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Nut Consumption, Lipids, and Risk of a Coronary Event

GARY E. FRASER, M.B. CH.B., PH.D.

Center for Health Research, School of Public Health, Loma Linda University, Loma Linda, California, USA

Summary: In the past, many have avoided nuts because of their high fat content. The Dietary Approaches to Stop Hypertension (DASH) diet, however, recommends regular consumption of this food along with seeds and dried beans (4–5 servings per week) as part of a diet to control hypertension. Nuts are nutrient-dense and most of their fat is unsaturated. They are also perhaps the best natural source of vitamin E and are relatively concentrated repositories of dietary fiber, magnesium, potassium, and arginine, the dietary precursor of nitric oxide. Human feeding studies have demonstrated reductions of 8–12% in low-density lipoprotein (LDL) cholesterol when almonds and walnuts are substituted for more traditional fats. Other studies show that macadamias and hazelnuts appear at least as beneficial as fats in commonly recommended diets. Whether consuming modest quantities of nuts daily may promote weight gain is not known with certainty, but preliminary data suggest that this is unlikely. Four of the best and largest cohort studies in nutritional epidemiology have now reported that eating nuts frequently is associated with a decreased risk of coronary heart disease of the order of 30–50%. The findings are very consistent in subgroup analyses and unlikely to be due to confounding. Possible mechanisms include reduction in LDL cholesterol, the antioxidant actions of vitamin E, and the effects on the endothelium and platelet function of higher levels of nitric oxide. Although nuts may account for a relatively small percentage of dietary calories, the potential interacting effects of these factors on disease risk may be considerable.

Key words: nuts, lipids, coronary heart disease, vitamin E

Address for reprints:

Gary E. Fraser, M.B. CH.B., Ph.D.
Center for Health Research
School of Public Health, NH 2008
Loma Linda University
Loma Linda, CA 92350, USA

Introduction

For many years there has been a strong opinion that dietary habits affect coronary risk factors and hence probably the risk of a coronary event. The evidence is now overwhelming that consumption of dietary fats, oats, and other sources of fiber, as well as a small number of phytochemicals, affect blood lipids, and that consumption of alcohol, potassium, sodium, and a vegetarian diet influence blood pressure levels. However, there is much less direct evidence that diet affects the frequency of coronary events. This is probably largely related to the difficulties of accurately measuring dietary habits. A few good population studies have implicated dietary fats,[1, 2] as expected on the basis of nutritional research. Others could not show these effects. There is some support for the idea that fish consumption may be protective,[3] but surprisingly such an effect may be mainly seen at quite low intake.

Much of the practice of preventive cardiology is burdened with the problem of coercing reluctant patients to change habits which they enjoy (smoking, eating food high in saturated fat, physical inactivity). It is a pleasing change to note increasing evidence for a probably protective food that most people will eat more frequently with little persuasion. I refer to the consumption of modest quantities of nuts.

A Brief Note on the Chemistry of Nuts

Nuts are fatty foods and as such have been treated with caution in most previous dietary recommendations. Indeed, about 80% of the calories in most nuts come from fat, but this is largely monounsaturated (polyunsaturated in walnuts). Nuts also contain significant quantities of dietary fiber, potassium, magnesium, and copper. They are perhaps the best natural source of antioxidant vitamin E, and are also rich in arginine, the dietary precursor of nitric oxide.

In Tables I and II, as an example, the content of these factors is examined in almonds compared with a number of other common fatty foods of animal origin. In most cases, the contrast is quite dramatic, demonstrating that it is probably not appropriate to group nuts with meats and dairy products as is currently the case in the USDA food pyramid. More recent dietary recommendations such as those developed for the Dietary Approaches to Stop Hypertension (DASH) diet,[4, 5] by Oldways Foundation,[6] or those for vegetarians,[7] place nuts more appropriately with seeds and legumes. In addition, along

TABLE I The fat content (calories) of selected nuts and other common fatty foods of animal origin (per 100 g of food) [a]

	Total fat	SFA	MUFA	PUFA	UFA/SFA
Almonds	473	45	307	99	9.06
Walnuts	557	50	128	352	9.52
Filberts	563	41	442	54	11.98
Pecans	608	49	380	150	10.91
Pistachios	436	55	294	66	6.53
Macadamias	663	99	524	12	5.41
Peanuts	443	61	220	140	5.87
Beef, T-bone (trimmed)	191	77	80	7	1.14
Chicken, roasted	120	33	47	26	2.19
Whole milk	30	19	9	1	0.52
Eggs	101	30	40	13	1.76
Cheddar cheese	298	190	85	8	0.49

[a] Values taken from U.S. Dept. of Agriculture Handbooks: Composition of Foods.

Abbreviations: SFA = saturated fatty acids, MUFA = monounsaturated fatty acids, PUFA = polyunsaturated fatty acids, UFA = unsaturated fatty acids.

TABLE II Contents of selected food constituents in nuts and other common fatty foods of animal origin (per 100 g of food) [a]

	Vitamin E (mg) [b]	Dietary fiber (g) [c]	Mg^{2+} (mg)	Arginine (g)	Cholesterol (mg)
Almonds	16.1	11.2	296	2.5	0
Walnuts	3.1	4.8	169	2.1	0
Filberts	21.9	6.4	285	2.2	0
Pecans	2.7	6.5	128	1.1	0
Pistachios	4.5	10.8	158	2.2	0
Macadamias	[d]	5.2	117	0.8	0
Peanuts	6.3	8.8	180	3.5	0
Beef, T-bone (trimmed)	0.3	0	25	1.6	83
Chicken, roasted	0.4	0	23	1.7	107
Whole milk	0.04	0	13	0.1	14
Eggs	0.7	0	12	0.8	548
Cheddar cheese	0.4	0	28	0.9	105

[a] Data from U.S. Dept. of Agriculture Handbooks: Composition of Foods.

[b] Alpha-tocopherol equivalents. From the Nutrition Data System, Nutrition Coordinating Center. Univ. of Minnesota. Version 2.5, 1993.

[c] Dietary fiber taken from Spiller GA: Appendix I of *Handbook of Dietary Fiber in Human Nutrition*, Boca Raton, Fla.: CRC Press, 1993.

[d] Not available.

with many other vegetable foods, nuts are a storehouse for a large number of phytochemicals that are presently less well defined. However, these substances include at least certain flavonoids, other polyphenols, and sterols that may well have biological activity.

The Effect of Nut Consumption on Blood Cholesterol Levels

Several studies of various design have evaluated the effect of consumption of almonds, walnuts, hazelnuts and macadamias on blood cholesterol levels. A study of pecans is underway. Some have simply recommended nuts and nut oils as a supplement to be incorporated into the diet; others control the other fats in the diet and/or the foods for which the nuts are substituted.

Berry *et al.*[8,9] used either almonds, olive oil, or avocados as a source of fat in a diet, thus increasing the quantities of monounsaturated fats (MUFA), or walnuts, safflower, and soy to increase polyunsaturated fats (PUFA). These two diets were compared with each other or with a third high-carbohydrate diet in two separate studies. These studies were randomized crossover feeding trials involving 17 or 18 young men over two 12-week feeding periods. The investigators controlled the whole diet, with the MUFA and PUFA diets having 34% and 33% of calories as total fat, respectively. Compared with the baseline diet, both the high MUFA and high PUFA diets had quite similar effects, lowering total and LDL cholesterol levels 10–20% and not changing high-density lipoprotein (HDL) cholesterol. When compared with the high-carbohydrate diet, the high MUFA diet lowered total and LDL cholesterol.

Spiller *et al.* have reported three studies with an emphasis on the effect of almonds/almond oil on blood lipids. In the first study,[10] two groups totaling 30 hypercholesterolemic subjects were given careful dietary advice and quite different fatty supplements in a parallel study design. Each group participated in the study for 4 weeks. The first group adhered to a low-fat base diet plus a 100 g/day supplement of almonds. The second group had the same low-fat base diet, plus 48 g of fat from butter and cheese. While on the diets, the first group experienced a 15% drop in total cholesterol compared with the second group.

In the second study,[11] the almonds were supplemental to a partially controlled "usual" diet for which limited dietary advice was given. The foundation of the recommended "usual" diet was grains, beans, vegetables, fruit, and low-fat milk products. Meat and high-fat dairy products were minimized. The 26 men and women from a cardiac rehabilitation unit took a supplement of 100 g/day of almonds and almond oil for 9 weeks, on average consuming 37% of total calories as fat. Again, compared with the "usual diet", total and LDL cholesterol declined 9% and 12%, respectively.

For the third study,[12] Spiller *et al.* enrolled 48 hypercholesterolemic subjects with mean baseline total cholesterol of 251 mg/dl. Careful instructions were given to help subjects conform to a recommended baseline diet, which was then supplemented with either (1) 100 g almonds, (2) 48 g olive oil and 113 g cottage cheese, or (3) 85 g cheddar cheese, 28 g butter, each day for four weeks in a parallel study design. By the end of the study, total cholesterol levels had changed to

222 mg/dl, 240 mg/dl, and 263 mg/dl, respectively (differences significant $p < 0.001$). Similar significant changes were seen for LDL cholesterol, but there was virtually no effect on HDL cholesterol.

Sabaté *et al.*[13] conducted a carefully controlled crossover feeding study in 18 young men. All meals were fed during two 4-week dietary periods. In one diet, a basic diet was supplemented with 85 g/day of walnuts, and during the control period by equivalent fat calories from more traditional foods. Although both the control and the walnut diets contained only 30% of calories as fat, much of the fat in the latter was polyunsaturated, while the control diet had 10% of calories from each of saturated fatty acids, MUFA, and PUFA. Total cholesterol dropped 12.4%, LDL 16.3%, and a nonsignificant smaller drop was also seen in HDL cholesterol.

Another recently completed study of walnut supplementation in subjects with elevated serum cholesterol has also demonstrated significant lowering of lipid levels.[14] Abbey *et al.*[15] in Australia trained 16 men to record their fat consumption and then provided supplements to be added to the basic diet. The first supplement was constructed to match the fatty acid profile of the Australian diet, the second consisted of 84 g of MUFA-rich almonds, and the third of 68 g of PUFA-rich walnuts. During successive 3-week periods, LDL cholesterol was lower by 10.3% and 8.9%, respectively, with almonds and walnuts, whereas HDL cholesterol did not change.

Two other studies have evaluated the effects of supplementing relatively low-fat, high-carbohydrate diets with macadamia nuts.[16, 17] In each case, despite the increase in total fat, as most of this was monounsaturated, blood lipid levels did not change, except for a nonsignificant 9% rise in HDL cholesterol. Finally, a feeding study of 70 children and 104 adults, in which the intervention was a supplement of hazelnuts, will soon be reported. Again the effects on blood lipids appeared beneficial, with an increase in HDL and a fall in LDL cholesterol. There was no significant change in body weight.[18]

Nut Consumption and Obesity

Some worry that advocating increased use of a fatty food may further aggravate the serious problem of obesity in the United States. This important question cannot yet be clearly addressed with data, but a few clues suggest that this may not be the case. A study in rats indicates that just as different types of dietary fatty acids affect blood cholesterol differently, the same may be true of their effects on body fat. When fed calories as saturated fat, they increased body fat much more and "burned" much less (as indicated by the respiratory quotient), than those fed equivalent polyunsaturated fat calories.[19]

Several investigators have noted that in certain human nut feeding studies that included only limited dietary advice, weight gain was not a problem despite supplements of several hundred calories of nuts and/or nut fat each day.[11, 17, 20] We have almost completed a study that formally tested the hypothesis that adding a supplement of 320 calories of almonds daily with no dietary advice does not change body weight. Preliminary results suggest that this is so.[21] Suggested explanations for such a possible result include a satiety effect of nuts compensating for the additional nut calories by decreased intake of other foods; limited absorption of the fat due to the nut fiber or poor mastication; or an unexplained metabolic effect whereby nut fats are "burned" rather than stored, perhaps associated with a higher metabolic rate.

Directly Observed Associations between Nut Consumption and Risk of Coronary Heart Disease Events

We first observed[22] that those who consume nuts frequently had an approximately 50% lower risk of either a fatal or a nonfatal coronary event than those who eat nuts rarely. There was an apparent dose–response association (Fig. 1) shown in a cohort study of 34,000 non-Hispanic, Caucasian California Seventh-Day Adventists. The number of events in Figure 1 is, of course, reflective of the total number of subjects at risk in each group as well as the CHD risk. Of these Adventist subjects, nearly 25% ate nuts five times each week or more. However, many others rarely ate nuts, so a comparison with good statistical power was possible. It was impressive to us that however we divided the data, the "nut effect" was always seen. Men, women, vegetarians, omnivores, hypertensives, nonhypertensives, relatively obese or relatively thin subjects, older or younger subjects, who ate large quantities of nuts, all had a substantially lower CHD risk than their counterparts eating lower quantities of nuts (Table III). Multivariate analyses, adjusting for traditional risk factors and several other foods, did not change these findings in any important way. We have subsequently reported[23] that a protective association with nut consumption is still clearly found in the oldest-old Adventists (over age 84 years), and that in multivariate analyses, African American Adventists who consume nuts more frequently experience a lower total mortality.[24] Other results show that the consumers of larger quantities of nuts in the non-Hispanic, Caucasian Adventists population have lower total mortality.[25] Lifetable analyses indicate that consumers of high quantities

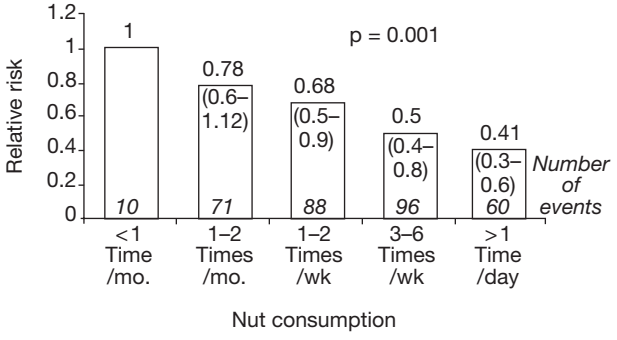

FIG. 1 Estimated relative risk for all fatal coronary heart diseases, stratified for age and sex: The Adventist Health Study.

TABLE III Associations between nut consumption and risk of coronary heart disease in various subgroups of the Adventist Health Study Population

	Relative risk Frequency of nut consumption			
Subgroup	< 1/week	1–4/week	> 4/week	p Values
Men	1.00	0.87	0.40	< 0.001
Women	1.00	0.56	0.51	< 0.001
Age < 80 years	1.00	0.88	0.48	< 0.001
Age ≥ 80 years	1.00	0.56	0.45	< 0.001
Normotensive	1.00	0.79	0.40	< 0.001
Hypertensive	1.00	0.75	0.81	NS
Vegetarian	1.00	0.58	0.42	< 0.001
Nonvegetarian	1.00	0.97	0.54	< 0.05
BMI ≤ 23.9	1.00	0.58	0.47	< 0.001
BMI > 23.9	1.00	0.80	0.52	< 0.01
Low exercise	1.00	0.62	0.63	< 0.05
Higher exercise	1.00	0.77	0.38	< 0.001
White bread only	1.00	0.57	0.46	0.07
Other breads or mixed	1.00	0.74	0.48	< 0.001

Abbreviations: BMI = body mass index, which had a mean value of 23.9 in this population, p = test of differences between categories of nut consumption, NS = not significant.

of nuts experience an extra 5.6 years of life expectancy free of coronary disease and an 18% lifetime risk of CHD compared with 30% in consumers of low quantities of nuts.[26]

The Iowa Women's Study[27, 28] of 34,000 women also found that higher nut consumption was associated with a 40% reduction in risk. This was despite the fact that, in this population, the highest category of nut consumption was relatively low at greater than once per week. They speculated that this was partly due to the vitamin E content of nuts, as adjustment for vitamin E reduced the apparent protection to 28%.

Findings from the 86,000 nurses in the Nurses' Health Study[29] confirm previous observations. After adjusting for traditional risk factors, those consuming nuts frequently (at least five ounces/week) had a 39% reduction (p = 0.007) in fatal CHD events and a 32% reduction (p = 0.04) in nonfatal myocardial infarction compared with those eating less than 1 ounce of nuts per week. Further adjustment for intake of dietary fats, fiber, vegetables, and fruits did not greatly change these results. The authors also reported results in 32 different subgroups of the population. In every case, those consuming higher quantities of nuts had a lower risk than those "almost never" consuming nuts, and in 25 and 29 of these subgroups p for trend was < 0.05 or 0.01, respectively, a remarkable degree of consistency. Their analyses suggested that these findings applied to peanuts as well as tree nuts. Peanuts are legumes but have a nutrient profile broadly similar to other nuts.

Finally, the Physicians' Health Study of 22,000 male physicians found a significantly decreasing risk of cardiac death and sudden death as nut consumption increased.[30] These trends persisted on multivariate adjustment.

Discussion

Data from several feeding trials, in which quantities of various types of nuts were added to the diet, consistently suggest that such supplements are at least as effective as or superior to fats in the recommended Step I American Heart Association diet. Levels of LDL are equal to or better than those observed when subjects eat the recommended diet. In view of the nutrient profile of nuts, this is not a surprise and indeed is predicted by the Keys equation.[31]

In addition, the consistent findings now from four of the largest and best cohort studies in nutritional epidemiology are impressive by directly associating nut consumption with reduced risk of CHD events. As far as we know, there are no other foods that have been so consistently associated with a marked reduction in CHD risk. When seeking evidence of causality, it is wise to require repetition of the finding in good studies from diverse populations. While further evidence is awaited with interest, such findings in California Seventh-Day Adventists (men and women separately), women in Iowa, and large groups of U.S. nurses and physicians, already supply a good deal of diversity. The robustness of the findings among many subgroups in two of these studies makes it exceedingly unlikely that these results are due to chance alone.

However, the epidemiologic studies are observational and confounding could still be a problem in theory. Are the nut-eaters different in some other way that accounts for the decreased risk? Theoretical consideration[32] suggests that a spurious two-fold effect due only to confounding requires the confounding factor to be a very strong risk factor and to be tightly linked or correlating with the factor of interest, in this case nut consumption. Such an unknown strong confounder is very elusive and we doubt that it exists. The four cohort studies have all adjusted for most of the known CHD risk factors, with only modest change in the magnitude of the apparent effect. Indeed the Nurses' Health Study even adjusted for hyperlipidemia, even though this may be an intermediary on any causal path between nut consumption and decreased risk.

As most persons who eat nuts eat relatively small quantities, how may these produce such strong apparent effects on risk of CHD? Based on the various nut-feeding studies, one would expect that the quantities of nuts that even daily consumers generally eat would reduce total cholesterol at most by 10%. This would be expected to result in a reduction in CHD events of approximately 25%, yet the studies observe 35–50 % reductions. This suggests that other factors influence these findings. A 50 g serving of nuts will exceed the recommended daily allowance for vitamin E, and this may well add or even interact with the antiatherogenic effects of lower blood cholesterol levels. Finally, there is also the possibility that the relatively high content of arginine in nuts may help raise levels of endogenous nitric oxide, which promotes normal endothelial function and has effects to inhibit platelet aggregation, monocyte adherence, chemotoxis, and vascular smooth muscle proliferation.[33] That this may occur with oral supplementation requires further support but has been shown to be effective in rabbits and mice,[34] and possibly in humans with baseline en-

dothelial dysfunction.[35–37] Some of these studies have also found that the oral arginine inhibits platelet aggregation.[35, 36] Thus there is the possibility that nuts may provide antiatherogenic effects by lowering blood LDL cholesterol levels, reducing LDL particle oxidation, reducing platelet aggregability, and improving endothelial function. If all this were to prove the case, the salutary effects of nuts when eaten in modest quantities would be less surprising.

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