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.
often established for pharmacological therapies.\textsuperscript{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.\textsuperscript{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 prescription of lipid-lowering regimens, patients enrolled in health-care programs are without filled prescriptions for 20% of the year.\textsuperscript{12} Presumably, adherence to prescribed health-care programs are without filled prescriptions for over prescription of lipid-lowering regimens, patients enrolled in health-care programs are without filled prescriptions for 20% of the year.\textsuperscript{12}

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.\textsuperscript{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.\textsuperscript{18}

**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.\textsuperscript{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.\textsuperscript{16,17}

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Jacobs et al. studied 34 492 postmenopausal women in 1986, aged between 55 and 69 and at baseline were free of CHD.\textsuperscript{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.\textsuperscript{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 post-menopausal hormones and multivitamins.\textsuperscript{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.\textsuperscript{22}

**Dietary fiber**

Several studies suggest that the consumption of high-fiber diets, especially those enriched in cereal fiber, reduces the risk of CHD.\textsuperscript{23} Morris et al. studied 337 healthy, middle-aged men between 1955 and 1966.\textsuperscript{24} Men with a high-energy intake had a lower rate of CHD than the rest, and, 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.\textsuperscript{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 prescription of lipid-lowering regimens, patients enrolled in health-care programs are without filled prescriptions for 20% of the year.\textsuperscript{12} Presumably, adherence to prescribed health-care programs are without filled prescriptions for 20% of the year.\textsuperscript{12}

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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. 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.

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. 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). 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 Study 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. Grasses, especially whole-grains, fruits and vegetables contain a wide range of nutrients and phytochemicals that may be beneficial to human health. Rimm et al. prospectively examined the relationship between intakes of folate and vitamin B₁₂ in relation to non-fatal myocardial infarction and fatal CHD in the women from the Nurses Health Study. 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 B₁₂ (median intake, 4.6 mg/day vs 1.1 mg/day). The RR dropped to 0.55 when both folate and B₁₂ 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. This study demonstrated that plasma folic acid concentrations increased and plasma homocysteine decreased proportionally 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. 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. 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. Hughes and Ong conducted a cross-sectional study of 726 subjects aged 30–69 years. 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.

References
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