

Effects of vegetarian diets on blood pressure

Yoko Yokoyama^{1,2}
Kazuo Tsubota^{2,3}
Mitsuhiro Watanabe^{1,2,4,5}

¹Graduate School of Media and Governance, Keio University, Fujisawa, Kanagawa, ²Health Science Laboratory,

³Department of Ophthalmology,

⁴Department of Internal Medicine, Keio University School of Medicine, Tokyo, ⁵Faculty of Environment and Information Studies, Keio University, Fujisawa, Kanagawa, Japan

Abstract: Hypertension is a major independent risk factor for coronary artery diseases, and the prevalence of hypertension is continuously increasing. Diet is an important factor that can be modified to prevent hypertension. According to the US Department of Health and Human Services, dietary patterns are defined as the quantities, proportions, and variety or combinations of different foods and beverages in diets and the frequency with which they are habitually consumed. In this review, the vegetarian dietary pattern is introduced with a focus on the effect on blood pressure (BP). Although the available evidence is limited, according to a previous meta-analysis of controlled trials, vegetarian dietary patterns significantly reduced systolic and diastolic BPs. One of the common features of a vegetarian diet is weight loss, which might, at least partially, explain the effect on BP. Other possible factors such as sodium, potassium, protein, amino acids, vitamin B-12, antioxidants, fiber, and the microbiome are introduced as possible mechanisms. Further studies are needed with non-Western populations to determine the most effective vegetarian dietary pattern and to explore the exact mechanisms by which these dietary patterns affect BP.

Keywords: vegetarian diet, plant-based diet, blood pressure, hypertension, meta-analysis

Introduction

Hypertension is a major independent risk factor for coronary artery diseases, irrespective of age, race, or sex.¹ According to the World Health Organization, hypertension is the cause of at least 45% of deaths due to heart disease and 51% of deaths due to stroke.² The number of people with hypertension has gradually increased from 600 million in 1980 to 1 billion in 2008.³ According to the Centers for Disease Control and Prevention, 32.5% of adults aged ≥ 20 years have hypertension, defined as high blood pressure (BP) and/or are taking antihypertensive medications.⁴ This high prevalence highlights the importance of utilizing public health approaches for the prevention of hypertension.

Diet is an important factor that can be modified to prevent hypertension. Sufficient evidence supports the role of modifiable factors, including diet, body weight, physical activity, and alcohol intake in the development of hypertension. Dietary modifications have been shown to be particularly effective in preventing and managing hypertension.⁵ Nutritional epidemiology typically examines diseases while considering a single or few nutrients or foods.⁶ Hu indicated that the results of nutrient analysis can be difficult to interpret as individuals do not consume nutrients in isolation. Dietary interventions may be easier to implement and more comprehensive when they are initiated as changes in the overall dietary pattern.⁶

Correspondence: Yoko Yokoyama
Graduate School of Media and Governance, Keio University, 5322 Endo, Fujisawa 252-0882, Kanagawa, Japan
Tel +81 466 48 5099
Email yyokoyama-kyt@umin.ac.jp



Vegetarian dietary pattern and BP

Dietary patterns are defined as “the quantities, proportions, variety, or combinations of different foods and beverages in diets, and the frequency with which they are habitually consumed” by the US Department of Health and Human Services.⁷ In this paper, vegetarian dietary patterns are introduced while considering their influence on BP.

According to the position statement issued by the American Dietetic Association, now called the Academy of Nutrition and Dietetics, a vegetarian diet is defined as “one that does not include meat (including fowl) or seafood, or products containing those foods.”⁸ Although this is considered the standard definition, it has not been used by all researchers reporting the outcomes of vegetarian diets. Therefore, in this paper, vegetarian diets are defined as dietary patterns that exclude or rarely include meats; some vegetarian diets include dairy products, egg, and fish. All vegetarian diets emphasize the consumption of foods of plant origin, particularly vegetables, grains, legumes, and fruits. The definition used in this paper was based on articles included in a recent meta-analysis and prospective cohort studies with a high percentage of vegetarian participants.

Results from cross-sectional studies

The information in this section is based on three cross-sectional studies with high percentages of vegetarian participants:⁹ the Adventist Health Study-2¹⁰ (36%), European Prospective Investigation into Cancer and Nutrition-Oxford (EPIC-Oxford)¹¹ (33%), and the UK Women’s Cohort Study¹² (29%; Table 1).

BP was compared according to the dietary pattern in 500 white participants in the Adventist Health Study-2 cohort.

The dietary patterns were determined using a validated food frequency questionnaire that asked their usual or average diet during the past year. Individuals consuming a vegan–vegetarian diet (consume meat, fish, and dairy products less than once a month) had a lower prevalence of hypertension (defined as systolic BP >139 mmHg, diastolic BP >89 mmHg, or taking prescribed antihypertensive medications) than omnivorous individuals (odds ratio [OR] =0.37; 95% confidence interval [CI], 0.19–0.74). Moreover, lacto-ovo vegetarians (consume meat and/or fish less than once a month and dairy products more than once a month) also had a lower estimated odds of hypertension (OR=0.57; 95% CI, 0.36–0.92).¹⁰ However, after adjusting for body mass index (BMI), the ORs were not statistically significant, suggesting that the effect of vegetarian diets on BP is partly mediated by the effect on BMI.

In the EPIC-Oxford study, BP was evaluated in 1,790 men and 6,873 women. Participants were allocated to four diet groups according to the answers to questions regarding their dietary habits for meat, fish, dairy products, and egg. Systolic and diastolic BPs were significantly lower in the vegan group than in any other group (meat eaters, fish eaters, lacto-ovo vegetarian) after adjustment for age. However, the relationships were not significant after adjustment for age and BMI.¹¹ Other dietary factors, including saturated fat intake and polyunsaturated fat to unsaturated fat ratio, were associated with BP in both sexes; alcohol intake and carbohydrate intake were related to BP only in men, and calcium intake was associated with BP only in women.

The prevalence of hypertension was compared between vegetarians and omnivores in the UK Women’s Cohort Study.

Table 1 Characteristics of the observational studies included in the review

Study (country)	Participants (N)	Groups	Age (years)	Men (%)	BMI (kg/m ²)	Sodium (g)
Adventist Health Study-2 ¹⁰ (US and Canada)	500	Vegan (n=49)	67.6	29	24.0	3.5 ^c
		Lacto-ovo (n=184)	63.5	37	25.1	3.9 ^c
		Partial vegetarian (n=69)	61.4	32	26.3	3.8 ^c
		Nonvegetarian (n=198)	61.0	38	29.5	3.8 ^c
EPIC-Oxford ^{11a} (UK)	8,663	Vegans (n=612)	40/37 ^b	37.6	22.6/22.0 ^b	2.8/2.5 ^b
		Vegetarians (n=3,123)	45/41 ^b	20.1	23.4/22.8 ^b	3.0/2.6 ^b
		Fish eaters (n=1,404)	49/44 ^b	16.6	23.5/22.8 ^b	3.0/2.7 ^b
		Meat eaters (n=3,524)	54/51 ^b	19.8	24.6/24.1 ^b	3.0/2.7 ^b
		UK Women’s Cohort ¹² (UK)	35,372	Vegetarians (n=6,478)	49	0
Other fish eaters (n=3,286)	50	0		23.3	NR	
Oily fish eaters (n=870)	51	0		23.2	NR	
Meat eaters (n=24,738)	54	0		25.0	NR	

Notes: ^aBlood pressures were compared for participants without self-reported hypertension. ^bMale/female. ^cThis sodium intake data was only available from the overall Adventist Health Study-2 cohort (n=71,751), as reported by Rizzo et al.²⁸

Abbreviations: BMI, body mass index; NR, not reported.

Vegetarians were defined as participants who ate meat or fish less than once a week, as determined using a food frequency questionnaire. Vegetarians had a lower prevalence of hypertension than meat eaters (11.4% vs 19.6%)¹² and also had lower BMIs (23.3 kg/m² vs 25.0 kg/m²) and alcohol intake (45% vs 54%).

These three cross-sectional studies, with high percentages of vegetarian participants, showed that vegetarian diets were related to not only lower prevalence of hypertension or BP but also lower BMI. After adjustment for BMI, the relationships between a vegetarian diet and BP were no longer significant in some studies. Therefore, BMI might be a very important factor for the relationship between vegetarian diets and BP. Although the results from cross-sectional studies cannot indicate causality, they might reflect the relatively longer effects of vegetarian diets.

Results from a meta-analysis

A recent meta-analysis was conducted, for which the MEDLINE and Web of Science databases were searched for articles published in English. Seven clinical trials and 32 observational studies were included. The details of the inclusion and exclusion criteria are provided elsewhere.¹³ An overview of the seven trials^{14–20} included in the meta-analysis, representing 311 participants (mean age, 44.5 years), are provided in Table 2. All the studies were open (non-masked) controlled trials conducted for 6–52 weeks (mean, 15.7 weeks). Vegan diets were examined in two trials,^{19,20} a lacto-vegetarian diet in one trial,¹⁶ and lacto-ovo-vegetarian diets in four trials.^{14,15,17,18} The intervention methods differed among the studies. For instance, Hakala

and Karvetti counseled participants to follow a specific dietary pattern.¹⁶ In other studies, some food was provided for each participant to consume. Results from studies that counseled participants on diet might be useful in that they also test the ability of humans to adhere to a diet. However, studies that provided food are useful to elucidate biologic mechanisms because they ensure that the patient is exposed to the specific vegetarian dietary pattern.

The consumption of vegetarian diets was associated with a reduction in mean systolic BP (−4.8 mmHg; 95% CI, −6.6 to −3.1; $P < 0.001$) and diastolic BP (−2.2 mmHg; 95% CI, −3.5 to −1.0; $P < 0.001$) compared with the consumption of omnivorous diets.¹³ According to Whelton et al, a reduction in systolic BP of 5 mmHg resulted in a 14% overall reduction in mortality due to stroke, 9% reduction in mortality due to cardiovascular heart disease, and 7% decrease in all-cause mortality.²¹ Consistent results were observed in another meta-analysis of observational studies (N=21,604), in which the consumption of vegetarian diets was associated with a lower mean systolic BP (−6.9 mmHg; 95% CI, −9.1 to −4.7).¹³ Because of statistically significant heterogeneity in the meta-analysis of observational studies, the heterogeneous factors were examined using meta-regression. The number of men, baseline systolic and diastolic BPs, and BMI were significant, indicating that the associations between vegetarian diets and BP were stronger among men and participants with higher baseline systolic and diastolic BPs and higher BMIs.

These findings from cross-sectional studies and meta-analyses are consistent with those of a previous review of observational studies; compared with the BPs of nonvegetarians, the systolic BP of vegetarians was 3–14 mmHg lower, and

Table 2 Characteristics of clinical trials included in the meta-analysis

References (country; year)	Participants (N)	Groups	Age (years)	Men (%)	BMI (kg/m ²) or weight (kg)	Sodium (g)
Ferdowsian et al ²⁰ (US; 2010)	113	Vegan (n=68)	46.0	26.5	98.7 kg	2.0
		Omnivorous (n=45)	42.0	4.4	100.1 kg	1.9
Nicholson et al ¹⁹ (US; 1999)	11	Vegan (n=7)	51.0	57.1	96.7 kg	NR
		Omnivorous (n=4)	60.0	50.0	97.0 kg	NR
Sciarrone et al ¹⁸ (Australia; 1993)	20	Lacto-ovo (n=10)	41.1	100	25.5 kg/m ²	2.6
		Omnivorous (n=10)	40.8	100	25.0 kg/m ²	2.2
Hakala and Karvetti ¹⁶ (Finland; 1989)	73	Lacto (n=31)	Mean 38.0*	25.8	34.4 kg/m ²	NR
		Omnivorous (n=42)		23.8	34.4 kg/m ²	NR
Kestin et al ¹⁷ (Australia; 1989)	17	Lacto-ovo (crossover)	Mean 44.0*	Mean 100*	Mean 25.5 kg/m ² *	3.4
		Omnivorous				3.5
Margetts et al ¹⁵ (Australia; 1986)	39	Lacto-ovo (crossover)	Mean 49.9*	Mean 71.8*	Mean 27.6 kg/m ² *	2.9
		Omnivorous				2.7
Rouse et al ¹⁴ (Australia; 1983)	38	Lacto-ovo (crossover)	Mean 40.1*	Mean 50.0*	Mean 23.7 kg/m ² *	NR
		Omnivorous				

Note: *Data was not available for individual groups, and is instead given as combined mean data for both groups.

Abbreviations: BMI, body mass index; NR, not reported.

diastolic BP was 5–6 mmHg lower.²² In addition, randomized controlled trials (RCTs) have shown that BP is lower when animal products are replaced with plant-based products in both normotensive and hypertensive participants.²² The Dietary Approaches to Stop Hypertension (DASH) study showed that a diet rich in vegetables and fruits reduced systolic BP by –5.5 mmHg ($P<0.001$) and diastolic BP by –3 mmHg ($P<0.001$).²³ The DASH study was partly based on the observation that vegetarian diets are associated with a significantly reduced risk of hypertension.²⁴

Possible mechanisms

Dietary pattern analysis focuses on the overall diet rather than individual nutrients. Although an approach utilizing a dietary pattern reveals the effectiveness of a real-world diet on diseases, it cannot identify the particular nutrients responsible for the disease. Therefore, Hu recommended that an observed association with a dietary pattern should be evaluated with the results from individual nutrient analyses.⁶ According to the Academy of Nutrition and Dietetics, the characteristics of a vegetarian dietary pattern include lower saturated fat and cholesterol levels and higher dietary fiber, magnesium, potassium, vitamins C and E, folate, carotenoid, flavonoid, and other phytochemical levels.⁸ In this paper, we discuss possible mechanisms of the distinctive characteristics in a vegetarian dietary pattern.

Energy intake

Particularly, the low energy intake in vegetarian diets might be attributable to the lower energy density of the diet, owing to higher fiber and lower fat content.

According to a recent meta-analysis of clinical trials, body weight decreases with the consumption of a vegetarian diet.²⁵ Because obesity is one of the main diet-related risk factors of hypertension,⁹ reducing body weight could be an important intermediate variable. However, because studies controlling for body weight have still demonstrated a BP-lowering effect of vegetarian diets, weight differences do not fully explain the observed BP differences.¹⁴

Sodium

Compared with the Western diet, vegetarian diets might be lower in sodium;^{26,27} however, no clear differences in sodium intake between nonvegetarians and vegetarians have been reported,²⁸ or some vegetarians have a higher sodium intake.²⁹ Sodium intake among studies included in this paper is shown in Tables 1 and 2. Overall, sodium intake was lower in the vegetarian diets.

In a recent meta-analysis of 107 RCTs, there was a strong dose–response relationship between reduced sodium intake and BP.³⁰ A 2.3 g reduction in sodium per day was associated with a 3.82 mmHg reduction in BP (95% CI, 3.08–4.55).³⁰ The DASH dietary pattern also focuses on vegetable and fruit consumption; in trials that controlled sodium intake, the DASH diet had a BP-lowering effect beyond sodium reduction alone.^{23,31} Further studies are needed to investigate the effects of vegetarian diets, with controlled sodium intake, on BP.

Potassium

Potassium is abundant in vegetarian diets,²⁸ and a meta-analysis of RCTs reported that potassium supplementation decreases BP.^{32,33} Moreover, a high potassium intake increases vasodilation and the glomerular filtration rate, while decreasing renin levels, renal sodium reabsorption, reactive oxygen species production, and platelet aggregation.³⁴ Other minerals, such as magnesium and calcium, were inversely associated with BP in the INTERMAP (INTERNational collaborative study of MACronutrients, micronutrients and blood Pressure) study, which was conducted in four countries (USA, UK, People's Republic of China, and Japan).³⁵ In a meta-analysis of magnesium supplementation, both systolic (3–4 mmHg) and diastolic (2–3 mmHg) BPs decreased.³⁶

Protein source

The INTERMAP study suggested that plant protein intake (2.8% energy) was associated with a 2.1 mmHg reduction in systolic BP.³⁷ Other prospective cohort studies also indicated that plant protein intake is associated with BP reduction³⁸ or a lower risk of incident hypertension.³⁹ A recent meta-analysis of trials that were stratified by plant protein or animal protein indicated no differences with protein from plant or animal sources.⁴⁰ However, the sample size of this meta-analysis was small (three trials, $N=327$ for plant protein; four trials, $N=574$ for animal protein), and the effects of plant or animal protein were not directly compared. Hence, further intervention studies and meta-analyses are needed to understand the effects of different sources of protein on BP.

Amino acids

Previous studies have suggested that plasma concentrations and intake of amino acids were different among vegetarians and omnivores.^{41,42} In the INTERMAP study, glutamic acid intake was higher among those consuming predominantly plant protein, as compared with those consuming predominantly animal protein.⁴³ A two-standard deviation higher intake of glutamic acid (4.7% of total protein) was associated with a

1.5 mmHg lower systolic BP.⁴³ Glutamic acid is a precursor of arginine, which is itself a precursor for the vasodilator nitrous oxide (NO)^{44,45} and may contribute to lowering of BP.

In the EPIC-Oxford cohort, plasma amino acid concentrations were compared between vegetarians and meat eaters in 392 men, aged 30–49 years. Amino acids such as lysine, methionine, tryptophan, and tyrosine were significantly lower, and alanine and glycine were higher in vegans than in meat eaters.⁴⁶ Lysine competes with arginine for transport into the cell,^{47,48} and arginine deficiency is associated with endothelial inflammation and immune dysfunction in humans.⁴⁹ Therefore, the lysine/arginine ratio may be important in understanding the BP-lowering effect. Compared with animal protein, plant proteins contain lower lysine levels and a low lysine/arginine ratio.⁵⁰ Therefore, plant protein, with a low lysine/arginine ratio, could reduce BP by stimulating NO production. A recent, small (N=30), randomized crossover trial was conducted to clarify the effect of changing the dietary lysine/arginine ratio on cardiovascular risk factors,⁵⁰ by providing 30 healthy adults with a low (0.7) or high (1.4) lysine/arginine ratio diet. After 35 days of the intervention, no difference was observed in BP.⁵⁰ However, the effectiveness of long-term consumption of a low lysine/arginine ratio diet has not been clarified.

A 2-year prospective cohort study (N=92) showed that dietary intake of methionine and alanine is associated with increased BP.⁵¹ Methionine is a homocysteine precursor that can increase BP by increasing the levels of asymmetric dimethylarginine – a competitive inhibitor of NO.⁵² Methionine is abundant in animal protein and scarce in plant protein;⁵³ therefore, a predominantly plant-based protein diet might have a lower methionine content. A metabolic phenotyping analysis, as part of the INTERMAP study, showed that urinary alanine excretion was associated with higher BP.⁵⁴ In the same study, dietary alanine was higher in people consuming a predominantly animal diet than in people ingesting a predominantly plant diet.³⁷

Vitamin B-12

In addition to the nutrients already described, vegans and vegetarians may have lower intakes of some nutrients such as vitamin B-12, vitamin D, calcium, zinc, and long-chain n-3 fatty acids.⁸ Vitamin B-12 deficiency is highly prevalent in vegetarians, particularly in vegans who do not consume vitamin B-12 fortified food or supplements.⁵⁵ Woo et al highlighted that, despite the protective effects of vegan diets on cardiovascular-related risk in some studies, vegan diets can have an adverse effect on arterial endothelial function and carotid intima-media thickness in Chinese vegetarians

with suboptimal vitamin B-12 levels and normal or high salt intake.⁵⁵ Vitamin B-12 deficiency results in increased homocysteine levels, which are related to arterial endothelial dysfunction and are an independent risk factor for cardiovascular disease.⁵⁶ Pawlak suggested that vitamin B-12 deficiency may ameliorate the benefit of a vegetarian diet for cardiovascular diseases.⁵⁷ Therefore, interactions with nutrients that are often deficient in some vegetarians should also be considered.

Antioxidants

Vegetables and fruits are rich in antioxidants. A 6-month RCT revealed that increased consumption of vegetables and fruits was related to increased antioxidant intake such as alpha-carotene, beta-carotene, lutein, b-cryptoxanthin, and ascorbic acid.⁵⁸ In addition, when compared with a control group, the group with a higher consumption of vegetables and fruits had significantly greater reductions in systolic (–4.0 mmHg; $P<0.0001$) and diastolic (–1.5 mmHg; $P=0.02$) BPs.⁵⁸

Fiber

Fiber is predominantly present in plant-based foods, and vegetarian diets have the largest amount of fiber. A recent meta-analysis of 24 RCTs revealed that dietary fiber supplementation (average dose, 11.5 g/d) reduced diastolic BP by –1.26 mmHg (95% CI, –2.04 to –0.48) and nonsignificantly reduced systolic BP by –1.13 mmHg (95% CI, –2.49 to 0.23).⁵⁹ Another meta-analysis of 25 RCTs indicated that dietary fiber intake was associated with a –1.65 mmHg (95% CI, –2.70 to –0.61) reduction in diastolic BP and a nonsignificant –1.15 mmHg (95% CI, –2.68 to 0.39) reduction in systolic BP.²¹ The effect of dietary fiber supplementation on both systolic and diastolic BPs was stronger and more significant in hypertensive patients.²¹ Although data are not sufficient to determine the effectiveness of dietary fiber supplementation for the reduction in BP, dietary fiber might explain part of the effectiveness of dietary pattern interventions.

Microbiome

The human gut microbiota can rapidly change with dietary fiber supplementation⁶⁰ or by excluding animal-based foods.⁶¹ The gut microbiota might contribute to the development of cardiovascular disease, including arteriosclerosis and hypertension.⁶² Toxic metabolites, such as p-cresol sulfate, indoxyl sulfate, and trimethylamine N-oxide (TMAO) are produced by gut microbiota through the fermentation of proteins.^{63–65} Previous trials showed that the average p-cresol sulfate excretion was 62% lower and average indoxyl sulfate secretion was 58% lower in participants consuming a vegetarian diet than

in those consuming an omnivorous diet.⁶⁶ p-Cresol sulfate and indoxyl sulfate are associated with vascular disease and mortality in patients with chronic kidney disease (CKD).^{67,68} The plasma TMAO concentration in patients with CKD was significantly higher than that in patients without CKD, and the plasma TMAO level was associated with a 2.8-fold increased risk of mortality. TMAO is produced by the metabolism of dietary choline, phosphatidylcholine, and L-carnitine by microbiota.^{64,69–71} A higher plasma TMAO level is primarily due to gut microbial action, as genes play only a minor role in determining TMAO levels in humans.⁷² However, a direct association between TMAO and BP has not been investigated. Recent basic research using a rat model showed that the TMAO level does not affect BP in normotensive animals, but it contributed to the hypertensive effect of angiotensin II.⁷³

Conclusion

Although the available evidence is not sufficient for robust conclusions, the results from cross-sectional studies with a higher prevalence of vegetarian diets or meta-analyses of trials indicate that a vegetarian dietary pattern is related to a lower BP. The effectiveness of a vegetarian dietary pattern might partly be explained by weight reductions. Any dietary pattern is composed of several nutrients or foods; therefore, its effect may reflect the synergetic effects of several nutrients or foods. Further studies are needed with a higher intake of sodium or animal products in non-Western populations. In addition, we were unable to determine which vegetarian dietary pattern (eg, vegan, lacto-vegetarian, lacto-ovo vegetarian, pesco-vegetarian) is better. Studies to clarify the possible mechanisms of typical nutrients in vegetarian diets and their synergetic effects are also needed.

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Disclosure

The authors report no conflicts of interest in this work.

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