

Thematic Article

Candidate foods in the Asia–Pacific region for cardiovascular protection: relevance of grains and grain-based foods to coronary heart disease

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This review elucidates the importance of healthy dietary and lifestyle habits to reduce morbidity and mortality associated with coronary heart disease (CHD), stroke and cardiovascular diseases. Given published evidence of the poor compliance, increased cost, and decreased benefit/risk ratios of medical therapies, individuals (and populations) are encouraged to adopt healthy life habits. The three most atherogenic dietary risk factors are saturated fat, cholesterol and obesity. Dietary patterns associated with the consumption of grains and grain-based foods predict risk of CHD independently of other life habits. Epidemiological and intervention studies elucidating the strong protective associations of grains, cereal fibers and anti-oxidant vitamins on CHD are reviewed. In summary, the consumption of grains and grain-based cereals is repeatedly associated with the ingestion of many nutrients, e.g., dietary fiber and anti-oxidants, that alter energy balance and nutrient intakes to positively affect cardiovascular health, especially when combined with healthy life habits.

Key words: cardiovascular disease, cereal, dietary fiber, folic acid, homocysteine.

What is the incidence of cardiovascular diseases?

The most recent statistics show that cardiovascular diseases (CVD) account for >25% of all deaths in many countries (Table 1). In the USA, CVD is the number one killer, accounting for one of every 2.4 deaths. Deaths from coronary heart disease (CHD) accounts for <30% of all CVD-related deaths in China and Japan, whereas CHD deaths represent 49.3–69.5% of the CVD-related deaths in many westernized countries (Table 1). Hypertension is the most prevalent form of CVD. It is estimated that the life expectancy of Americans would rise by almost 7 years if all forms of CVD were eliminated.¹

What are the risk factors for cardiovascular disease?

The risk factors for CVD are tobacco smoke, age, sex, race, hypercholesterolemia, physical inactivity, diabetes mellitus and obesity. Exposure to tobacco smoke and physical activity reflect behavioral factors whereas aging, sex and race are risk factors which individuals cannot control. Iso *et al.* documented a 70% fall in stroke mortality and 20% decline in CHD in Japan over the past 30 years which was associated with decreased rates of smoking and reduced consumption of salt, meat and dairy products.² However, they also reported a recent increase in CHD among Japanese urban males and emphasized the need for vigorous prevention efforts to avoid elevated blood lipid levels and to reduce smoking. This paper will focus on CHD risk factors that are significantly influenced by dietary choices, namely hypercholesterolemia, diabetes mellitus and obesity.

Adiposity is related to diabetes incidence and intra-abdominal fat is significantly associated with increased risk of diabetes.³ Blood cholesterol concentration is an important and modifiable risk factor for CHD. Dietary recommendations

advise people to make choices that reduce cardiovascular and CHD risk. As people do not always choose lifelong dietary habits and lifestyles to reduce their risk of CHD, it is relevant to determine if short-term changes, that is, <5 years, in life habits will significantly influence the CHD process.

Is it ever too late to ameliorate risk factors?

The best evidence that midlife changes in life habits and risk factors are important in preventing cardiovascular events is derived from clinical trials. For example, the Scandinavian Simvastatin Survival Study in which hypercholesterolemic patients with CHD received lipid-lowering medications documented a 34% reduction in major coronary events, a 42% decrease in coronary mortality and a 30% reduction in total mortality.⁴ Pignone *et al.* conducted a meta-analysis of primary prevention studies published between 1994 and 1996.⁵ The clinical trials included in the analysis were of 3–7 years in duration. Pignone *et al.* found that pharmacologic lipid-lowering therapies reduced the relative risk of CHD events, that is, non-fatal myocardial infarction or CHD death, by 30% compared to placebo.⁵ It appears that the cessation of smoking or pharmacologically-induced reductions in blood pressure and serum cholesterol concentrations are associated with reduced risk of CHD and most of the benefit may occur within 5 years.^{6–10} Nevertheless, age is still the most important determinant of coronary risk and lower age limits are

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Table 1. Death rates for coronary heart disease, stroke, cardiovascular disease and all causes in selected countries*

Country	CHD	Men aged 35–74			Total	Women aged 35–74			Total
		Stroke	CVD			CHD	Stroke	CVD	
China – Rural (1994)	54	230	393	1357	36	151	275	868	
China – Urban (1994)	100	251	409	1079	69	170	296	716	
United States (1997)	214	43	389	1054	88	34	192	632	
New Zealand (1994)	287	60	419	994	113	44	196	607	
England/Wales (1997)	267	57	390	946	96	44	180	585	
Italy (1993)	150	64	304	953	72	26	131	504	
Australia (1995)	202	44	298	840	73	31	129	466	
Canada (1995)	200	38	299	894	42	40	131	457	
Japan (1997)	57	79	186	743	20	41	85	341	

*Most recent year available, rate per 100 000 population. CHD, coronary heart disease; CVD, cardiovascular disease.

Source: <http://www.americanheart.org/statistics>.

often established for pharmacological therapies.^{5,11} Thus, there is an importance of adopting good life habits to reduce CHD risk, especially in populations who may not have access to pharmacologic interventions.

Should life habits be emphasized over medical therapies?

Changes in life habits, including dietary choices, are the foundation of all disease prevention programs. One reason is that the benefit of medical therapy is lower in individuals at a lower risk of CHD, whereas the risk of potential adverse effects of the medications is similar in all individuals, regardless of their risk factors. In fact, the risk of adverse effects may even be greater because of the potential for longer use in low risk individuals. The benefit/risk ratio of life habits is much more favorable than medical therapies. Secondly, the lifelong cumulative cost of medical therapy increases dramatically when interventions are targeted towards an increased number of lower-risk individuals for more years.¹¹ Perhaps more importantly, even when medical therapies are implemented, that is, prescription of lipid-lowering regimens, patients enrolled in health-care programs are without filled prescriptions for over one-third of the year.¹² Presumably, adherence to prescribed medical therapies would be worse in patients without health insurance who have to pay for their own medications. Given poor compliance, cost and benefit/risk ratios of medical therapies, it is important that health professionals and government agencies continue to urge individuals to embrace dietary practices and lifestyles (physical activity, exposure to tobacco smoke) that ameliorate CHD risk.

What should people eat to reduce their risk of coronary heart disease?

The three most atherogenic dietary risk factors for CHD are saturated fat, cholesterol and obesity.^{13,14} Dietary recommendations to general healthy populations encourage life habits (proper diet, regular exercise) that reduce the risk of obesity, hypercholesterolemia and diabetes mellitus. Once individuals have CHD, the American Heart Association Step I and II diets are recommended, whereby complex carbohydrates are used to substitute for reductions in the consumption of total fat, saturated fat and cholesterol and to replace some of the energy lost through a reduction in fat intake. National sample data and epidemiological studies have shown that the risk factors for CHD, including

hypercholesterolemia and hypertension, are not much different between young men in Japan and the US.¹⁵ The focus of this review is to highlight the importance of grains and grain-based foods in maintaining normal serum cholesterol levels and preventing oxidative damage to the cardiovascular system.

Grains and grain-based foods

A recent meta-analysis by Tang *et al.* concluded that dietary advice to free-living subjects can be expected to reduce total blood cholesterol by 3–6%, depending upon the type and intensity of the diet advocated.¹⁶ One of the benefits of low-fat, high-carbohydrate diets is that they are also associated with significant weight loss (2–3 kg), which is directly associated with reductions in serum cholesterol concentrations.^{16,17} It has also been shown that regular consumption of ready-to-eat breakfast cereals is associated with reduced intakes of total and saturated fat intakes and reductions in serum cholesterol levels.¹⁸

Jacobs *et al.* studied 34 492 postmenopausal women in 1986, aged between 55 and 69 and at baseline were free of CHD.¹⁹ The quintiles for whole-grain intakes were 0.2, 0.9, 1.2, 1.9 and 3.2 servings/day, but the lower risk of CHD with higher whole-grain intake was not explained by fiber or other constituents of whole-grains. In a 10-year epidemiological study of 7552 women aged between 38 and 63 without any previous history of CVD or diabetes, Liu *et al.* reported an inverse relationship between whole-grain intake and CHD risk.²⁰ The lack of a specific effect of dietary fiber intake with CHD in these studies may reflect associations between life habits and the intake of whole-grains, as whole-grain intakes are associated with differences in food choices, smoking, exercise, use of postmenopausal hormones and multivitamins.²¹ Despite the limitations of food frequency questionnaires, the consumption of dietary patterns including grains and grain-based foods predict risk of CHD independently of other life habits.²²

Dietary fiber

Several studies suggest that the consumption of high-fiber diets, especially those enriched in cereal fiber, reduces the risk of CHD.²³ Morris *et al.* studied 337 healthy, middle-aged men between 1955 and 1966.²⁴ Men with a high-energy intake had a lower rate of CHD than the rest, and,

independently of this, so did men with a high intake of dietary fiber from cereals. Erkkila *et al.* studied 253 patients with CHD that were not using lipid-lowering medications.²⁵ Patients in the lowest quartile of cereal product intake had higher total and low-density lipoprotein (LDL) cholesterol concentrations than those in the other three quartiles. Patients in the lowest quartile of whole-grain product intake had the highest total cholesterol concentrations and both of these associations remained after adjusting for the consumption of fat (g/day). The main findings of this study were that dietary fiber intake was inversely correlated with total cholesterol concentration and serum triglycerides. This relationship was observed as both fiber intake (g/1000 kcal) and as intake of foods rich in dietary fiber. Although meta-studies typically find a negative association between water-soluble fiber intakes and total cholesterol concentrations, this study found that high intakes of dietary fiber (water-soluble and insoluble) and cereal products were associated with lowered serum cholesterol concentrations.^{26,27}

The Health Professionals Follow-up Study tracked 43 757 US male health professionals, aged between 40 and 75 who were initially free of diagnosed CHD and diabetes, for 6 years.²⁸ The age-adjusted relative risk (RR) for total myocardial infarction was 0.59 among men with the highest quartile of total dietary fiber intake (median 28.0 g/day) compared with men with the lowest quartile (median, 12.4 g/day). The age-adjusted RR for fatal myocardial infarction in the highest quartile was 0.45, which was observed in the lowest quartile of fiber intake. Cereal fiber was strongly associated with a reduced risk of total myocardial infarction for each 10 g increase in cereal fiber/day.

The Nurses' Health Study, a large prospective cohort study of 68 782 women, aged between 37 and 64, over 10 years (beginning 1984). Wolk *et al.* reported that the RR for major CHD events was 0.53 for women in the highest quintile of total dietary fiber intake (median, 22.9 g/day) compared with women in the lowest quintile (median, 11.5 g/day).²⁹ For a 10 g/day increase in total dietary fiber intake (the difference between lowest and highest quintiles), the multivariate RR was 0.81. Among sources of dietary fiber (e.g., cereal, vegetables, fruit), only cereal fiber was strongly associated with a reduced risk of CHD (multivariate RR = 0.63).

The Alpha-Tocopherol, Beta-Carotene Cancer Prevention Study³⁰ was a randomized, double-blind, placebo-controlled trial with daily supplementation of alpha-tocopherol and/or beta-carotene in 21 930 men, aged between 50 and 69, free of diagnosed CHD for 6.1 years. Men in this study had average fiber intakes of 26.7 g/day. The most important contributor of fiber was whole-grain breads: rye, wheat, oats and barley. Water-soluble fiber intake was slightly more strongly associated with reduced coronary death than water-insoluble fiber. Cereal fiber, but not vegetable or fruit fiber, had a significant inverse association with coronary death. This study concluded that independent of other risk factors, greater intake of foods rich in fiber can substantially reduce the risk of CHD, and particularly coronary death, in middle-aged men who smoke cigarettes.

Thus, epidemiological studies in both men and women have found strong protective associations of grains and cereal fibers on coronary heart disease.

Anti-oxidants

New research suggests that dietary anti-oxidants may play an important protective role in the etiology of CVD. Several reports now associate elevated plasma homocysteine levels and oxidative stress with arteriosclerotic vascular disease.^{31,32} Grains, especially whole-grains, fruits and vegetables contain a wide range of nutrients and phytochemicals that may be beneficial to human health.³² Rimm *et al.* prospectively examined the relationship between intakes of folate and vitamin B₆ in relation to non-fatal myocardial infarction and fatal CHD in the women from the Nurses Health Study.³³ After controlling for cardiovascular risk factors (including smoking, hypertension, and intake of alcohol, fiber, vitamin E, saturated, polyunsaturated and trans-fats), the RR of CHD between extreme quintiles were 0.69 for folate (median intake, 696 µg/day vs 158 µg/day) and 0.67 for vitamin B₆ (median intake, 4.6 mg/day vs 1.1 mg/day). The RR dropped to 0.55 when both folate and B₆ intakes were compared with the opposite extreme. Although the exact role of folic acid fortification on vascular disease remains undetermined, Malinow *et al.* conducted a randomized, double-blind, placebo-controlled, cross-over study in 75 individuals with CHD.³⁴ This study demonstrated that plasma folic acid concentrations increased and plasma homocysteine decreased proportionately with the folic acid content of the breakfast cereal. Consumption of ready-to-eat breakfast cereals, typically containing 100–400 µg folic acid per serving can be important sources of folic acid and the cessation of intake of commercially available breakfast cereals is associated with increased homocysteine concentrations.³⁵

Folic acid is, however, only one of many anti-oxidants found in grains, fruits and vegetables. One measure of anti-oxidant activity is expressed as Trolox equivalents (TE). Miller *et al.* reported that a 41 g serving of ready-to-eat-breakfast cereals provided 1120 TE, whereas a 85 g serving of vegetables and fruits provided 380 and 1020 TE, respectively.³² These findings help explain results from prospective studies reporting that the consumption of foods rich in anti-oxidant vitamins and fiber reduce CHD risk. The Scottish Heart Health Study prospectively studied 11 629 men and women from 1984 to 1993. Todd *et al.* reported that higher levels of anti-oxidant vitamins appeared to increase CHD survival for men, with little evidence of a benefit in women, but that increased dietary fiber intake was associated with a significantly protective effect for incident CHD and mortality.³⁶ Hughes and Ong conducted a cross-sectional study of 726 subjects aged 30–69 years.³⁷ They hypothesized that differences in blood concentrations of folate, vitamin B₁₂ and homocysteine partly explain increased incidence in CHD in South Asian Indians versus South Asian Malays and Chinese. It was observed that plasma folate and vitamin B₁₂ concentrations were lower in the Indian individuals but plasma homocysteine concentrations were not different. This suggests that regional diets and lifestyles do affect CHD incidence.

Observational data suggest that high serum or dietary levels of vitamin E and beta-carotene may be associated with a lower risk of CVD. The Alpha-Tocopherol Beta-Carotene Cancer Prevention Study found that vitamin E supplementation had little effect on the numbers of deaths from cardiovascular causes, including CHD, myocardial

infarction or stroke.^{38,39} This was similar to the findings of the Heart Outcomes Prevention Evaluation (HOPE) study.⁴⁰ However, Liu *et al.* did find that higher intakes of whole-grain foods were associated with a lower risk of ischemic stroke among women.²¹ Thus, epidemiological and intervention trials have still not come up with a consistent understanding of the relationship between anti-oxidant vitamins, like vitamin E, and cardiovascular incidence and mortality.

Conclusions

In summary, given the associations among dietary and life habit choices, it is difficult to elucidate mechanisms of action of specific bioactive components found in foods. Despite the limitations of epidemiological and intervention trials, the consumption of grains and grain-based cereals is repeatedly associated with the ingestion of many nutrients that alter energy balance and nutrients intakes, for example, dietary fiber and anti-oxidants, to positively affect cardiovascular health, especially when combined with healthy life habits.

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