Mini-review

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Effect of the vegetarian diet on non-communicable diseases

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Abstract

A vegetarian diet generally includes plenty of vegetables and fruits, which are rich in phytochemicals, antioxidants, fiber, magnesium, vitamins C and E, Fe^{3+}, folic acid and n-6 polyunsaturated fatty acid (PUFA), and is low in cholesterol, total fat and saturated fatty acid, sodium, Fe^{2+}, zinc, vitamin A, B_{12} and D, and especially n-3 PUFA. Mortality from all-cause, ischemic heart disease, and circulatory and cerebrovascular diseases was significantly lower in vegetarians than in omnivorous populations. Compared with omnivores, the incidence of cancer and type 2 diabetes was also significantly lower in vegetarians. However, vegetarians have a number of increased risk factors for non-communicable diseases such as increased plasma homocysteine, mean platelet volume and platelet aggregability compared with omnivores, which are associated with low intake of vitamin B_{12} and n-3 PUFA. Based on the present data, it would seem appropriate for vegetarians to carefully design their diet, specifically focusing on increasing their intake of vitamin B_{12} and n-3 PUFA to further reduce already low mortality and morbidity from non-communicable diseases.

Keywords: vegetarian, non-communicable diseases; mortality; ischemic heart disease; cancer; type 2 diabetes; homocysteine; mean platelet volume; platelet aggregation

INTRODUCTION

Non-communicable diseases (NCDs), also known as chronic diseases, are those which cannot be passed from person to person. They are generally slow-progressing and long-duration diseases. It is well established that NCDs are the leading cause of death in the world, responsible for 63% of the 57 million deaths that occurred in 2008.[1] There are four main types of NCDs: cardiovascular diseases (coronary heart disease and cerebrovascular disease), cancers, chronic respiratory diseases (such as chronic obstructed pulmonary disease and asthma) and diabetes, which account for 36 million deaths. In most middle- and high-income countries, NCDs were responsible for more deaths than all other causes of death combined, with almost all high-income countries reporting the proportion of NCD deaths to total deaths to be more than 70%.[2]

Globally increasing prevalence of NCDs is associated with ageing, rapid unplanned urbanization and the globalization of unhealthy lifestyles. Unhealthy lifestyles include unhealthy diets, physical inactivity, exposure to tobacco smoke and harmful use of alcohol. In particular, globalization of unhealthy diets may result in raised blood pressure, increased serum glucose and lipids, overweight and obesity. These are called 'intermediate risk factors', which can lead to cardiovascular disease and diabetes.[3]

Becoming a vegetarian has become increasingly popular over the past decade, with many people turning to vegetarianism in an attempt to achieve better health. A vegetarian is someone whose diet excludes all animal flesh. There are different types of vegetarianism, which include or exclude various foods.[4] Strict vegans and Su vegetarians (such as Buddhism in China) exclude all animal products, including eggs, dairy, beeswax and honey, leather products and goose-fat shoe polish, as well as vegetables in the *Allium* genus such as garlic, onion, spring onion, scallions and leeks. They also avoid products that may use animal ingredients not included in their labels or which use animal products in their manufacturing, e.g. cheeses that use animal rennet (enzymes from animal stomach lining), gelatin (from animal skin, bones and connective tissue), some sugars that are whitened with bone char (e.g. cane sugar but not beet sugar) and alcohol clarified with gelatin or crushed shellfish and sturgeon.[4] Raw veganism includes only fresh and uncooked fruit, nuts, seeds, and vegetables. Fruitarianism permits only fruit, nuts, seeds, and other plant matter that can be gathered without harming the plant. A lacto-ovo-vegetarian diet includes both eggs and dairy products, an ovo-vegetarian diet includes eggs but not dairy products, and a lacto-vegetarian diet includes dairy products but not eggs. Pescetarian (pesco-vegetarian) has been described as someone whose diet includes fish but no other meat. In addition, some individuals claim themselves to be semi-vegetarian. However, this has been debated by most vegetarian groups or societies because semi-vegetarian diets include fish, other seafood, and possibly poultry, whereas it is stated that vegetarians must exclude all animal flesh.

Compared with an omnivorous diet, a vegetarian diet includes plenty of fruits and vegetables. In general, vegetarian diets are rich in fiber, magnesium, phytochemicals, antioxidants, vitamins C and E, Fe^{3+}, folic acid and n-6 polyunsaturated fatty acid (PUFA), but low in cholesterol, total fat and saturated fatty acid, sodium, Fe^{2+}, zinc, vitamins A, B_{12} and D, and especially n-3 PUFA.[4]

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Low intake of cholesterol, total fat, SFA and sodium, and high intake of phytochemicals, antioxidants and fiber in vegetarians, are associated with health advantages including decreased mortality and morbidity of NCDs.[4]

It is unclear whether vegetarians have adequate levels of vitamin D. Vitamin D can be either consumed from the diet or synthesized in humans from cholesterol following adequate exposure from the sun. Vegetarians have a lower intake of vitamin D; however, they do not necessarily have lower vitamin D status (serum/plasma 25-hydroxyvitamin D) compared with omnivores. Studies from Poland[5] and the UK[6] reported that vegetarians and vegans have lower serum/plasma 25-hydroxyvitamin D. However, Adventist Health Study-2 from the USA[7] found that serum/plasma 25-hydroxyvitamin D concentrations were not associated with vegetarian status. The possible reasons for the variable results include inadequate exposure to sunlight, dark skin, potentially adequate intake by individuals who are lacto- or lacto-ovo-vegetarians *versus* vegans, use of supplements or supplemented foods etc.

VEGETARIAN DIET AND CARDIOVASCULAR DISEASE

Results from epidemiological studies showed that vegetarians have lower mortality from ischemic heart disease (IHD) compared with omnivores. A recent meta-analysis of seven prospective cohort studies with a total of 124 706 participants[8] showed that vegetarians had a 29% (relative risk (RR) = 0.71; 95% CI: 0.56–0.87) lower mortality from IHD, 16% lower mortality from circulatory diseases (RR = 0.84; 95% CI: 0.54–1.14) and a 12% lower mortality from cerebrovascular disease (RR = 0.88; 95% CI: 0.70–1.06) compared with omnivores.

An earlier review of five prospective studies, which included 76 172 men and women aged 16–89 years, of the 8330 deaths before the age of 90 years which were recorded after a mean 10.6 years' follow-up, 2264 deaths resulted from IHD.[9] Compared with omnivores, mortality from IHD was 24% (death rate ratio 0.76, 95% CI: 0.62–0.94) lower in vegetarians. Mortality among vegetarians varied significantly with age at death: rate ratio (OR), which were 0.55 (95% CI: 0.35–0.85), 0.69 (95% CI: 0.53–0.90) and 0.92 (95% CI: 0.73–1.16) for deaths from IHD at ages <65, 65–79 and 80–89 years, respectively. Subgroup analysis from the same authors showed that mortality rate of IHD was 34% lower in lacto-ovo-vegetarians, 26% lower in vegans, 34% lower in fish eaters but not meat eaters and 20% lower in occasional meat eaters compared with regular meat eaters.[10]

Results from a California Seventh-Day Adventists cohort with 34 192 subjects showed that RR for fatal IHD in men who ate beef ≥3 times/week was 2.31.[11] Compared with omnivores, lifetime risk of IHD was reduced by 37% in male vegetarians. A total of 44 561 men and women (34% vegetarians) living in England and Scotland participated in the European Prospective Investigation into Cancer and Nutrition (EPIC)–Oxford study.[12] There were 1235 IHD cases recorded after an average follow-up of 11.6 years. Compared with omnivores, vegetarians had a 32% lower risk (hazard ratio (HR): 0.68; 95% CI: 0.58, 0.81) of IHD.

Compared with omnivores, lower mortality of IHD in vegetarians was associated with decreased blood pressure, plasma total cholesterol (TC), triacylglycerol (TAG) and low-density lipoprotein cholesterol (LDL-C) levels, serum lipoprotein(a) concentration, ratios of TC/high-density lipoprotein cholesterol (HDL-C), LDL-C/HDL-C and TAG/HDL-C, body mass index, waist-to-hip ratio, plasma factor VII activity and serum ferritin levels.[13] These factors are known to reduce the risk of cardiovascular disease and diabetes.

However, there is concern that vegetarians, and particularly those with strict vegan and Su vegetarian diets that are not well designed , may have an inadequate intake of several important nutrients, particularly Fe, Zn, vitamin B_{12} and n-3 PUFA, which are associated with some disadvantages and health risks.[4] Studies have shown that vegetarians, especially strict vegans, tend to have lower serum levels of vitamin B_{12} compared with omnivores. Serum vitamin B_{12} concentration was significantly negatively correlated with plasma homocysteine.[14–16] Remethylation of homocysteine to methionine requires vitamin B_{12} (methylcobalamin form) as a coenzyme for homocysteine methyltransferase (methionine synthetase) and N^5-methyltetrahydrofolate as a methyl donor.[17] Vitamin B_{12} is essential for new cell synthesis, blood formation and maintenance of the nervous system. Vitamin B_{12} as a coenzyme increases the utilization of folic acid and metabolism of carbohydrate, fat and protein etc. In the vitamins, B_{12} is the only one containing a mineral (cobalt); therefore it is also known as the red vitamin. Seafood, animal meats, eggs and liver are good sources of vitamin B_{12}. Vitamin B_{12} is not found in plant foods; however, seaweed may contain vitamin B_{12} analogs, which are reliable sources of active vitamin B_{12}.[4] Lacto-ovo-vegetarians may obtain vitamin B_{12} from eggs and dairy products. Vegans could get some very limited vitamin B_{12} from fermented soybean products, seaweed and edible fungi (like mushrooms) from farms or in the wild, which may be contaminated with bacteria found in the soil.[4]

Low dietary intake of n-3 PUFA in vegetarians is associated with decreased tissue levels of n-3 PUFA,[18,19] which is associated with a number of risk factors for NCDs. Plasma homocysteine concentration was significantly negatively correlated with plasma phospholipid concentration of total n-3 PUFA ($r = -0.270$, $P = 0.002$), 22:6n-3 ($r = -0.286$, $P = 0.001$), 20:5n-3 ($r = -0.226$, $P = 0.009$), 22:5n-3 ($r = -0.182$, $P = 0.036$) and the ratio n-3/n-6 PUFA ($r = -0.265$, $P = 0.002$) and significantly positively correlated with 20:4n-6 ($r = 0.180$, $P = 0.037$). In the partial correlation analysis, after controlling for serum vitamin B_{12} and folate concentrations, plasma homocysteine was significantly negatively correlated with plasma phospholipid concentration of total n-3 ($r = -0.182$, $P = 0.038$), 22:6n-3 ($r = -0.205$, $P = 0.019$) and the ratio n-3/n-6 PUFA ($r = -0.174$, $P = 0.048$) in a cross-sectional vegetarian study.[19]

Adenosine 5′-diphosphate and collagen-induced *ex vivo* whole blood platelet aggregation were significantly lower in both high and moderate meat-eater groups than in both vegan and lacto-ovo-vegetarian groups. In an intervention study, collagen, arachidonic acid, adenosine 5′-diphosphate and epinephrine-stimulated platelet aggregation in either maximum percentage or slope were significantly reduced after 10 vegetarians were supplemented with 700 mg per day each of 22:6n-3 and 20:5n-3 for 8 weeks. Both 22:6n-3 and 20:5n-3 were significantly incorporated into plasma lipids.[20]

Mean platelet volume was significantly lower in high and moderate meat-eater and lacto-ovo-vegetarian groups than in vegans.[21] Increased mean platelet volume in vegans suggests the presence of larger and activated platelets. Evidence from case–control studies has indicated that an increased mean platelet volume is an independent risk factor for acute myocardial infarction and for acute and/or non-acute cerebral ischemia. Large platelets, in such cases, have been shown to have increased reactivity. When platelets become activated, they change from

their normal resting disk-like structure to assume a spherical shape, and their volume increases substantially, leading to the potential for thrombus formation.[4] In multiple linear regression analysis, after controlling for potential confounding factors such as dietary group, body mass index, age, exercise, dietary intake of PUFA, saturated fat, cholesterol, carbohydrate and fiber, mean platelet volume was still strongly negatively correlated with platelet PL 22:5n-3 ($P = 0.001$) and 20:3n-6 ($P = 0.003$). The data suggest that 22:5n-3 and 20:3n-6 may play a critical role in the structural function of the platelet membrane.[21]

This, in conjunction with increased platelet aggregability, suggests there should be an increased thrombosis tendency in vegans. Platelet aggregation is associated with low dietary intake of n-3 PUFA. Platelet aggregation is initiated by thromboxane A_2, a potent platelet aggregation agent and vascular contractor, produced from 20:4n-6 in the platelet membrane.[22] The 20:5n-3 is released from phospholipids of the platelet membrane and acts as a 'false' substrate to compete with 20:4n-6 for access to cyclooxygenase and produces an alternative form of thromboxane A_3, which is relatively inactive in promoting platelet aggregation and vasoconstriction. This situation can lead to a reduced thromboxane A_2 production and thus a lower thrombosis tendency.[23] A vegetarian diet with a high n-6/n-3 PUFA ratio can cause a high tissue ratio of n-6/n-3 PUFA, and an increased ratio of 20:4n-6/20:5n-3, which may promote production of thromboxane A_2, leading to increased platelet aggregability.[4]

VEGETARIAN DIET AND CANCERS

Results from prospective cohort, population and case–control studies found that vegetarians have a lower incidence of cancer compared with omnivores. A meta-analysis of seven prospective cohort studies with a total of 124 706 participants[8] showed that vegetarians had an 18% (RR = 0.82; 95% CI: 0.67–0.97) lower cancer incidence compared with omnivores. In a cohort of 61 566 British men and women consisting of 32 403 omnivores, 8562 pescetarian and 20 601 vegetarians[24] there were 3350 incident cancer cases reported after an average follow-up of 12.2 years. In this study, 2204 were omnivores, 317 were pescetarian and 829 were vegetarians. Compared with omnivores, RRs for stomach cancer were 0.29 (95% CI: 0.07–1.20) in pescetarians and 0.36 (0.16–0.78) in vegetarians; RRs for ovarian cancer were 0.37 (0.18–0.77) in pescetarians and 0.69 (0.45–1.07) in vegetarians; RRs for bladder cancer were 0.81 (0.36–1.81) in pescetarians and 0.47 (0.25–0.89) in vegetarians; RRs for cancers of the lymphatic and hematopoietic tissues were 0.85 (0.56–1.29) in pescetarian and 0.55 (0.39–0.78) in vegetarians, and RRs for all cancers were 0.82 (0.73–0.93) in pescetarians and 0.88 (0.81–0.96) in vegetarians.

In the Adventist Health Study-2, with 69 120 participants, 2939 cancer cases were identified.[25] Compared with omnivores, the multivariate HR of overall cancer risk was 0.92 (95% CI: 0.85–0.99) for vegetarians; gastrointestinal tract cancer was also significantly lower in vegetarians (HR, 0.76; 95% CI: 0.63–0.90). Vegans have a lower risk for overall (HR, 0.84; 95% CI: 0.72–0.99) and female-specific cancer (HR, 0.66; 95% CI: 0.47–0.92) compared with other dietary patterns. A cohort of California Seventh-Day Adventists with 34 192 subjects showed that RR of the colon and prostate cancers were significantly higher in omnivores (RR of 1.88 and 1.54, respectively), and frequent beef consumers also had a higher risk of bladder cancer compared with vegetarians.[11] In a cohort of Nutrition, Lifestyle and Colorectal Cancer Incidence, with 10 998 men and women, 95 cases of colorectal cancer were diagnosed after 17 years.[26] The relative risk was 0.85 (95% CI: 0.55–1.32) in vegetarians compared with omnivores.

There is no significant correlation between vegetarians and risk of breast cancer. In a population-based case–control study among South Asian migrant women from the Indian subcontinent living in England, 240 breast cancer cases were identified during 1995–1999. For each case, two age-matched South Asian controls were randomly recruited from the age–sex register of the case practice.[27] Compared with omnivores, the odds ratio of breast cancer was 0.77 (95% CI: 0.50–1.18) in lifelong vegetarians adjusted for socio-demographic and reproductive variables. A cohort study of European Prospective Investigation into Cancer and Nutrition involving 37 643 British women, of which 31% were vegetarians,[28] 585 women were recorded with breast cancer during 7.4 years of follow-up. The multivariable-adjusted hazard ratio for breast cancer in vegetarians was 0.91 (95% CI: 0.72–1.14).

VEGETARIAN DIET AND TYPE 2 DIABETES

Results from prospective cohort, population and case–control studies found that vegetarians have a lower prevalence of type 2 diabetes compared with non-vegetarians.

In the Adventist Health Study-2, 60 903 subjects (22 434 males and 38 469 females) aged 30 years or older were recruited from Seventh-Day Adventist Church members across North America in 2002–2006.[29] Prevalence rates of type 2 diabetes were 2.9% in vegans, 3.2% in lacto-ovo-vegetarians, 4.8% in pescetarians, 6.1% in semi-vegetarians and 7.6% in omnivores. Compared with omnivores, OR of type 2 diabetes was 0.51 (95% CI: 0.40–0.66) for vegans, 0.54 (0.49–0.60) for lacto-ovo-vegetarians, 0.70 (0.61–0.80) for pescetarians and 0.76 (0.65–0.90) for semi-vegetarians adjusted for age, sex, body mass index (BMI), physical activity, ethnicity, television watching, education, income, sleep habits and alcohol use.

A study involving 40.387 (15 200 males and 26 187 females) non-diabetic participants (17.3% blacks) aged $\geq$30 years was carried out in the USA and Canada. Demographic, anthropometric, lifestyle and dietary data were collected for these subjects.[30] After 2 years' follow-up, information on the development of diabetes was elicited from a questionnaire. Cases of diabetes were 0.54% in vegans, 1.08% in lacto-ovo-vegetarians, 1.29% in pescetarians, 0.92% in semi-vegetarians and 2.12% in omnivores. Risk of type 2 diabetes increased from 0.381 (OR; 95% CI: 0.236–0.617) in vegans, 0.618 (0.503–0.760) in lacto-ovo-vegetarians and 0.486 (0.312–0.755) in semi-vegetarians compared with omnivores controlled for age, gender, BMI, physical activity, education, income, television watching, sleep, alcohol use and smoking. Compared with white subjects, blacks had a higher risk of type 2 diabetes (OR 1.364; 95% CI: 1.093–1.702).

A study in Seventh-Day Adventists consisted of 407 Barbadian Seventh-Day Adventists (SDAs), aged from 25 to 74 years. Of these subjects, 153 (37.6%) were males and 254 were (62.4%) females and 43.5% were vegetarians.[31] Compared with omnivores, the prevalence rates of diabetes was lower in long-term vegetarians. In a prospective cohort study of the Adventist Mortality Study and Adventist Health Study (California, USA), 8401 healthy subjects aged 45–88 years were recruited.[32] During the 17 years follow-up, there were 543 diabetes cases identified. Compared with long-term vegetarian, incidence risk of diabetes was 74% (OR = 1.74; 95%

CI: 1.36–2.22) higher for omnivores who consistently consumed meat weekly over a 17-year interval. After controlling for body weight and weight change, weekly meat intake remained a critical risk factor for diabetes (OR = 1.38; 95% CI: 1.06–1.68). Lower prevalence of type 2 diabetes in vegetarians compared with omnivores has also been reported in different populations.[11,33]

One hundred and sixty-nine healthy Chinese lacto-vegetarians and 126 healthy omnivore men aged 21–76 years were recruited for a cross-sectional study.[34] Compared with omnivores, vegetarians have a significantly lower fasting serum glucose concentration, and higher homeostasis model assessment β-cell function and insulin secretion index, which indicates vegetarians have increased insulin sensitivity. In a cross-sectional study, 98 Chinese healthy female adults aged 31–45 years (49 were female Buddhist lacto-vegetarians; 49 were omnivores) from Taiwan participated in the study.[35] Compared with omnivores, vegetarians had significantly lower fasting plasma concentrations of glucose (mean ± SEM: 4.7 ± 0.05 *vs*. 4.9 ± 0.05 mmol L^{-1}), insulin (median: 35.3 *vs*. 50.6 pmol L^{-1}) and insulin resistance index (HOMA) (median: 1.10 *vs*. 1.56). Ninety-five healthy Slovak Republic long-term lacto-ovo-vegetarians (duration of vegetarianism 10.2 ± 0.5 years) and 107 healthy omnivores (traditional western diet) aged 19–64 years participated in a study[36] which demonstrated that serum concentration of glucose and insulin and values of insulin resistance IR (HOMA) were significantly lower in vegetarians than in omnivores: 4.47 ± 0.05 *vs*. 4.71 ± 0.07 mmol L^{-1}, 4.96 ± 0.23 *vs*. 7.32 ± 0.41 mU L^{-1} and 0.99 ± 0.05 *vs*. 1.59 ± 0.10, respectively.

Studies from clinical trials revealed that vegetarian diet improves insulin resistance compared with conventional diet in type 2 diabetic subjects.

In a 24-week intervention study, 74 type 2 diabetes patients, aged 30–70 years old with HbA1c between 6% and 11% were randomly divided into either the vegetarian diet group ($n = 37$, 17 males and 20 females), or the control group ($n = 37$, 18 males and 19 females) which received a conventional diabetic diet for 12 weeks.[37] Both group diets were isocaloric and all meals were provided during the study. In the second 12 weeks, the diet was combined with aerobic exercise. Insulin sensitivity was significantly increased in the vegetarian diet group compared with the control group ($P = 0.04$). Plasma concentrations of leptin significantly decreased ($P = 0.02$) and adiponectin significantly increased ($P = 0.02$) in the vegetarian group at 24 weeks compared with baseline.

A randomized clinical trial of type 2 diabetic patients showed that a low-fat vegan diet improves glycemic control.[38] In the study, 99 type 2 diabetic patients with fasting plasma glucose concentration >6.9 mmol L^{-1}, aged 27–82 years, were randomly assigned to a low-fat vegan diet group ($n = 49$, 22 males 27 females) or a control group which followed the American Diabetes Association (ADA) guidelines ($n = 50$). Participants were evaluated at baseline and 22 weeks. Forty-three percent (21 of 49) of subjects in the vegan group and 26% (13 of 50) in the control group reduced their diabetes medications. HbA1c decreased 0.96% and 0.56% in the vegan group and control group ($P = 0.089$), respectively. HbA1c decreased 1.23 points in the vegan group compared with 0.38 points in the control group when those who changed medications were excluded ($P = 0.01$). An average of 6.5 kg body weight loss in the vegan group and 3.1 kg loss in the control group ($P = 0.001$) was achieved. Body weight change correlated with HbA1c change ($r = 0.51$, $n = 57$, $P = 0.0001$).

In conclusion, vegetarian diets are rich in phytochemicals, antioxidants, fiber, magnesium, vitamins C and E, Fe^{3+}, folic acid and n-6 PUFA, and low in cholesterol, total fat and saturated fatty acid, sodium, Fe^{2+}, zinc, vitamins A, B_{12} and D, and especially n-3 PUFA. Compared with omnivores, all-cause mortality and mortality from NCDs such as ischemic heart disease, circulatory and cerebrovascular diseases, and type 2 diabetes were significantly lower in vegetarians. All cancer incidences, except breast cancer, were significantly lower in vegetarians than in omnivores. However, a poorly designed vegetarian diet may lead to certain increased risk factors of NCDs such as plasma homocysteine, mean platelet volume and platelet aggregability. It is suggested that vegetarians should increase their dietary intake of vitamin B_{12} and n-3 PUFA to further reduce already low mortality and morbidity of NCDs.

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