











Dietary intervention for the management of hypertension in Asia

Hao-Chih Chang MD¹  | Hao-Min Cheng MD, PhD^{1,2,3,4}  | Chen-Huan Chen MD^{1,2,3,4}  |
 Tzung-Dau Wang MD, PhD⁵  | Arieska Ann Soenarta MD⁶ | Yuda Turana MD, PhD⁷  |
 Boon Wee Teo MB, BCh⁸  | Jam Chin Tay MBBS, FAMS⁹  | Kelvin Tsoi BSc, PhD¹⁰  |
 Ji-Guang Wang MD, PhD¹¹  | Kazuomi Kario MD, PhD¹² 

¹Department of Medicine, Taipei Veterans General Hospital Su-Ao and Yuan-Shan Branch, Yilan, Taiwan

²Faculty of Medicine, National Yang-Ming University School of Medicine, Taipei, Taiwan

³Department of Medical Education, Center for Evidence-based Medicine, Taipei Veterans General Hospital, Taipei, Taiwan

⁴Institute of Public Health and Community Medicine Research Center, National Yang-Ming University School of Medicine, Taipei, Taiwan

⁵Division of Cardiology, National Taiwan University Hospital, Taipei, Taiwan

⁶Department of Cardiology and Vascular Medicine, Faculty of Medicine, University of Indonesia-National Cardiovascular Center, Harapan Kita, Jakarta, Indonesia

⁷School of Medicine and Health Sciences, Atma Jaya Catholic University of Indonesia, Jakarta, Indonesia

⁸Division of Nephrology Department of Medicine, Yong Loo Lin School of Medicine, Singapore, Singapore

⁹Department of General Medicine, Tan Tock Seng Hospital, Singapore, Singapore

¹⁰JC School of Public Health and Primary Care, The Chinese University of Hong Kong, Shatin, Hong Kong, China

¹¹Department of Hypertension, Centre for Epidemiological Studies and Clinical Trials, the Shanghai Institute of Hypertension, Shanghai Key Laboratory of Hypertension, Ruijin Hospital, Shanghai Jiaotong University School of Medicine, Shanghai, China

¹²Division of Cardiovascular Medicine, Department of Medicine, Jichi Medical University School of Medicine, Tochigi, Japan

Correspondence

Hao-Min Cheng, No. 201, Sec. 2, Shipai Road, Beitou District, Taipei, Taiwan 11267, R.O.C.
 Email: hmcheng@vghtpe.gov.tw

Abstract

Hypertension is among the leading global risks for premature death. As the risks substantially increase along with the elevated blood pressure, a small reduction of blood pressure could have prevented numerous cardiovascular events in general population. Evidence has shown that dietary intervention is a cost-effective strategy that has been broadly advocated in the published guidelines. However, the implementation could be limited by different food cultures. This review details the mechanisms of each dietary intervention approach, evidence, and the implications in Asian populations, and the perspective of future research.

1 | INTRODUCTION

Hypertension is a leading risk factor contributing to increased global disease burden and premature death.¹ Regardless of the definition of hypertension, blood pressure (BP) is a continuous and independent

variable for adverse cardiovascular events.² The risk of cardiovascular diseases progressively increased throughout the range of both systolic and diastolic BP in all age groups, including the pre-hypertensive range (systolic BP of 120 to 139 mmHg and diastolic BP of 80 to 89 mmHg).³ A small reduction of systolic or diastolic BP by lifestyle modification

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could have a great impact on the numbers of adverse cardiovascular events prevented.⁴ Of all the lifestyle changes, dietary intervention plays a predominant role and has been advocated as an initial treatment for pre-hypertension and throughout all the stages of hypertension. Although dietary modifications have been universally recommended in the published guidelines, their mechanisms of action have not been reviewed and the implications may vary among different Asian populations. The purpose of this review article is to summarize the mechanisms of action in each dietary approach, also the evidence and their applications in Asian populations.

2 | DIETARY PATTERNS

In the contemporary hypertension guidelines, there have been two types of recommendations on dietary intervention: dietary patterns and regulations relating to specific electrolyte intake. Considering that the effect of an individual nutrient may be too small to detect, targeting the whole dietary patterns with synergic efficacy of lowering BP over individual nutrients have been advocated. The most well-established diets are the Dietary Approaches to Stop Hypertension (DASH) diet and Mediterranean diet. The DASH diet, a dietary pattern rich in fruits, vegetables, low-fat dairy foods, reduced amount of saturated fat, total fat, and cholesterol, has been proved to substantially reduce systolic BP by 11.4 mmHg and diastolic BP by 5.5 mmHg in hypertensive patients,⁵ whereas the Mediterranean diet, rich in fruits, vegetables, legumes, nuts, and olive oil with moderate intakes of fish, dairy, wine, and low intakes of meat, was shown to reduce systolic BP by 5.5 mmHg and diastolic BP of 1.7 mmHg compared with typical diet.⁶ Given that the implementation of Mediterranean diet may be limited by dietary cultures in different regions, the DASH-type dietary patterns are more recommended in both western and Asian guidelines as the integral part of lifestyle modifications (Table 1).

2.1 | Mechanisms of action

The mechanisms of the BP-lowering effect of the DASH diet have been evaluated in previous studies. It has been previously demonstrated that DASH diet can provide potassium, magnesium, and calcium at levels close to the 75th percentile of the United States consumption while maintaining sodium content similar to that of the control diet based on the analysis of the nutrient composition of the DASH diet.⁵ Despite the change of specific nutrient component, the available evidence does not indicate that any specific nutrient could be responsible for effects of the DASH diet on BP changes. In a sub-analysis of the randomized controlled DASH-Sodium trial, Akita and colleagues⁷ found that DASH diet steepens the pressure-natriuresis curve, suggesting a natriuretic action of the DASH diet. The natriuretic effect of the DASH diet has also been exemplified by its interaction with the renin-angiotensin system (RAS), resulting in increased plasma renin activity and aldosterone levels.^{8,9} In another randomized controlled study enrolling 20

unmedicated hypertensive adults, DASH diet intervention was shown to be associated with increased nitric oxide bioavailability and reduced pulse wave velocity.¹⁰ Considering the complexity of the change in whole dietary pattern, the BP-lowering effect could result from multiple mechanisms and is hard to be explained by a single mechanism.

2.2 | Evidence and application in Asia

However, the application of DASH diet in Asian countries may be limited by the large differences in dietary culture and taste preferences. Modified DASH diet, tailored for Asian food culture but with the same nutrition composition as conventional DASH diet, has been shown to effectively reduce BP and is more acceptable by Asian populations (Table 2).¹¹ It could be promoted as an alternative strategy in Asian countries, if more evidence supports. In addition to the DASH diet, some Asian dietary patterns have also been reported to lower the risk of hypertension. The frequency of spicy food consumption is inversely associated with the risk of hypertension in Chinese female adults.¹² Curry food intake is correlated with the reduced serum levels of heavy metals, also the prevalence of hypertension in Koreans.¹³ However, their underlying mechanisms and whether the findings could be extrapolated to other populations warrant more investigation. Until further evidence supports, we suggest following the principles of the DASH diet as the main dietary pattern to reduce BP.

3 | SODIUM RESTRICTION

In addition to the dietary patterns, high dietary sodium intake is also associated with the development and progression of hypertension,¹⁴ and such association is nonlinear and is more pronounced in persons consuming high-sodium diets, with hypertension, or older ages.¹⁵ Meta-analysis has shown that every 100 mmol reduction in sodium (equivalent to 2.3 g sodium/day) is associated with a fall in systolic BP of 5.8 mmHg.¹⁶ It is noteworthy that the BP-lowering effect of salt restriction is on top of the healthy dietary pattern. The DASH-Sodium trial demonstrated that combined dietary sodium restriction (<100 mmol/day; equivalent to 2.3 g sodium/day) and DASH diet substantially lowered BP more effectively than either alone.¹⁷ Salt restriction is therefore recommended in all published guidelines for preventing cardiovascular disease on top of the healthy dietary patterns (Table 1).

3.1 | Mechanisms of action

The mechanism of salt intake and elevated BP has been broadly discussed. Excessive sodium intake not only results in fluid retention, enhanced sympathetic activity, increased vasoconstriction, but also vascular, myocardial remodeling, and renal damages in the long run.^{18,19} Although sodium restriction lowers BP in a dose-response

TABLE 1 Summary of dietary intervention for the management of hypertension in different guidelines

Guidelines	Dietary pattern	Salt/sodium ^a	Potassium	Alcohol	Body weight
ACC/AHA 2017 ²⁹	DASH diet	<1.5 g/day (sodium)	3.5–5.0 g/day	Men <2 drinks/day ^b Women <1 drink/day ^b	Ideal body weight
ESC/ESH 2018 ³⁰	Increased vegetables/ fruits, fish, nuts, unsaturated fatty acid; low consumption of red meat; low-fat dairy products	<5 g/day (salt)	N/A	Men <14 units/day ^c Women <8 units/day ^c	BMI: 20–25 Waist: men < 94 cm Women < 80 cm
TSOC/THS 2017 ³⁵	DASH diet	2–4 g/day (sodium)	N/A	Men <30 g/day Women <20 g/day	BMI: 22.5–25
Chinese 2018 ⁴⁴	Reasonable meal, balanced diet	<6 g/day (salt)	Increase intake	Men <25 g/day Women <15 g/day	BMI < 24 Waist: men < 90 cm Women < 85 cm
JSH 2019 ³¹	Increased vegetables/ fruits; reduced saturated fatty acid/ cholesterol; increased polyunsaturated fatty acids; low-fat dairy products	<6 g/day (salt)	N/A	Men < 20–30 ml/day Women <10–20 ml/ day	BMI < 25
KSH 2018 ³²	Increased vegetables/ fruits, fish, nuts, and unsaturated fatty acids; low consumption of meat; low-fat dairy products	<6 g/day (salt)	N/A	Men < 20–30 g/day Women < 10–20 g/ day	BMI < 25

Abbreviations: ACC/AHA, American College of Cardiology/American Heart Association; BMI, body mass index; DASH, Dietary Approaches to Stop Hypertension; ESC/ESH, European Society of Cardiology/European Society of Hypertension; JSH, Japanese Society of Hypertension; KSH, Korean Society of Hypertension; TSOC/THS, Taiwan Society of Cardiology/Taiwan Hypertensive Society.

^a1 g sodium = 43.5 mmol sodium = salt (g)/2.5

^b1 standard drink: roughly 14 g of pure alcohol.

^c1 unit: 125 ml of wine or 250 ml of beer.

relationship,¹⁷ there seems to be a discordant association between sodium intake, BP levels, and cardiovascular outcomes. Studies have observed that there is a J-shape association between sodium intake and risk of adverse cardiovascular events.²⁰ Both high and low sodium intake are associated with increased mortality. Meta-analysis showed that low sodium intake (<100 mmol/day) is associated with increased renin activity, also the levels of aldosterone and catecholamines.²¹ Reduction in sodium intake appears to activate the sympathetic system with impairment of BP homeostasis in hypertensive patients.²² Low sodium diet also affects membrane sodium transport in animal studies.^{22,23}

3.2 | Evidence and application in Asia

The significant BP-lowering effect of sodium restriction has been proved by randomized controlled trials in Asian populations (Table 2).^{24–28} Apart from the western guidelines that more strictly recommend <3.75 g to 5 g/day,^{29,30} the daily salt restriction is lessened to <6 g/day in Japanese, Korean, and Chinese guidelines for a higher average salt consumption in Asian populations (Table 1).^{31,32} Monosodium glutamate, a flavor enhancer and one of the major

source of salt intake in Chinese populations, is associated with the higher increase in BP.³³ Thus, regulation on the additive of monosodium glutamate may be a more prior way to advocate sodium restriction in Asian countries. However, whether the recommendation of low sodium intake by current guideline panels is supported by robust evidence has been challenged recently.³⁴ It should be noted that most guidelines do not recommend a lower limit for daily sodium intake except that Taiwan Society of Cardiology/Taiwan Hypertensive Society 2017 hypertension guideline suggests that the optimal daily sodium consumption should be at 2–4 g/day, with a lower limit of >2 g/day.³⁵ In this clinical review, based upon observational studies, it may be more reasonable to suggest a population-level mean target of <5 g/day in populations with mean sodium intake of >5 g/day, while awaiting the results of large randomized controlled trials determining the effects of sodium reduction on incidence of cardiovascular events and mortality.³⁴

4 | POTASSIUM SUPPLEMENTATION

In contrast to dietary salt, potassium intake is inversely correlated with BP. A higher level of potassium intake has been reported to

TABLE 2 Clinical trials of dietary intervention in Asian populations

Trials	Year	Study design	Dietary interventions	Durations	Efficacy
Dietary patterns					
Kawamura and colleagues ¹¹	2011–2012	Single-arm, open-label	Modified DASH diet (n = 58)	2 months	↓BMI, ↓BP, ↓fasting glucose, ↓fasting insulin
Sodium restriction					
Brito-Ashurst and colleagues ²⁴	2008–2009	Randomized-controlled, open-label	Tailored low-salt diet advice (n = 28) vs. standard low-salt diet advice (n = 28)	6 months	↓systolic BP, ↓diastolic BP
Jessani and colleagues ²⁵	Published in 2008	Randomized-controlled, crossover	Low-sodium diet: 20 mEq/day (n = 200)	1 week	↓systolic BP
Mu and colleagues ²⁶	Published in 2009	Randomized-controlled, single blind	Salt restriction: 50–100 mmol/day (n = 110) vs. added-potassium-and-calcium: 10mmol/day (n = 101) vs. control (n = 114)	2 years	↓systolic BP, ↓diastolic BP
Nakano and colleagues ²⁷	2012–2014	Randomized-controlled, open-label	Nutritional education: salt < 6 g/day (n = 51) vs. control (n = 44)	3 months	↓24-h systolic BP
Zhou and colleagues ²⁸	Published in 2012	Randomized-controlled, double blind	Salt substitute (reduced-sodium, high-potassium) (n = 224) vs. normal salt (n = 238)	2 years	↓systolic BP, ↓diastolic BP
Potassium supplementation					
Kawano and colleagues ⁴²	Published in 1998	Randomized, crossover	Potassium supplementation: 64 mmol/day (n = 55)	4 weeks	↓office, home, 24-h BP
Gu and colleagues ⁴³	Published in 2001	Randomized-controlled, double blind	Potassium supplementation: 60mmol/d (n = 75) vs. placebo (n = 75)	12 weeks	↓systolic BP

Abbreviations: BMI, body mass index; BP, blood pressure; DASH, Dietary Approaches to Stop Hypertension.

blunt the effect of sodium intake on BP,³⁶ whereas low dietary potassium intake may potentiate salt sensitivity and synergistically lead to higher BP.³⁷ A lower ratio of sodium-to-potassium dietary intake is significantly associated with the more reduction of BP than the corresponding levels of either alone.³⁸

4.1 | Mechanisms of action

The protective effect of high-potassium diet against increased BP may be conceivably correlated with the modulation of sodium and potassium by renal tubules. In a small-scaled randomized controlled study enrolling 22 hypertensive patients, potassium supplementation lowered BP and was associated with increased natriuresis.³⁹ It has been shown that a high-potassium intake may suppress sodium retention via down-regulation of the thiazide-sensitive sodium-chloride cotransporter.⁴⁰ Although potassium supplementation has been proposed to lower BP, the data are not entirely consistent.⁴¹ Therefore, potassium replenishment was not literally recommended in most of the guidelines, except that American College of Cardiology (ACC)/American Heart Association (AHA) 2017 guideline recommends daily potassium intake at 3.5–5.0 g/day (Table 1).²⁹

4.2 | Evidence and application in Asia

Potassium supplementation has been shown to significantly lower BP in Asian populations (Table 2).^{42,43} Although the Chinese 2018 guidelines suggested to increase potassium intake,⁴⁴ the optimal target is not clearly defined (Table 1). It is worth indicating that the average daily potassium intake is less in Asian populations. Rice instead of potato is the staple food in Asian cuisines that contains less potassium (25 mg vs. 500 mg per 100 g of rice vs. potato). This is a very important dietary issue for Asian and leads to the significant between-ethnicity difference in daily potassium intake (men: Japanese 1.9 g/day, Chinese 1.5 g/day, British 2.9 g/day, and American 2.5 g/day; women: Japanese 1.9 g/day, Chinese 1.5 g/day, British 2.4 g/day, and American 2.0 g/day).⁴⁵ Although we do not have to change our dietary habit, sufficient potassium supplementation could become a critical issue for the rice-consuming Asian countries. Randomized controlled trial has shown that potassium does not need to be given in the form of potassium chloride to lower BP.⁴⁶ Increasing the consumption of food rich in potassium is the preferable way to increase potassium intake.²⁹ We therefore suggest following a healthy dietary pattern, such as the potassium-rich DASH diet or a diet rich in fruits and vegetables, as the principal way to replenish daily potassium intake for Asian populations.

5 | CALORIE RESTRICTION

Not only the dietary intake, some of the diet-related factors are also associated with high BP. Epidemiological studies have consistently shown a direct correlation between body mass index (BMI) and BP,⁴⁷ and the relationships of BP to waist circumference or central fat distribution are even more evident.⁴⁸

5.1 | Mechanisms of action

The pathophysiological implications of adiposity on elevated BP have been discussed. Studies have shown that obesity may lead to excessive sodium and fluid retention via the up-regulation of RAS and the excessively secreted leptin by adipose tissue. Obesity also contributes to insulin resistance with hyperinsulinemia that attenuates renal sodium excretion.⁴⁹ The disturbed sodium and fluid homeostasis that sustain hypertension, however, could be reversed by body weight loss.⁵⁰ In a meta-analysis, an average body weight loss of 5.1 kg by means of lifestyle modifications is associated with a mean reduction of 4.4 mmHg in systolic BP and 3.6 mmHg in diastolic BP.⁵¹ Body weight control is therefore recommended in all the published guidelines.

5.2 | Evidence and application in Asia

While the ACC/AHA 2017 guideline recommended keeping ideal body weight,²⁹ the European Society of Cardiology/European Society of Hypertension 2018 guidelines suggested to aim at healthy BMI (20–25 kg/m²) with waist circumference of <94 cm in men and <80 cm in women.³⁰ Like the European guidelines, most Asian guidelines also recommended to keep BMI less than 24–25 kg/m² as possible (Table 1). Since dietary intake and obesity are both closely associated with hypertension, the causal relationship has been investigated. Food security, as developed by the World Food Program, is the measure for food frequency and dietary diversity. The inability to consume qualified or diverse food is correlated with the development of hypertension and adverse cardiovascular events. It has been also reported that the effect of food security on hypertension is mediated through the abnormal body shape.⁵² Therefore, to reduce the development of hypertension, dietary intervention with calorie restriction in keeping the ideal body weight (BMI) or shape (waist circumference) at goals plays an essential role.

6 | FUTURE PERSPECTIVE

Although dietary interventions consist of different approaches to reduce BP, there are some similarities in between. Except that salt restriction directly decreases the sodium intake, other dietary interventions are associated with the modulation of renal sodium excretion. Both the DASH dietary pattern and potassium supplementation

exert increased natriuretic effect, while body weight loss may reverse the sodium and fluid retention. Considering the similar mechanisms of action, whether the BP-lowering effects are additive if combined or as an alternative to another remain unclear. In addition, both DASH and sodium restriction are shown to activate RAS, which may raise the concerns of increased cardiovascular risk.⁵³ To what extent we should recommend on the sodium restriction, and whether the joint effects of reduced BP could be translated to the improved cardiovascular outcomes require more clinical studies to clarify the issues. Furthermore, although average BP being regarded as an indicator of cardiovascular risk, recent meta-analysis suggested that BP oscillation adds significant prognostic information beyond traditional risk factors.⁵⁴ Prospective clinical trials with pre-specified goals can be warrant to evaluate the effects of dietary interventions on BP variability.

7 | CONCLUSIONS

Dietary intervention plays an essential role in the management of hypertension and is one of the most cost-effective measures to improve public health outcomes. Although the recommended daily intake amount may vary in Asian guidelines, we suggest to follow the DASH-type dietary pattern, sodium restriction less than 5 g/day in population level, and BMI goal of less than 25 kg/m² as the principal measure for Asian populations to keep BP at goals. More prospective interventional trials should be conducted to clarify the lower limit of daily sodium intake, joint effects of the different dietary approaches, and their effects on the long-term cardiovascular outcomes.

CONFLICT OF INTERESTS

HM Cheng received speakers honorarium and sponsorship to attend conferences and CME seminars from Eli Lilly and AstraZeneca; Pfizer Inc; Bayer AG; Boehringer Ingelheim Pharmaceuticals, Inc; Daiichi Sankyo, Novartis Pharmaceuticals, Inc; SERVIER; Co., Pharmaceuticals Corporation; Sanofi; TAKEDA Pharmaceuticals International and served as an advisor or consultant for ApoDx Technology, Inc CH Chen reports personal fees from Novartis, Sanofi, Daiichi Sankyo, SERVIER, and Boehringer Ingelheim Pharmaceuticals, Inc JG Wang reports having received research grants from Chendu Di-Ao and Omron, and lecture and consulting fees from Astra-Zeneca, Novartis, Omron, Servier, and Takeda. K Kario reports research grants from Omron Healthcare, Fukuda Denshi, A&D, Pfizer Japan, and honoraria from Omron Healthcare. All other authors report no potential conflicts of interest in relation to this article.

AUTHOR CONTRIBUTIONS

HM Cheng and CH Chen contributed to the conception and design of the article. HC Chang interpreted the relevant literature and drafted the article. HM Cheng revised it critically. All authors substantially contributed the important intellectual content and suggestion during manuscript drafting, and accept accountability for the overall work.

ORCID

Hao-Chih Chang  <https://orcid.org/0000-0002-6256-2194>
 Hao-Min Cheng  <https://orcid.org/0000-0002-3885-6600>
 Chen-Huan Chen  <https://orcid.org/0000-0002-9262-0287>
 Tzung-Dau Wang  <https://orcid.org/0000-0002-7180-3607>
 Yuda Turana  <https://orcid.org/0000-0003-4527-0285>
 Boon Wee Teo  <https://orcid.org/0000-0002-4911-8507>
 Jam Chin Tay  <https://orcid.org/0000-0001-7657-4383>
 Kelvin Tsoi  <https://orcid.org/0000-0001-5580-7686>
 Ji-Guang Wang  <https://orcid.org/0000-0001-8511-1524>
 Kazuomi Kario  <https://orcid.org/0000-0002-8251-4480>

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