

Modification of Dietary Habits for Prevention of Gout in Japanese People: Gout and Diet

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To cite this article:

Takashi Koguchi. Modification of Dietary Habits for Prevention of Gout in Japanese People: Gout and Diet. *American Journal of Health Research*. Vol. 9, No. 5, 2021, pp. 176-189. doi: 10.11648/j.ajhr.20210905.16

Received: August 1, 2021; **Accepted:** September 1, 2021; **Published:** September 10, 2021

Abstract: The prevalence of gout in Japan has increased markedly since the 1960s. This phenomenon is thought to be attributed to the westernization of the Japanese diet since 1955. The objective of this article is to propose a preventive method for gout through the evaluation of recent dietary habits in Japanese people. In this article, the author suggests what foods should be chosen in proper diet or dietary pattern in Japanese people referencing the results of clinical research reported. Furthermore, this article suggests essentials of behavior for prevention of gout and its comorbidities. Diet and dietary pattern for the prevention of gout in Japanese people (especially adults) are suggested as follows: avoidance of purine-rich diet, uric acid-prone dietary pattern, animal foods dietary pattern, and the Western diet; encourage high fruit and soybean products diet, less protein-rich and more vegetable/fruit-rich materials diet, soybean products and fruit dietary pattern, polyphenol-rich dietary pattern, higher adherence to the Mediterranean diet (the traditional Mediterranean diet) and its dietary pattern, higher adherence to the Dietary Approaches to Stop Hypertension (DASH) diet and its dietary pattern, and vegetarian diet (plant-based diet). Referring to or adopting dietary patterns such as the Mediterranean diet, the DASH diet, and vegetarian diet (plant-based diet), the author wishes to emphasize that Japanese people should eat a diet in which consciously selects foods rich in dietary fiber, vitamin A, vitamin B₁, vitamin B₂, vitamin B₆, calcium, potassium, magnesium, and zinc and decreases intakes of fat (especially animal fat) and salt. Modification of behavior (diet, alcohol, body weight, physical activity, and tobacco) for the prevention of gout and its comorbidities in Japanese adult people is suggested as follows: avoidance of the Western diet and its dietary pattern; encourage higher adherence to the Mediterranean diet (the traditional Mediterranean diet) and its dietary pattern, higher adherence to the DASH diet and its dietary pattern, and vegetarian diet (plant-based diet); limiting alcohol consumption; weight management including proper calorie intake; weight loss for overweight and obese people; adequate physical exercise (e.g., moderate intensity aerobic exercise for 30 minutes on 5-7 days per week, vigorous intensity aerobic physical activity for 75 minutes per week); and smoking cessation. The above behavior for the prevention of gout may also play a helpful role in the prevention of gout and its comorbidities.

Keywords: Comorbidities of Gout, Dietary Habits, Gout, Hyperuricemia, The Mediterranean Diet, The DASH Diet, Uric Acid

1. Introduction

The global burden of gout is substantial and seems to have been increasing in many parts of the world including Japan over the past 50 years [1-4]. A high serum uric acid (SUA) concentration (hyperuricemia) is frequently associated with gout [5]. The Japanese Society of Gout and Uric & Nucleic Acids [6] has stated that hyperuricemia is a risk factor for gout (as uratosi). In the US National Health and Nutrition Examination Survey (NHANES) 2007-2008, the

comorbidities of individuals with hyperuricemia, gout, or both hyperuricemia and gout were hypertension, chronic kidney disease (CKD), obesity (body mass index: BMI ≥ 30 kg/m²), diabetes mellitus, nephrolithiasis, and cardiovascular disease (CVD) (myocardial infarction, heart failure, stroke), though the prevalence of the comorbidities of gout are different from those of hyperuricemia or both hyperuricemia and gout [7]. Considering that gout often coexists with other important diseases, the author wishes to emphasize the importance of dietary habits for decreasing SUA concentrations to prevent

gout. It is also important to maintain SUA concentration within the normal physiological range in order to exert the beneficial effects of the antioxidant properties of uric acid (UA), such as its neuroprotective action [8] and prevention of bone loss and osteoporosis [9].

In the articles in this series reported by Koguchi [10-12], modification of dietary habits for the prevention of gout in Japanese people (especially adults) is suggested as follows: avoidance of excessive intake of saturated fatty acids and cholesterol; replacement of saturated fatty acids with mono- and polyunsaturated ones (especially n-3 polyunsaturated fatty acids); limiting the intake of meat, organ meats high in purine content (e.g., liver, kidney), confectioneries (sugary foods including desserts and sweets), and sugar-sweetened beverages; limiting or decreasing intake of fat (especially animal fat), salt, oils and fats, and seasonings and condiments (soy paste, soy sauce, and sauce); limiting alcohol and

alcoholic beverage consumption; encourage intake of fiber-rich foods (e.g., cereals, whole grains, high-fiber bread), eggs, milk and dairy products (especially low-fat dairy products), legumes, seeds and nuts, fruit, vegetables, and coffee; increase intake of foods rich in dietary fiber, vitamin A, vitamin B₁, vitamin B₂, vitamin B₆, calcium, potassium, magnesium, and zinc; and maintenance of good hydration.

Diets that lower SUA concentration and decrease hyperuricemia risk may have a beneficial effect on the prevention of gout. In this article, the author introduces clinical research reports that reveal association between diet or dietary pattern and SUA concentrations or hyperuricemia risk (Table 1) and suggests what foods should be chosen in proper diet or dietary pattern in Japanese people referencing the results of clinical research reported. Furthermore, this article suggests essentials of behavior for prevention of gout and its comorbidities.

Table 1. Association between food intake with plasma or serum uric acid concentrations, hyperuricemia risk, and gout risk in individuals with or without hyperuricemia or gout in clinical research.

Diet or Dietary Pattern	PUA or SUA	Hyperuricemia risk	Gout risk
High-protein diet	↓ * [13-17]		
Purine-free diet	↓ [20]		
Purine-rich diet	↑ [27-33]		
High fruit and soybean products diet	↓ [44]		
Less protein-rich and more vegetable/fruit-rich materials diet	↓ [45, 46]		
Calorie restricted diet composed of 40% carbohydrate including whole grains, 30% protein, and 30% fat	↓ [47]		
A dietary urate index dietary pattern	↑ [48]		
Uric acid-prone dietary pattern	↑ [49]		
Soybean products and fruit dietary pattern		↓ [50]	
Animal foods dietary pattern		↑ [51]	
The Western diet			↑ [1, 52]
The Western dietary pattern		↔ [50]	
The Mediterranean diet	↓ [83, 110]		
Higher adherence to the Mediterranean diet	↓ [84-86]	↓ [81, 84, 85]	
The DASH diet	↓ [118]		
Higher adherence to the DASH diet			↓ [52]
Vegetarian diet			↓ [133]

* ↑, Increase; ↓, Decrease; ↔, No influence on risk. Abbreviation: The DASH diet, The Dietary Approaches to Stop Hypertension diet; PUA, plasma uric acid; SUA, serum uric acid.

2. Effect of Diet on Plasma or Serum Uric Acid Concentrations

2.1. High-protein Diet

High-protein diet was associated with increased urinary uric acid (UUA) excretion and lowered serum uric acid (SUA) levels [13-17]. High in vegetable protein (specifically, wheat gluten) protein diet (27% of total energy from protein) lowered SUA concentrations in hyperlipidemia in a randomized, crossover trial [18]. Higher intake of total protein was associated with increased gout risk in a prospective study [19].

2.2. Purine-free Diet

An observational study found that a strict purine-free diet reduced serum uric acid (SUA) level by 15-20% [20]. Some of these restrictions can lead to reduction of life quality. Many

researchers [21-24] have announced that traditional low purine diets are generally unpalatable and nutritionally poor, and they are not usually recommended. Fam [21] and Schlesinger [25] have also stated that a rigid purine-free diet can rarely be sustained for a long period of time.

2.3. Purine-rich Diet

Purine-rich foods include animal meat (i.e., beef, pork, lamb, organ meats, and meat extracts), seafood (i.e., fish fillets, tuna, shrimp, lobster, clams, etc.), plants (i.e., yeast extracts, peas, beans, lentils, asparagus, cauliflowers, spinach, mushrooms, bamboo shoots), seaweed (e.g., nori, wakame), seasonings (i.e., soup stock, oyster sauce, consommé, Chinese soup, etc.) [6, 26]. By contrast, dairy products (i.e., milk, cheese, yogurt, ice cream), grains and their products (i.e., bread, pasta, cereals), nuts, fruit, vegetables, sugars and sweets, sugar-sweetened beverages, and alcoholic beverages are low in purine [6, 26]. Eggs and milk contained no purine

[6, 26]. The amounts of purines in distilled liquor (i.e., whiskey, brandy, shochu, awamori) and plum wine do not almost contain (0-0.4 mg/100mL) and those in beer and wine were 3.3-9.8 mg/100mL and 0.4-1.6 mg/100mL, respectively [6, 26]. The Ministry of Health, Labour and Welfare in Japan have not been investigated the daily intake of purines in Japanese people yet.

Purine, such as ribonucleic acid (RNA), adenosine-5'-monophosphate (5'-AMP), guanosine-5'-monophosphate (5'-GMP), inosine-5'-monophosphate (5'-IMP), hypoxanthine, and adenine, increased plasma uric acid (PUA) or serum uric acid (SUA) concentrations [27-33]. Schlesinger [25] stated that the variation in hyperuricemia and gout with different purine-rich foods may be explained by the variation in the amounts and types of purine content and their bioavailability for purine-to-uric acid metabolism. Bowering et al. [29] found that daily administration of 4 g of RNA to healthy subjects doubled the uric acid (UA) pool, increasing serum uric acid (SUA) concentration, and increasing urinary uric acid (UUA) excretion, which cause overproduction-type hyperuricemia. Brulé et al. [34], Yokozawa et al. [35, 36], and Koguchi et al. [37] reported that dietary adenine caused experimental underexcretion-type hyperuricemia through renal dysfunction in rats, which seems to be due to the 2,8-dihydroxyadenine nephrolithiasis. Considering the maximum recommended amount of nucleic acid from the daily diet, long-term excessive intake of adenine-rich foods which is containing 50 mg or more adenine in 100 g of food [e.g., animal liver, legumes (soybeans, peas, lentils, white beans, green beans, red beans, etc.) [6, 26]] can cause elevated SUA levels due to decreased kidney function. It is necessary to limit the amount of one serving of purine-rich foods, especially adenine.

Havlik et al. [38] found that protein-rich vegetable-based meat substitutes are more suitable for dietary considerations in a low-purine diet for subjects with hyperuricemia.

In a case-crossover study, there was a dose-response relationship between increasing purine intake and risk of gout flares and the impact of plant purine on gout attacks was substantially smaller than purine from animal sources in gout patients [39].

The guidelines for the management of gout have stated the following view for purine intake in patients of gout: (1) limit purine intake [40]; (2) avoidance of purine intake [6]; (3) a daily intake of purine should be less than 400mg [6]; (4) recommendation for a purine-low diet [41]; and (5) encourage diets rich in plant foods inclusion of soybeans and vegetable sources of protein, but high-purine foods at the same time avoid [42]. Japanese Urological Association., Japanese Society of Endourology., Japanese Society on Urolithiasis Research [43] has recommended refraining from overdose of purines for patients with urolithiasis.

2.4. High Fruit and Soybean Products Diet

In an open randomized controlled trial, Zhang et al. [44] found that the standard diet (dietary guidelines for hyperuricemia) and high fruit and soybean products diet

decreased serum uric acid (SUA) concentrations in Chinese asymptomatic hyperuricemia adults. They [44] stated that high fruit and soybean products dietary intervention could be an effective alternative to a standard diet for achieving clinically important reductions in SUA concentrations for asymptomatic hyperuricemia adults.

2.5. Less Protein-rich and More Vegetable/Fruit-rich Materials Diet

In a clinical trial, Kanbara et al. [45, 46] reported that the less protein-rich and more vegetable/fruit-rich materials diet significantly decreased serum uric acid (SUA) concentrations and significantly increased urinary uric acid (UUA) excretion and uric acid (UA) clearance, compared with the protein-rich and less vegetable/fruit materials diet. These reports suggest that urine alkalization by eating less protein-rich and more vegetable/fruits-rich materials diet is important and effective for promoting UA excretion [45, 46].

2.6. Calorie Restricted Diet Composed of 40% Carbohydrate Including Whole Grains, 30% Protein, and 30% Fat

In an observational study performed by Dessein et al. [47], thirteen non-diabetic men with gout (median age 50, range 38-62) ingested calorie restricted diet (1,600 kcal a day) composed of 40% carbohydrate [replacement of refined carbohydrates (e.g., white flour, white rice) with complex ones (e.g., whole wheat flour, brown rice)], 30% protein, and 30% fat [replacement of saturated fats (e.g., dairy fats, meat fat) with mono- and polyunsaturated fats (e.g., macadamia nuts, almonds, peanuts and peanut butter, olive oil, canola oil, avocados)] for 16 weeks. The mean serum uric acid (SUA) concentration decreased by 18% in gouty patients after four months of dietary intervention. This was accompanied by a 67% reduction in monthly gouty attack frequency. This pilot study also reduced weight and had beneficial effects on dyslipidemia in gout. Dessein et al. [47] have stated that weight reduction associated with a change in proportional macronutrient intake is beneficial, reducing the SUA levels and dyslipidemia in gout.

3. Effect of Dietary Pattern on Plasma or Serum Uric Acid Concentrations and Hyperuricemia

3.1. A dietary Urate Index Dietary Pattern

In a large prospective cohort study, a dietary urate index was positively associated with serum uric acid (SUA) concentrations in the total population (Whites and African Americans) [48]. A dietary urate index was as follows: (1) added sugars (teaspoons/d or approximately 4.2g/day); (2) alcoholic beverages (drinks/d, with one drink defined as 12 fl oz of beer, 5fl oz of wine or 1.5 fl oz of eighty-proof distilled spirits; 1 g = approximately 0.03 fl oz); (3) ounce equivalents/d of red meats (1oz = 28.3 g); (4) ounce equivalents/d of fish (sum of fish high and low in n-3 fatty

acids); (5) cup equivalents/d of legumes; (6) cup equivalents/d of dairy products (milk, cheese and yogurt); (7) dietary vitamin C from foods in mg/day; and (8) caffeine from all sources (g/day) [48].

3.2. Uric Acid-prone Dietary Pattern

In a cross-sectional study of 266 ethnic Chinese adults in Taiwan, there was a positive association between the “uric acid-prone (composes of meat, seafood, organ meat, eggs and beverages)” dietary pattern and plasma uric acid (PUA) concentrations after adjusted for age, gender and body mass index (BMI) [49].

3.3. Soybean Products and Fruit Dietary Pattern

In a case-control study in Chinese adults, there was a negative association between the “soybean products and fruit (high in soybean products, fruit, vegetables and starchy tubers)” dietary pattern and the risk of asymptomatic hyperuricemia [serum uric acid (SUA) level > 7.0 mg/ dL (416.4 μ mol/L) among men and > 6.0 mg/dL (356.9 μ mol/L) among women], independent of blood lipids [50].

3.4. Animal Foods Dietary Pattern

In a case-control study in Chinese adults, there was a positive association between the “animal products and fried food (high in pork, eggs, animal giblets, poultry and fried wheat products while low in fruit and vegetables)” dietary pattern and the risk of asymptomatic hyperuricemia [serum uric acid (SUA) level > 7.0 mg/ dL (416.4 μ mol/L) among men and > 6.0 mg/dL (356.9 μ mol/L) among women] [50]. In a case-control study, the animal foods dietary pattern characterized by higher intake of an animal organ, seafood and processed meat products was associated with higher prevalence of newly diagnosed hyperuricemia in a Chinese population [51].

4. Effect of Diet and Dietary Pattern on Plasma or Serum Uric Acid Concentrations, Hyperuricemia, and Gout

4.1. The Western Diet

4.1.1. The Western Diet

The Western diet is characterized by high intake of red and processed meats, animal fat, beverages sweetened with sugar, sweets, desserts, French fries, and refined grains contains many foods and low intake of fresh fruit and vegetables and low-fat dairy products [1, 52, 53]. The Western diet was associated with low fiber intake, which is often accompanied by elevated levels of inflammatory biomarkers such as serum C-reactive protein, tumor necrosis factor-alpha (TNF- α), and interleukin-6 (IL-6) [54-56]. The Western diet was associated with increased risk of gout [1, 52] and chronic kidney disease (CKD) [53, 57].

4.1.2. The Western Dietary Pattern

The “Western (high in beef, lamb, cake, and beverages including juice and alcoholic beverages)” dietary pattern was not associated with the risk of asymptomatic hyperuricemia in a case-control study in China [50]. Increased intake of fried foods was associated with increased hyperuricemia risk [58].

The Western dietary pattern was associated with increased risk of rapid estimated glomerular filtration rate (eGFR) decline of ≥ 3 mL/min/1.73m² per year [59], type 2 diabetes mellitus [60] and coronary heart disease (CHD) [61].

4.2. Polyphenol-rich Dietary Pattern

Plant foods contain polyphenols [62]. Polyphenols such as procyanidins from grape seeds [63], quercetin [64-66], myricetin [64, 65], kaempferol [64], puerarin [64], chlorogenic acid [67], apigenin [68], luteolin [66, 68], genistein [65], theaflavin [69], and tea catechins [e.g., catechin, epicatechin, (-)-epigallocatechin, (-)-epicatechin-3-gallate, (-)-epigallocatechin-3-gallate] [70] inhibit xanthine oxidase activity, thus suppressing uric acid (UA) production. In a randomized, double-blinded, placebo-controlled, crossover trial, quercetin significantly reduced plasma uric acid (PUA) concentration (approximately 8%) compared with baseline (before ingestion of quercetin) [71]. The consumption of isoflavones was inversely associated with the presence of hyperuricemia in women [72].

The foods that high in the above polyphenols (> 3.0 mg/100 g FW or > 3.0 mg /100mL) are alcoholic beverages (rose wine, red wine), beverages (apple pure juice, coffee beverage, rowanberry pure juice, chocolate milk, plum pure juice, apple pure juice, fox grape pure juice, pear pure juice), cocoa (chocolates, cocoa powders), herbs (common sage, common thyme, lemon verbenas, Italian oreganos, marjoram, Mexican oreganos, rosemaries), fruit (blackberries, black currants, black elderberries, European cranberries, apricots, grapes, fox grapes, nectarines, peaches, plums, red raspberries, sour cherries, strawberries, sweet cherries, quinces, loquats, apples, pears, custard apples), nuts (almonds, hazelnuts, pecan nuts, pistachio nuts), legumes (common beans, broad bean seeds, soybeans), soy products (soy paste, soy bacon, soy flour, soy meat, soy tempe, soy tofu), spices (capers, caraways, cloves, cumin), vegetables (black olives, broad bean pods, broccoli, globe artichokes), tea infusions (black tea infusion, green tea infusion, oolong tea infusion), herb infusions (peppermint tea) [73]. Dietary polyphenol intake in the US was ~ 1 g/day [74]. The Ministry of Health, Labour and Welfare in Japan have not been investigated the daily intake of polyphenols in Japanese people yet. Since it has reported that excessive intake of some polyphenols resulted in growth depression in animals [75], it must take care of excessive intake of polyphenols.

Dietary polyphenols and polyphenol-rich foods exert antioxidant effect [76] and anti-inflammatory effects [76-78].

A polyphenol-rich dietary pattern, such as the Mediterranean diet, is likely to play a role in its anti-inflammatory effect and downregulation of cellular and circulating inflammatory biomarkers related to atherosclerosis in subjects at high risk of cardiovascular disease (CVD), as

reviewed in detail by Ríos-Hoyo et al. [76], Mena et al. [79], and Medina-Remón et al. [80]. also suggest that high polyphenol intake improves cardiovascular risk factors—mainly systolic and diastolic blood pressure and the lipid profile.

4.3. The Mediterranean Diet

4.3.1. Higher Adherence to the Mediterranean Diet (The Traditional Mediterranean Diet)

The traditional Mediterranean diet is characterized by a high intake of fruit, vegetables, legumes, olive oil, nuts, and whole grain; moderate consumption of wine, dairy products, and poultry; and a low consumption of red meat, sweet beverages, creams, and pastries [81].

Plasma uric acid (PUA) concentration on the consumption of the vegetable-soup “gazpacho” (500 mL/day) for 14 days was significantly lower than that at baseline (before drinking the soup) in healthy men [82].

In an intervention study in patients with hyperuricemia [Mean serum uric acid (SUA) concentration: 9.12 mg/dL (542.46 μ mol/L)] for 6 months, the Mediterranean diet provoked a 20% reduction in serum uric acid (SUA) concentration [Mean SUA concentration 6.92 mg/dL (411.6 μ mol/L)] after the first month and SUA concentrations remained constant for five months [Mean SUA concentration 6.1–6.4 mg/dL (362.8–380.7 μ mol/L)] in patients with hyperuricemia [Mean SUA concentration 9.12 mg/dL (542.5 μ mol/L)] [83].

Higher adherence to the Mediterranean diet was associated with decreased SUA concentrations [84–86] and a lower likelihood of hyperuricemia [84, 85]. In the PREDIMED trial, a greater baseline adherence to the Mediterranean diet was associated with a lower risk of hyperuricemia in elderly Mediterranean participants at high cardiovascular risk [81]. However, the effects of the Mediterranean diet on patients with gout or hyperuricemia have not yet been studied sufficiently. There is a need for more studies in gout to see if the Mediterranean diet may prevent gout or reduce gouty attacks.

The Mediterranean diet has antioxidant [87] and anti-inflammatory properties [88]. Decrease in serum C-reactive protein levels have been also observed in the Mediterranean diet with olive oil [79, 88]. The Mediterranean diet with olive oil reduced plasma C-reactive protein level by 0.54 mg/L compared with a low-fat diet [88]. An energy-unrestricted Mediterranean diet, supplemented with extra-virgin olive oil or nuts, had a lower rate of major cardiovascular events compared to a reduced-fat diet [89]. In an intervention study, eating the Mediterranean diet for 3 months improved rheumatoid arthritis [90].

Higher adherence to the Mediterranean diet was significantly associated with lower levels of lipid biomarkers (LDL-cholesterol and apo B) [86], renal function indicators (creatinine and uric acid) [86], systolic blood pressure [91] and diastolic blood pressure [86, 91], and hepatic function biomarkers (serum γ -glutamyl-transpeptidase and glutamate-pyruvate transaminase) [86].

Greater adherence to the Mediterranean diet was associated with decreased risk of renal function [92], chronic kidney disease (CKD) [93, 94], obesity [95], cardiovascular disease (CVD) [96–100], cancer [76, 101], Parkinson’s disease [101], Alzheimer’s disease [101], dementia and dementia progression [102], noncontrolled asthma [103], and renal-cause mortality [92].

Higher adherence to the alternate Mediterranean diet was significantly associated with decreased risk of type 2 diabetes mellitus [104], all-cause mortality [105], CVD-cause mortality [105], and cancer mortality [105].

In the National Kidney Foundation’s Kidney Disease Outcomes Quality Initiative (KDOQI) clinical practice guideline for nutrition in CKD (CKD stages 1–5D, nondialysis, maintenance hemodialysis, peritoneal dialysis, posttransplantation, transplant) [106], the Mediterranean diet improves lipid profiles in adults with CKD 1–5 not on dialysis or posttransplantation with or without dyslipidemia to CKD. The Mediterranean diet is encouraged for the prevention and/or management of type 2 diabetes mellitus [107, 108].

4.3.2. The Mediterranean Dietary Pattern

The Mediterranean dietary pattern has health benefits. The Mediterranean dietary pattern can be characterized by the following four essential dietary indicators: (1) Monounsaturated to saturated fatty acid ratio (range: 1.6 to 2.0); (2) Intake of dietary fiber (41 to 62 g/person/day); (3) Antioxidant capacity of the whole diet (3500 to 5300 trolox equivalent/person/day); and (4) Phytosterols intake (370 to 555 mg/person/day) [109].

A systematic review reported by Vedder et al. [110] concluded that diet interventions, including low-calorie diet (but not fasting), purine-low diets, and different variations of the Mediterranean diet, were able to decrease serum uric acid (SUA) concentrations in patients with asymptomatic hyperuricemia or gout. The range in SUA change after the above-mentioned interventions (excluding fasting) was + 0.3 to – 2.9 mg/dL [110]. According to the EULAR guideline, this implicates a required decrease of 0.5 to 3.7 mg/dL to achieve target levels [41].

The Mediterranean dietary pattern reduced weight gain [110, 111] and improved lipid profiles [110]. The Mediterranean dietary pattern was associated with decreased risk of overweight or obesity [112], all-cause mortality [113], and cancer-cause mortality [113].

4.4. The Dietary Approaches to Stop Hypertension (DASH) Diet

4.4.1. Higher Adherence to the Dietary Approaches to Stop Hypertension (DASH) Diet

The Dietary Approaches to Stop Hypertension (DASH) diet emphasizes high intake of fruit, vegetables, nuts and legumes, low fat dairy foods, and whole grains; low intake of sodium, sweets including sweetened beverages, red meat, processed meat, saturated fats, and total fats [114–116]. The composition of macronutrient and mineral of the DASH diet are as follows: total fat, 27% of calories; saturated fat, 6% of calories;

cholesterol, 150 mg; protein, 18% of calories; carbohydrate, 55% of calories; fiber, 30 g; sodium, 2,300 mg; potassium, 4,700 mg; calcium, 1,250 mg; magnesium, 500 mg [116, 117].

In a randomized, crossover feeding trial in 103 adults with prehypertension or stage 1 hypertension, the DASH diet reduced serum uric acid (SUA) concentration compared with the control diet (-0.35 mg/dL [95% confidence interval (95%CI) [-0.65, -0.05], $P=0.02$], and this effect was greater among participants with hyperuricemia (-1.29 mg/dL [95%CI -2.50, -0.08]) [118]. In the DASH diet groups, medium sodium intake (a target of 120 mmol/day) and high sodium intake (a target of 180 mmol/day) lowered SUA concentrations compared to low sodium intake (a target of 60 mmol/day), respectively [118]. In case of the DASH diet, 2,300 mg of sodium intake per day in adults with prehypertension or stage 1 hypertension seems to be appropriate.

In a randomized trial of African Americans with controlled hypertension from an urban clinic, partial replacement of diet with DASH foods lowered SUA concentrations compared with higher baseline SUA concentrations (SUA concentration > 8 mg/dL) [119]. Baseline changes in SUA concentrations were inversely associated with changes in systolic blood pressure, diastolic blood pressure, and urine sodium excretion in African Americans with controlled hypertension from an urban clinic [119]. In a randomized-controlled trial, 103 pre-hypertensive or hypertensive adults (SUA concentration \geq 6 mg/dL), for 90 days, the DASH diet lowered SUA concentrations compared to the typical American diet at 90 days [120].

Higher adherence to the DASH diet was associated with decreased risk of gout [52], kidney disease [121], overweight/obesity [116], type 2 diabetes mellitus [103, 116, 122], chronic heart disease [123], coronary heart disease (CHD) [123], stroke [123], kidney stones [124], rapid estimated glomerular filtration rate (eGFR) decline [59], dementia and dementia progression [125], all-cause mortality [105, 125], renal-cause mortality [92], CVD-cause mortality [105, 125], stroke-cause mortality [125], and cancer-cause mortality [105, 125]. Higher adherence to the DASH diet improved renal function by 15% compared to lower adherence [92].

Higher adherence to the DASH diet was inversely associated with waist circumference and diastolic blood pressure [86]. A meta-analysis showed that the DASH diet reduced systolic blood pressure and diastolic blood pressure [126, 127]. In a randomized controlled outpatient feeding trial, the DASH diet has shown a reduction of total, LDL-, and HDL-cholesterol concentrations [128].

The guidelines have encouraged the DASH diet for patients with type 2 diabetes mellitus [107] and hypertension [129]. The National Kidney Foundation-Kidney Disease Outcomes Quality Initiative Guidelines on Hypertension and Antihypertensive Agents in CKD recommended a modified version of the DASH diet (protein intake: 0.6-0.8 g/kg/day; phosphorus intake: 0.8-1.0 g/day; potassium intake: 2-4 g/day) for persons with CKD stages 3 and 4 (eGFR between 15 and 59 mL/min/1.73 m²) [130].

4.4.2. The Dietary Approaches to Stop Hypertension (DASH) Dietary Pattern

The DASH dietary pattern, which is a diet rich in fruit, vegetables, nuts and legumes, low-fat dairy products and whole grains, and with low intake of sodium, sugar-sweetened beverages, and red and processed meats, was associated with a lower risk of gout, suggesting that its effect of lowering serum uric acid (SUA) levels in individuals with hyperuricemia translates to a lower risk of gout [52].

4.5. Vegetarian Diet (Plant-based Diet)

Vegetarians avoid purine-rich meat and seafood, while consuming more vegetables, whole grains, seeds and nuts [131, 132].

In two separate prospective cohort studies from the Tzu Chi population (Taiwanese), a vegetarian diet (vs a nonvegetarian diet) was associated with a lower risk of gout [133]. Taiwanese vegetarians had a lower intake of dairy, eggs, coffee, tea, sugar sweetened beverages, and higher intakes of soybeans, fruit, vegetables, dietary fiber, vitamin C, and avoiding meat and fish, compared with Taiwanese nonvegetarians [133].

Fruit, vegetables, and various herbs consist of many phytochemicals, and other micronutrient compounds that have been shown to inhibit uric acid (UA) synthesis [134], including olive leaf constituents [68], certain Indian medicinal plants [135], DKB114, which is a mixture of *Chrysanthemum Indicum* Linne flower and *Cinnamomum Cassia* (L.) J. Presl Bark extracts [136] inhibit xanthine oxidase activity, thus suppressing uric acid (UA) production. A Chinese herbal decoction (Diclofenac Sodium Enteric-coated Tablets or Meloxicam Tablets) decreased serum uric acid (SUA) levels in gout patients [137]. Phytochemicals, which are found in fruit, vegetables, grains, beans, and other plants, may attenuate the nucleotide-binding and oligomerization domain-like receptor, leucine-rich repeat and pyrin domain-containing 3 (NLRP3) pathway [138, 139]. Since vegetarian diets tend to contain lower saturated fat, higher unsaturated fat and phytochemical-rich plant foods [131, 132], vegetarian diets may prevent inflammatory responses that trigger gout attacks by dampening the activation of nucleotide-binding and oligomerization domain-like receptor, leucine-rich repeat and pyrin domain-containing 3 (NLRP3) inflammasome [138, 140].

The risk of UA crystallization was highest during the ingestion of the self-selected meat diet and the Western-type diet, but the ingestion of the vegetarian diet led to a significant reduction in the risk of UA crystallization by 93% compared to the Western-type diet [141].

Vegetarian diets have been shown to lower blood pressures in a meta-analysis of randomized, controlled trials (systolic blood pressure (SBP): -4.8 mmHg and diastolic blood pressure (DBP): -2.2 mmHg) [142] and in a prospective cohort study (odds ratio: 0.66, 95% CI: 0.50, 0.87) [143]. Vegetarian diets have been shown to reduce gout-associated comorbidities, such as hypertension [142, 143], diabetes mellitus [144, 145], and cardiovascular diseases (CVD) [146].

4.6. The Mediterranean Diet, the Dietary Approaches to Stop Hypertension (DASH) Diet, and Vegetarian Diet (Plant-based Diet)

Both the Mediterranean diet and the DASH diet include a high intake of fruit, vegetables, whole-grain cereals, legumes and nuts, together with a moderate consumption of fish and low-fat dairy products, and low consumption of meat, meat products, and sweets and commercial pastries. Therefore, the Mediterranean diet and the DASH diet would be possible to play a role in the prevention of gout and its comorbidities including various lifestyle-related diseases. In the category of Mediterranean-style diet, the DASH diet is most probably best defined and evidence based regarding cardiovascular risk factors [110]. The DASH diet is a moderate form of a plant-rich diet and is described as being similar to “lacto-ovo vegetarian” diet [147]. The American Diabetes Association (ADA) [107] has encouraged the Mediterranean diet, the DASH diet, and plant-based diet for the management of type 2 diabetes and prediabetes.

5. Essentials of Behavior for Prevention of Gout and Its Comorbidities

5.1. Modification of Behavior Except for Dietary Habits for Patients with Gout and Its Comorbidities in the Guidelines

5.1.1. Weight Management

The guidelines have recommended weight loss for overweight and obese people with gout [5, 6, 40, 41], or hypertension [129, 148-150] or diabetes mellitus [107, 108, 148, 150] or cardiovascular diseases (CVD) [148, 150, 151].

5.1.2. Physical Activity

Physical activity for the management of patients with gout [5, 6, 41], kidney stone (urolithiasis) [152], hypertension [129, 148, 150], and diabetes mellitus [107, 148, 150, 153], and healthy adults for the prevention of cardiovascular diseases (CVD) [148, 150, 151] is recommended in each guideline.

The guidelines have recommended vigorous intensity aerobic physical activity for patients with gout [6], hypertension [149], diabetes mellitus [107], and healthy adults for the prevention of CVD [148, 150] and moderate intensity aerobic exercise for patients with hypertension [129] and healthy adults for the prevention of CVD [148, 150, 151].

5.1.3. Treatment of Tobacco Use

Smoking cessation for the management of gout [5], chronic kidney disease (CKD) [154], hypertension [129], diabetes mellitus [107, 148], and for the prevention of cardiovascular diseases (CVD) [148, 150, 151] is recommended in each guideline.

5.2. Essentials of Behavior for Prevention of Gout and Its Comorbidities

The Western diet was associated with increased risk of gout,

which may explain the increasing prevalence of gout in Western countries [1, 52]. It seems that one of the factors contributing to the increase in the number of gout patients in Japan is due to the westernization of the diet, although gout is associated with environmental factors, such as dietary habits [155], alcohol consumption [155], aging [156], comorbidities [156], select lifestyle factors [156], physical function [157], and physical health-related quality of life [158, 159]. The Japanese Society of Gout and Uric & Nucleic Acids [6] has stated that the increase in gout patients is attributed to changes in environmental factors rather than genetic background: they consider that environmental factors (e.g., purine intake, fructose intake, meat and visceral intake, alcohol consumption, strenuous muscle exercise, stress, obesity) and hyperuricemia is a risk factor for gout (as uratosi) [6]. Prevention of gout may involve behavior for the prevention and suppression of hyperuricemia from viewpoint of lowering SUA levels.

Modification of behavior (diet, alcohol, body weight, physical activity, and tobacco) for the prevention of gout in Japanese adult people is suggested as follows: avoidance of the Western diet and its dietary pattern; encourage higher adherence to the Mediterranean diet (the traditional Mediterranean diet) and its dietary pattern, higher adherence to the Dietary Approaches to Stop Hypertension (DASH) diet and its dietary pattern, and vegetarian diet (plant-based diet); limiting alcohol consumption; weight management including proper calorie intake; weight loss for overweight and obese people; adequate physical exercise (e.g., moderate intensity aerobic exercise for 30 minutes on 5-7 days per week, vigorous intensity aerobic physical activity for 75 minutes per week); and smoking cessation. The above behavior for the prevention of gout with proper choices of foods may also play a helpful role in the prevention of gout and its comorbidities.

6. Conclusion

The number of patients with gout has been increasing steadily in Japan [1-4]. Thus, the objective of this article was to propose a preventive method for gout through the evaluation of recent eating habits in Japan. Modification of dietary habits for the prevention of gout in Japanese people (especially adults) is suggested as follows: avoidance of excessive intake of saturated fatty acids and cholesterol; replacement of saturated fatty acids with mono- and polyunsaturated ones (especially n-3 polyunsaturated fatty acids); limiting the intake of meat, organ meats high in purine content (e.g., liver, kidney), confectioneries (sugary foods including desserts and sweets), and sugar-sweetened beverages; limiting or decreasing intake of fat (especially animal fat), salt, oils and fats, and seasonings and condiments (soy paste, soy sauce, and sauce); limiting alcohol and alcoholic beverage consumption; encourage intake of fiber-rich foods (e.g., cereals, whole grains, high-fiber bread), eggs, milk and dairy products (especially low-fat dairy products), legumes, seeds and nuts, fruit, vegetables, and coffee; increase intake of foods rich in dietary fiber, vitamin A, vitamin B₁, vitamin B₂, vitamin B₆, calcium, potassium,

magnesium, and zinc; avoidance of purine-rich diet, uric acid-prone dietary pattern, animal foods dietary pattern, and the Western diet; encourage high fruit and soybean products diet, less protein-rich and more vegetable/fruit-rich materials diet, soybean products and fruit (high in soybean products, fruit, vegetables and starchy tubers) dietary pattern, polyphenol-rich dietary pattern, higher adherence to the Mediterranean diet (the traditional Mediterranean diet) and its dietary pattern, higher adherence to the Dietary Approaches to Stop Hypertension (DASH) diet and its dietary pattern, and vegetarian diet (plant-based diet); and maintenance of good hydration. From the results of several reports, Roman [156] has stated that weight loss, physical exercise, vitamin C supplementation, soy-containing products, low-fat milk, the DASH diet, and consumption of coffee and cherries have been linked to lowering serum uric acid (SUA) levels and a reduced incidence of acute gout attacks. The above modification of dietary habits for the prevention of gout in Japanese people may also play a helpful role in the prevention of cardiovascular disease (CVD). The American College of Cardiology and the American Heart Association [150], with respect to the prevention of CVD, have encouraged the intake of fruit, vegetables, legumes, nuts, whole grains, and fish, and have proposed minimizing the consumption of trans fats, added sugars (including sugar-sweetened beverages), red meats, sodium, and saturated fats. It is speculated that consuming these foods corresponds to the prevention of gout, but excessive intake of fish should be avoided. To properly choose and consume the following foods that contain the above-mentioned nutrients is important for Japanese people; that is to say, meat (poultry), seafood (salmon, sardines, tuna, trout, mackerel), seeds and nuts (pumpkin seeds, chia seeds, sunflower seeds, almonds, sesame seeds, pistachio nuts, hazelnuts, pecan nuts, walnuts, and pine nuts), grains (white rice, bread), whole grains (brown rice, fortified ready-to-eat cereals, oatmeal), potatoes, mushrooms (maitake mushrooms, shiitake mushrooms), legumes (common beans, kidney beans, soybeans, chickpeas, lentils), seaweed, fruit (apples, apricots, avocados, bananas, blackberries, black currants, black elderberries, cherries, European cranberries, kiwi fruits, oranges, raisins, red raspberries, strawberries), vegetables (black olives, broad bean pods, broccoli, garlic, globe artichokes, spinach, carrots, parsley, tomatoes, peppers, radishes, cucumbers, Chinese cabbages, pickles), soy products (soy milk, tofu, soy meat), dairy products (milk, cheese, yogurt), eggs, spices (capers, caraways, cloves, cumin), oils (olive oil), coffee and tea (black tea, green tea), and chocolates and cocoa powders [160, 161]. Choosing and eating the above foods containing such nutrients and phytochemicals in the Mediterranean diet, the DASH diet, and vegetarian diet (plant-based diet) may also lead to prevent gout and its comorbidities [e.g., chronic kidney disease (CKD) [162], obesity [163], diabetes mellitus [108, 163], and CVD [163] caused by inflammation from elevated SUA concentrations. Referring to or adopting dietary patterns such as the Mediterranean diet, the DASH diet, and vegetarian diet (plant-based diet), the author wishes to emphasize that

Japanese people should eat a diet in which consciously selects foods rich in dietary fiber, vitamin A, vitamin B₁, vitamin B₂, vitamin B₆, calcium, potassium, magnesium, and zinc and decreases intakes of fat (especially animal fat) and salt. Maintaining SUA concentrations within the normal physiological range that leads to the prevention of gout may exert the beneficial effects of the antioxidant properties of uric acid (UA).

Conflict of Interest Statement

The author declares that there are no conflicts of interest.

Acknowledgements

The author thanks Prof. Eiko Ota (Kokugakuin University Tochigi Junior College), Ms. Yuko Itabashi, Ms. Tamae Yanagita, Ms. Nao Uzuka, and Ms. Yumi Kuwabara for furnishing references at Kokugakuin University Tochigi Gakuen Library.

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