Nut consumption, lipids, and risk of a coronary event

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In the past many have avoided nuts because of their high fat content. The Dietary Approaches to Stop Hypertension 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 fibre, magnesium, potassium and arginine, which is 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 the daily consumption of modest quantities of nuts may promote obesity 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 in 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 kilojules, the potential interacting effects of these factors on disease risk may be considerable.

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

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 fibre, also 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] and, surprisingly, such an effect may be seen at quite a low intake.

Much of the practice of preventive cardiology is burdened with the problem of coercing reluctant patients to change habits that they enjoy (smoking, eating food high in saturated fat, physical inactivity). It is a pleasing change to note the 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 energy in most nuts comes from fat, but this is largely monounsaturated (polyunsaturated in walnuts). Nuts also contain significant quantities of dietary fibre, 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.

As an example, the content of these factors is examined in nuts as compared with a number of other common fatty foods of animal origin in Tables 1 and 2.[4,5] 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 United States Department of Agriculture (DA) food pyramid. More recent dietary recommendations, such as those developed for the Dietary Approaches to Stop Hypertension (DASH) diet,[6,7] by the Oldways Foundation[8] or that for vegetarians,[9] place nuts more appropriately with seeds and legumes. In addition, along with many other vegetable foods, nuts are a storehouse for a large number of other phytochemicals, which 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

A number of studies of various design have evaluated the effect of consumption of almonds, walnuts, hazelnuts and

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Table 1. The fat content (calories) of selected nuts and other common fatty foods of animal origin (per 100 g of food)*

	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

*Values taken from US Department of Agriculture Handbooks.[4]
SFA, saturated fatty acids; MUFA, monounsaturated fatty acids; PUFA, polyunsaturated fatty acids; UFA, unsaturated fatty acids.

Table 2. Contents of selected food constituents in nuts and other common fatty foods of animal origin (100 g of food)†

	Vitamin E (mg)*	Dietary fibre (g)‡	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	NA	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

*Alpha-tocopherol equivalents. From the Nutrition Data System, Nutrition Coordinating Center, University of Minnesota, Version 2.5, 1993.
†Data from US Department of Agriculture Handbooks.[4]
‡Dietary fibre taken from Spiller.[5]
NA, not available.

macadamias on blood cholesterol levels. A study of pecans is under way. Some have simply given nuts and nut oils as a supplement to be incorporated into the diet. Others have controlled the other fats in the diet and/or the foods for which the nuts substituted.

Berry *et al.* used either almonds, olive oil and 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 have been compared to each other or to a third high carbohydrate diet in two separate studies.[10,11] These studies were randomized cross-over 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 joules as total fat, respectively. When compared to the baseline diet, both the high MUFA and high PUFA diets had quite similar effects; that is, lowering total and low-density lipoprotein (LDL) cholesterol levels 10–20% and not changing high-density lipoprotein (HDL) cholesterol. Compared to the high carbohydrate diet the high MUFA diet lowered total and LDL cholesterol.

Spiller and colleagues have reported three studies with an emphasis on the effect of almonds/almond oil on blood lipids. In the first study, two groups, totalling 30 hypercholesterolemic subjects, were given careful dietary advice and quite different fatty supplements in a parallel study design.[12] Each group participated in the study for four 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 to the second.

In the second study, the almonds were supplemental to a partially controlled 'usual' diet for which limited dietary advice was given.[13] 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, in comparison to the 'usual diet', total and LDL cholesterol declined 9% and 12%, respectively.

For the third study, Spiller and colleagues enrolled 48 hypercholesterolemic subjects with a mean baseline total cholesterol of 251 mg/dL.[14] Careful instructions were given to help subjects conform to a recommended baseline diet, which was then supplemented with either (i) 100 g almonds; (ii) 48 g olive oil and 113 g cottage cheese; or (iii) 85 g cheddar cheese, 28 g butter, each day for 4 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 and colleagues conducted a carefully controlled cross-over feeding study in 18 young men.[15] All meals were fed during two 4 week dietary periods. A basic diet was supplemented in one diet with 85 g/day of walnuts, and during the control period by the equivalent fat joules from more traditional foods. Although both the control and the walnut diets contained only 30% of energy as fat, much of the fat in the latter was polyunsaturated, while the control diet had 10% of energy from each of the saturated fatty acids, MUFA and PUFA. Total cholesterol dropped 12.4%, LDL 16.3% and a non-significant smaller drop was also seen in HDL cholesterol.

Abbey and colleagues in Australia trained 16 men to record their fat consumption and then provided supplements to be added to the basic diet.[16] The first supplement was constructed so as to match the fatty acid profile of the Australian diet, the second consisted of 84 g of MUFA-rich almonds and the third 68 g of PUFA-rich walnuts. During successive 3 week periods, LDL cholesterol was lowered 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.[17,18] In each case, despite the increase in total fat as most of this was monounsaturated, blood lipid levels did not change, except for a non-significant 9% rise in

HDL cholesterol. Finally, a feeding study has examined 70 children and 104 adults, where the intervention was a supplement of hazelnuts (R Solà *et al.*, unpubl. data, 1999). 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 bodyweight.

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 energy as saturated fat, the rats increased body fat much more and 'burned' much less (as indicated by the respiratory quotient) than those fed equivalent polyunsaturated fat joules.[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.[13,18,20] We have almost completed a study to formally test the hypothesis that adding a supplement of 76.2 joules of almonds daily with no dietary advice does not change bodyweight. Preliminary results suggest that this is so.[21] Suggested explanations for such a possible result include that the satiety effect of nuts might compensate for the additional nut joules by decreasing the intake of other foods; limited absorption of the fat due to the nut fibre or poor mastication; or an unexplained metabolic effect whereby nut fats are 'burned' rather than stored, which is perhaps associated with a higher metabolic rate.

Directly observed associations between nut consumption and risk of coronary heart disease events

We first observed that frequent nut consumers had an approximately 50% lower risk of either a fatal or non-fatal coronary event compared to those rarely eating nuts.[22] There was an apparent dose–response association (Fig. 1). This was in a cohort study of 34 000 Caucasian, Californian Seventh-day Adventists. The number of events in Fig. 1 is, of course, reflective of the total numbers of subjects at risk in each group, as well as the coronary heart disease (CHD) risk. Of these Adventist subjects, nearly 25% ate nuts five times each week or more; however, many others rarely ate nuts, so a good statistical comparison was possible. It was impressive to us that regardless of how we divided the data the 'nut effect' was always seen. Those men, women, vegetarians, omnivores, hypertensives, non-hypertensives, relatively obese or relatively thin subjects and older or younger subjects who consumed higher quantities of nuts, all had substantially lower CHD risk compared to those who ate less nuts (Table 3). Multivariate analyses, after adjusting for traditional risk factors and several other foods, did not change this finding in any important way. We have subsequently reported that a protective association with nut consumption is still clearly found in the oldest-old Adventists (over age 84 years),[23] and that in multivariate analyses, African-American Adventists experience a lower total mortality as they consume nuts more frequently.[24] Other results show that the those Caucasian Adventists who consume higher quantities of nuts in the population have lower total mortality.[25] Lifetable analyses indicate that those who consume higher quantities of nuts experience an extra 5.6 years life expectancy that is free of coronary disease, and an 18% life-

Table 3. Associations between nut consumption and risk of coronary heart disease in various subgroups of the Adventist health study population*

Subgroup	Relative risk Frequency of nut consumption < 1/week	1–4/week	> 4/week	*P*
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
Non-vegetarian	1.00	0.97	0.54	< 0.050
BMI ≤ 23.9	1.00	0.58	0.47	< 0.001
BMI > 23.9	1.00	0.80	0.52	< 0.010
Low exercise	1.00	0.62	0.63	< 0.050
Higher exercise	1.00	0.77	0.38	< 0.001
White bread only	1.00	0.57	0.46	0.070
Other breads or mixed	1.00	0.74	0.48	< 0.001

*BMI, body mass index, which had a mean value of 23.9 in this population; *P*, probability test of differences between categories of nut consumption; NS, not significant.

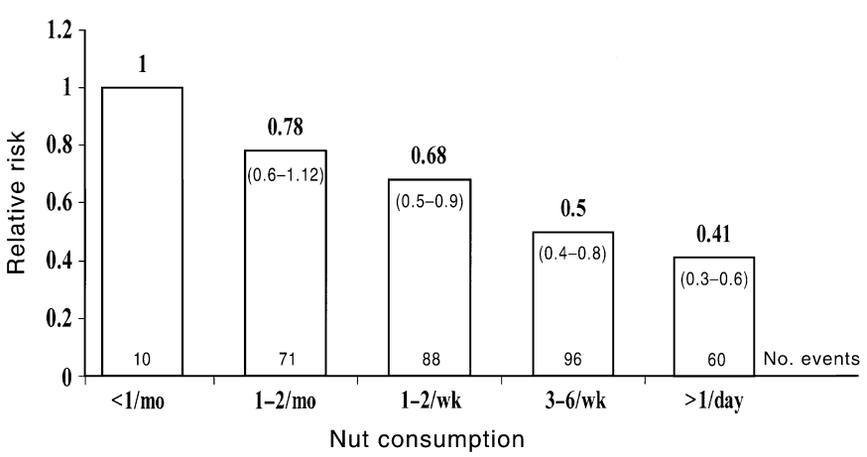

Figure 1. Estimated relative risk for all fatal coronary heart diseases, stratified for age and sex: The Adventist Health Study.

time risk of CHD compared to 30% for those who eat low quantities of nuts.[26]

The Iowa Women's Study of 34 000 women also found that higher nut consumption was associated with a 40% reduction in risk.[27,28] This was despite the fact that in this population the highest category of nut consumption was relatively low at more 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 confirm previous observations.[29] After adjusting for traditional risk factors, frequent nut consumers (at least 140 g/week) had a 39% reduction ($P = 0.007$) in fatal CHD events and a 32% reduction ($P = 0.04$) in non-fatal myocardial infarction compared to those eating less than 28 g of nuts per week. Further adjustment for intake of dietary fats, fibre, vegetables and fruits did not change these results greatly. The authors also reported results in 32 different subgroups of the population. For every case, those who consumed higher quantities of nuts had a lower risk than those who 'almost never' ate nuts, and in 25 and 29 of these subgroups probability (P) for trend was less than 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 that is 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 that correlated with increasing nut consumption.[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 fats in the recommended Step 1 American Heart Association Diet or superior. Levels of LDL are equal to or better than those observed when subjects follow 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 now consistent findings from three 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 as consistently associated with a marked reduction in CHD risk. When seeking evidence of causality, it is wise to obtain repetition of the finding in good studies that are from diverse populations. While further evidence is awaited with interest, such findings as those in California Seventh-day Adventists (men and women separately), women in Iowa and a large group of US nurses, already supplies a good deal of diversity. The robustness of the findings among many subgroups of two of these studies makes it exceedingly unlikely that these results are due to chance alone.

However, the epidemiological studies are observational and, in theory, confounding could still be a problem. Are the nut eaters different in some other way that accounts for the decreased risk? Theoretical consideration 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 correlated with the factor of interest, in this case nut consumption.[32] Such an unknown strong confounder is very elusive and we doubt that it exists. The three cohort studies have all been adjusted for most of the known CHD risk factors with only a 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 people 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 the quantities of nuts that even daily consumers generally eat would reduce total cholesterol by 10% at the most. 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 are operating. 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 anti-atherogenic 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 endothelial dysfunction.[35–37] Some of these studies have also found that the oral arginine inhibits platelet aggregation.[35,36] Thus there is the possibility the nuts may provide anti-atherogenic effects by lowering blood LDL cholesterol levels, reducing LDL particle oxidation, reducing the ability for platelets to aggregate and improving endothelial function. If all this were proved to be the case, the salutary effects of nuts when eaten in modest quantities would be less surprising.

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