIlhenny Co., Avery Island, Louisiana) to the unhealthy American diet.

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