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Original Article

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Risk Factors for Hyperuricemia or Gout in Men and Women: The Circulatory Risk in Communities Study (CIRCS)

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Aim: We aimed to examine sex-specific risk factors for hyperuricemia or gout in Japanese cohorts.

Methods: We followed up 3,188 men (mean age, 55.6 years) and 6,346 women (mean age, 54.1 years) without hyperuricemia, gout, or elevated liver enzymes at baseline from 1986 to 1990 for a median of 14.6 years. The participants were considered as having hyperuricemia or gout if their serum uric acid levels were ≥ 7.0 mg/dL or they were receiving treatment for hyperuricemia or gout during annual health checkups. The sex-specific multivariable hazard ratios (HRs) of hyperuricemia or gout incidence were calculated after adjustment for smoking and drinking status, body mass index, hypertension, diabetes, hypercholesterolemia, and hypertriglyceridemia using the Cox proportional-hazard model.

Results: During follow-up, 733 men and 355 women had hyperuricemia or gout. Among men, the multivariable HRs (95% confidence intervals) of hyperuricemia or gout were 1.23 (1.00–1.52) and 1.41 (1.13–1.75) for drinkers of <46 and ≥ 46 g ethanol/day, respectively, compared with non-drinkers; 1.00 (0.81–1.24) and 1.18 (0.93–1.50) for smokers of 1–19 and ≥ 20 cigarettes/day, respectively, compared with never smokers; and 1.41 (1.20–1.65) for hypertensive compared with non-hypertensive participants. The HRs for women were 1.02 (0.70–1.48), 1.66 (1.05–2.63), and 1.12 (0.88–1.42) for current drinkers, current smokers, and hypertensive participants, respectively. For both men and women, body mass index, diabetes, hypercholesterolemia, and hypertriglyceridemia were not associated with hyperuricemia or gout incidence.

Conclusions: Hypertension and alcohol drinking are risk factors for hyperuricemia or gout among men and smoking among women.

Key words: Uric acid, Risk factor, Cohort study, Epidemiology

Introduction

Uric acid is a purine metabolite, and high uric acid levels not only cause hyperuricemia or gout but were also associated with all-cause mortality[1)] and ischemic stroke incidence[2)] in both men and women as well as with cardiovascular mortality[1)] and stroke incidence in women[3)]. High serum uric acid levels

have also been associated with the incidence of hypertension[4], type 2 diabetes[5], metabolic syndrome[6], chronic kidney disease[7], and prevalence of impaired endothelial function[8], arterial stiffness and atherosclerosis in women[9].

Hyperuricemia or gout is more common in men[10], but in postmenopausal women, uric acid metabolism declines due to decreasing estrogen associated with menopause[11]. Recently, we reported that uric acid levels significantly increase during the menopausal period[12]. A typical risk factor for increasing uric acid levels is alcohol consumption[13]; however, studies investigating the risk factors for hyperuricemia or gout have often focused on men. The Health Professionals Follow-Up Study and cohort studies in Korea and Japan have reported that hypertension (≥ 140/90 mmHg)[14], being overweight (body mass index (BMI) ≥ 25 kg/m^2)[14, 15] or an increment of BMI of 2.64 kg/m^2 [16], and alcohol intake (≥ 15-g ethanol/day)[13] or increased intake of ≥ 25.3-g ethanol/day[16] were risk factors for hyperuricemia or gout in men. The risk factors for gout in women have been investigated in the Framingham Heart Study and a Taiwanese cohort study[17, 18]. The Framingham Heart Study demonstrated that obesity (BMI ≥ 30 kg/m^2), heavy drinking (≥ 28-g ethanol/day), and hypertension (≥ 140/90 mmHg or taking antihypertensive medication) were risk factors for gout in both men and women[17]. In a Taiwanese cohort study, BMI (≥ 24.0 kg/m^2), hypertriglyceridemia (>150 mg/dL for fasting), renal insufficiency (glomerular filtration rate < 60 mL/min/1.73 m^2), and high waist circumference (>90 and >80 cm for men and women, respectively) were risk factors for gout in both men and women and hypertension (≥ 135/85 mmHg) in men[18]. It is unclear whether such associations are similar in Japan, where the prevalence of gout is as low as 1.9% in men and <0.1% in women (based on beneficially of health insurance)[10], compared with 5.2% in men and 2.7% in women in the United States[19], 11.3% in men and 2.4% in women in Australia[18], and 8.2% in men and 2.3% in women in Taiwan[20].

Aim

In this study, we aimed to examine sex-specific risk factors for hyperuricemia or gout in a study of Japanese cohorts.

Methods

Study Population

The Circulatory Risk in Communities Study (CIRCS) is an ongoing dynamic community-based prospective study involving five Japanese communities. Details of the CIRCS protocol have been described elsewhere[21]. The participants were from the following four communities: Ikawa (Akita Prefecture), a farming community in northeastern Japan; Kyowa district in Chikusei City (Ibaraki Prefecture), a farming community in mid-eastern Japan; Minami-Takayasu, a district in Yao City (Osaka Prefecture), a suburb near Osaka City in mid-western Japan; and Noichi, a district in Konan City (Kochi Prefecture), a western rural community in Japan. The participants consisted of 4,831 men and 7,534 women aged 30–89 years who participated in baseline health checkups that included testing for serum uric acid between 1986 and 1990. We excluded participants found to have serum uric acid levels of 7.0 mg/dL or higher, or past or present history or treatment of hyperuricemia or gout based on the face-to-face interview, at baseline health checkups (708 men and 147 women). Those with aspartate aminotransferase (AST) and/or alanine aminotransferase (ALT) greater than 61 IU/L were excluded from the baseline survey as they likely had non-alcoholic fatty liver disease or non-alcoholic steatohepatitis and were at a higher risk of all-cause mortality (n=586)[22]. We further excluded those who did not participate in the annual health checkups after baseline (583 men and 807 women). Finally, 3,188 men and 6,346 women were included in this study **(Fig. 1)**.

Incidence of Hyperuricemia or Gout

During the follow-up period, annual health checkups were conducted at healthcare centers in the four communities. The participants were followed up to determine the first incidence of hyperuricemia or gout in the annual health checkups by the end of 2005 in Noichi, 2007 in Kyowa, and 2019 in Minami-Takayasu and Ikawa. For all participants at both baseline and follow-up, blood samples were collected while the participants were sitting, stored in silicone-filled glass tubes, and centrifuged. After 1990, the blood samples were collected in plastic serum separator gel tubes. The method and measurement instrument for serum uric acid levels were changed

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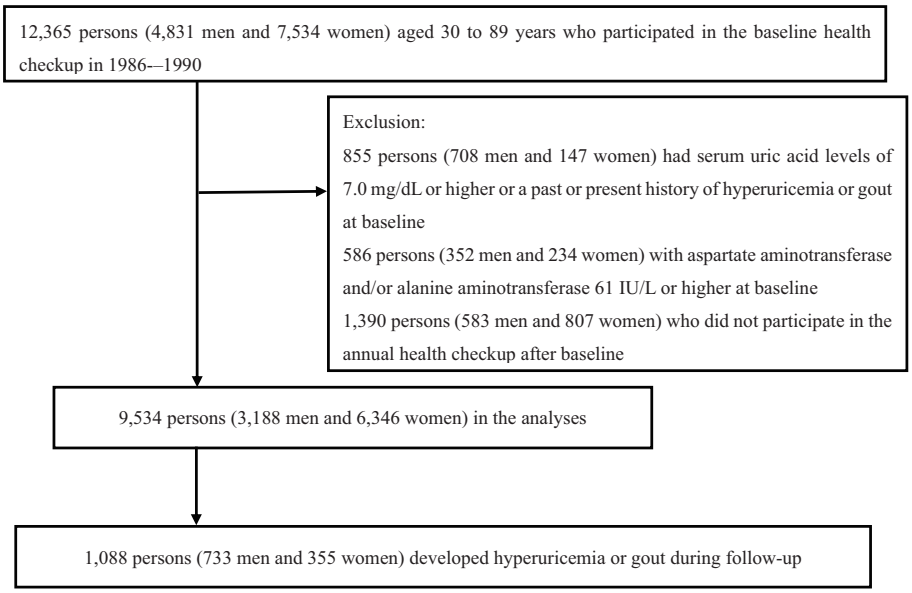

Fig. 1. Flow chart for the selection of the study participants

three times. Serum uric acid was first measured with the phosphotungstic acid method using an SMA-6/60 automatic analyzer (Technicon, Tarrytown, NY, USA) until September 1986, then the uricase method using a SMAC automatic analyzer (Technicon) until July 1993, the same uricase method using Autoanalyzer 7250 (Hitachi, Tokyo, Japan) until July 2001, and finally the uricase–peroxidase method using Autoanalyzer AU2700 (Olympus Corp., Tokyo, Japan).

Onset of hyperuricemia or gout were indicated by the use of treatment for hyperuricemia or gout in the face-to-face interviews and/or serum uric acid levels of 7.0 mg/dL or higher[23] in health checkups during follow-up. The definition of hyperuricemia in this study was similar to that in the previous one[24].

Measurements

Several risk factors were measured at baseline (1986–1990). A well-trained physician or nurses placed a standard mercury sphygmomanometer on the right arm of the seated participants after at least 5 min of rest to measure arterial systolic and phase 5 diastolic blood pressure. If the initial systolic blood pressure was ≥ 140 mmHg or the diastolic blood pressure was ≥ 90 mmHg, the physician repeated the measurement. In that case, the second measurement was used for analysis; otherwise, the first measurement was used. BMI was calculated as weight (kg) divided by the square of height (m^2). Serum total cholesterol was measured with the Liebermann–Burchard direct method using SMA-6/60 before September 1986 and an enzymatic method using the SMAC thereafter. Serum glucose was measured with the cupric–neocuproine method using SMA-6/60 before September 1986 and the hexokinase method using the SMAC thereafter. The values of serum glucose (mg/dL) measured using the cupric–neocuproine method were adjusted using a linear regression formula: serum glucose concentration (mg/dL) × 0.8546 + 9.7531. These measurements were performed at the Osaka Medical Center for Cancer and Cardiovascular Disease, an international member of the National Cholesterol Reference Method Laboratory Network in the United States[25], and Ibaraki Health Service Association. AST and ALT were measured with the Henry's method using SMA-6/60 before September 1986 and then the Tris buffer method using the SMAC thereafter. We calculated the estimated glomerular filtration rate (eGFR, mL/min/1.73 m^2) as follows: = 194 × (serum creatinine, mg/dL) − 1.094 × (age, year) − 0.287 (× 0.739 for women)[26]. Menopause was defined as menstruation not occurring for 6 months or more. Face-to-face interviews were conducted to determine the smoking status (never, former, current), number of cigarettes smoked per day, drinking status (never, former, current), usual weekly intake of alcohol evaluated by units of "go" (a traditional Japanese unit of volume corresponding to 23-g ethanol/day), menopause (yes, no), and consumption of antihypertensive, cholesterol-lowering, and antidiabetic medications.

Hypertension was defined as systolic blood pressure ≥ 140 mmHg and/or diastolic blood pressure

≥ 90 mmHg or use of antihypertensive medication. Non-fasting blood collection was defined as collection of blood <8 h after meal and fasting blood collection as ≥ 8 h after meal. Diabetes mellitus was defined as fasting blood glucose of ≥ 126 mg/dL, non-fasting blood glucose of ≥ 200 mg/dL, or antidiabetic medication use. Hypercholesterolemia was defined as serum total cholesterol of ≥ 220 mg/dL or use of cholesterol-lowering medication. Hypertriglyceridemia was defined as triglyceride level of ≥ 150 mg/dL for fasting or ≥ 175 mg/dL for non-fasting status.

Statistical Analysis

The age-adjusted sex-specific characteristics of participants who did or did not develop hyperuricemia or gout were compared using analysis of covariance and logistic regression models. The hazard ratios (HRs) and 95% confidence intervals (CIs) for the risk factors for hyperuricemia or gout were calculated using Cox proportional-hazard models: age-adjusted HRs, age- and uric acid-adjusted HRs, and multivariable HRs. The multivariable HRs were further adjusted for smoking status (never smoked, former smoker, current smoker of 1–19 or ≥ 20 cigarettes/day), drinking status (never drank, former drinker, current drinker of <46- or ≥ 46-g ethanol/day), BMI, eGFR, hypertension (yes or no), diabetes (yes or no), hypercholesterolemia (yes or no), hypertriglyceridemia (yes or no), and menopause (women only, yes or no) at baseline. We adjusted for uric acid levels at baseline because individuals with uric acid levels close to 7.0 mg/dL were at a higher risk of developing hyperuricemia or gout than those with lower uric acid levels. Because few women had a smoking status of ≥ 20 cigarettes/day or a drinking status of ≥ 46-g ethanol/day, the smoking status among women was classified into never, former, and current and the drinking status into never, former, and current. We used SAS version 9.4 (SAS Institute, Cary, NC, USA) for all analyses, and the statistical significance level was set to <0.05.

Ethical Considerations

Individual consent was not required for the analysis of this study as it was done as a secondary use of data obtained for public health practice on cardiovascular disease prevention in the local community at that time. In compliance with the relevant guidelines and regulations, information about the research and the use of data was publicly disclosed, and the participants were given the opportunity to decline the analysis of their data. The study was approved by the institutional review boards of Osaka Center for Cancer and Cardiovascular Disease Prevention, Osaka University, and the University of Tsukuba.

Results

During a median follow-up of 14.6 years, 733 men and 355 women developed hyperuricemia, of whom 10 men and 8 women started treatment for gout. The incidence rate was 17.7 per 1,000 person-years in men and 3.6 per 1,000 person-years in women. The mean ages at baseline were 55.6 and 54.1 years for men and women, respectively. The sex-specific baseline characteristics of the participants who did or did not develop hyperuricemia or gout are presented in **Table 1**. For both men and women, those with hyperuricemia or gout had higher BMI, blood pressure, and serum total cholesterol levels, lower eGFR, and a higher proportion of hypertension, hypercholesterolemia, hypertriglyceridemia, and antihypertensive medications. Men with hyperuricemia or gout were more likely to be current drinkers.

The sex-specific HRs and 95% CIs of hyperuricemia or gout according to potential risk factors are presented in **Table 2**. In the age-adjusted model, high BMI (≥ 25 kg/m^2), hypertension, hypercholesterolemia, hypertriglyceridemia (men and women), and current drinking status (men only) were associated with the risk of hyperuricemia or gout. Generally, further adjustment for baseline uric acid levels attenuated these associations, but the associations with hypertension, current drinking status (men) and smoking ≥ 20 cigarettes/day (men) and current smoking status (women) remained statistically significant. The adjustment for other confounders further attenuated these associations. For men, the multivariable HRs (95% CIs) of hyperuricemia or gout were 1.23 (1.00–1.52) and 1.41 (1.13–1.75) for drinkers of <46- and ≥ 46-g ethanol/day, respectively, compared with non-drinkers and 1.41 (1.20–1.65) for hypertensive compared with non-hypertensive participants. For women, the multivariable-adjusted HR (95% CIs) of hyperuricemia or gout was 1.66 (1.05–2.63) for current smokers compared with never smokers.

Discussion

This long-term community-based prospective study found that hypertension and current drinking status in men and current smoking status in women were associated with the incidence of hyperuricemia or gout. To the best of our knowledge, this study is one of the few studies in Asia[10, 20], where the prevalence and incidence of gout were lower than

Table 1. Sex-specific baseline characteristics of participants who did or did not develop hyperuricemia or gout

	Hyperuricemia or gout cases Mean (SD) or proportion	Noncases Mean (SD) or proportion	*P* value
Men, *n*	733	2455	
Age, years	53.1 (11.2)	56.3 (11.2)	<0.001
Current drinking, %	77.6	69.0	<0.001
Current smorking, %	55.7	56.8	0.17
Uric acid, mg/dL	6.0 (0.7)	5.1 (0.9)	<0.001
Body mass index, kg/m^2	23.3 (2.7)	22.6 (2.7)	<0.001
Systolic blood pressure, mmHg	134.2 (17.1)	131.6 (18.0)	<0.001
Distolic blood pressure, mmHg	82.6 (11.1)	80.0 (10.9)	<0.001
Antihypertensive medication, %	15.8	13.2	<0.001
Hypertension, %	43.8	36.1	<0.001
Diabetes, %	8.3	9.3	0.70
Serum total cholesterol, mg/dL	191.1 (33.2)	186.8 (31.6)	0.004
Cholesterol-lowering medication, %	0.3	0.3	0.81
Hypercholesterolemia, %	18.6	15.2	0.036
Hypertriglyceridemia, %	31.8	21.2	<0.001
eGFR, mL/min/1.73m^2	87.5 (20.1)	89.2 (20.0)	<0.001
Women, *n*	355	5991	
Age, years	54.5 (10.1)	54.0 (11.4)	0.40
Current drinking, %	9.3	9.0	0.74
Current smorking, %	5.9	5.2	0.52
Uric acid, mg/dL	5.2 (0.9)	4.2 (0.9)	<0.001
Body mass index, kg/m^2	24.2 (3.0)	23.1 (3.2)	<0.001
Systolic blood pressure, mmHg	133.5 (19.8)	130.0 (17.8)	<0.001
Distolic blood pressure, mmHg	79.7 (12.3)	77.6 (10.6)	<0.001
Antihypertensive medication, %	23.9	14.3	<0.001
Hypertension, %	40.8	33.2	<0.001
Diabetes, %	8.5	6.1	0.38
Serum total cholesterol, mg/dL	208.0 (38.9)	200.0 (34.9)	<0.001
Cholesterol-lowering medication, %	2.3	1.2	0.09
Hypercholesterolemia, %	35.2	27.0	0.001
Hypertriglyceridemia, %	23.9	16.7	<0.001
eGFR, mL/min/1.73m^2	82.2 (24.3)	92.6 (25.3)	<0.001
Menopause, %	66.8	62.3	0.59

Abbreviations: SD, standard deviation

those in the United States, Australia, and Europe[19, 27], that have prospectively investigated the risk factors for hyperuricemia or gout in women.

Hypertension decreases renal blood flow due to increased renal and systemic vascular resistance[28]. Tissue ischemia due to hypertension promotes uric acid reabsorption in the proximal tubules of the kidney and decreases uric acid excretion[29, 30]. The present study showed the association between hypertension and the incidence of hyperuricemia or gout in men, which was significantly consistent with the results of previous cohort studies. In the Health Professionals Follow-Up Study in the United States, 47,150 men were followed up for 12 years, and 730 of them developed gout. Men with hypertension had a higher risk of gout (HR=2.31 [1.96–2.72]) than those without hypertension[15]. In a cohort study of Korean male workers, 2,496 developed hyperuricemia over a follow-up period of 5.4 years, and the risk was higher in those with a blood pressure of 140/90 mmHg or higher or those taking hypertensive medication (HR=1.24 [1.10–1.39]) than in those with a blood pressure of 120/80 mmHg[14]. The Framingham Heart Study also reported that a blood pressure of ≥ 140/90 mmHg, indicating hypertension, was associated with the risk of gout in both men (HR=1.59 [1.12–2.24]) and women (HR=1.82 [1.06–3.14]) compared with a blood pressure of less than 140/90 mmHg[17]. A

Table 2. Sex-specific hazard ratios (95% CI) of incident hyperuricemia or gout according to potential risk factors

	Men					
	Person -years	Nunber of events, *n*	Incidence rate (per 1000 person- years)	Age-adjusted HR (95%Cl)	Age and uric acid adjusted HR (95%Cl)	Multivariable HR (95%Cl)[1]
Drinking status[2]						
Never	9029	131	14.5	Reference	Reference	Reference
Former	2012	33	16.4	1.16 (0.79, 1.70)	1.16 (0.79, 1.70)	1.18 (0.80, 1.74)
<46g ethanol/day	16768	303	18.1	1.28 (1.04, 1.58)	1.22 (0.99, 1.50)	1.23 (1.00, 1.52)
≥ 46g ethanol/day	13394	264	19.7	1.56 (1.25, 1.93)	1.44 (1.16, 1.78)	1.41 (1.13, 1.75)
Smoking status[2]						
Never	8242	146	17.7	Reference	Reference	Reference
Former	9582	178	18.6	0.98 (0.78, 1.22)	0.91 (0.73, 1.14)	0.89 (0.71, 1.11)
1-19 cigarettes/day	15432	256	16.6	0.94 (0.77, 1.16)	1.05 (0.86, 1.29)	1.00 (0.81, 1.24)
≥ 20 cigarettes/day	8024	152	18.9	1.14 (0.91, 1.44)	1.26 (1.00, 1.59)	1.18 (0.93, 1.50)
Body mass index, kg/m^2						
<18.5	1535	21	13.7	0.75 (0.48, 1.16)	0.94 (0.61, 1.46)	0.99 (0.63, 1.53)
18.5-24.9	31279	530	16.9	Reference	Reference	Reference
≥ 25	8533	182	21.3	1.29 (1.09, 1.53)	0.93 (0.78, 1.10)	0.86 (0.72, 1.04)
Hypertension, %						
No	28387	412	14.5	Reference	Reference	Reference
Yes	12960	321	24.8	1.85 (1.58, 2.15)	1.43 (1.23, 1.67)	1.41 (1.20, 1.65)
Diabetes						
No	38660	680	17.6	Reference	Reference	Reference
Yes	2657	52	19.6	1.14 (0.85, 1.51)	1.13 (0.85, 1.50)	1.03 (0.76, 1.38)
Hypercholesterolemia, %						
No	34995	597	17.1	Reference	Reference	Reference
Yes	6352	136	21.4	1.21 (1.00, 1.46)	0.91 (0.76, 1.10)	0.92 (0.76, 1.12)
Hypertriglyceridemia, %						
No	28836	424	14.7	Reference	Reference	Reference
Yes	9443	233	24.7	1.70 (1.44, 1.99)	1.13 (0.96, 1.33)	1.13 (0.95, 1.34)
	Women					
	Person -years	Nunber of events, *n*	Incidence rate (per 1000 person- years)	Age-adjusted HR (95%Cl)	Age and uric acid adjusted HR (95%Cl)	Multivariable HR (95%Cl)[1]
Drinking status[2]						
Never	87911	319	3.6	Reference	Reference	Reference
Former	924	3	3.2	-	-	-
<46g ethanol/day	8751	33	3.8	1.15 (0.80, 1.66)	1.09 (0.76, 1.57)	1.02 (0.70, 1.48)
≥ 46g ethanol/day						
Smoking status[2]						
Never	92060	328	3.6	Reference	Reference	Reference
Former	1168	6	5.1	1.37 (0.61, 3.08)	0.87 (0.39, 1.97)	0.86 (0.38, 1.95)
1-19 cigarettes/day	4378	21	4.8	1.52 (0.97, 2.38)	1.68 (1.07, 2.63)	1.66 (1.05, 2.63)
≥ 20 cigarettes/day						
Body mass index, kg/m^2						
<18.5	4722	7	1.5	0.49 (0.23, 1.03)	0.72 (0.34, 1.52)	0.70 (0.33, 1.49)
18.5-24.9	70571	216	3.1	Reference	Reference	Reference
≥ 25	22312	131	5.9	1.97 (1.58, 2.46)	1.21 (0.97, 1.52)	1.18 (0.94, 1.49)
Hypertension, %						
No	72902	210	2.9	Reference	Reference	Reference
Yes	24731	145	5.9	1.76 (1.40, 2.21)	1.16 (0.92, 1.46)	1.12 (0.88, 1.42)
Diabetes						
No	94770	341	3.6	Reference	Reference	Reference
Yes	2784	12	4.3	1.03 (0.57, 1.83)	0.80 (0.45, 1.44)	0.77 (0.43, 1.35)
Hypercholesterolemia, %						
No	73811	230	3.1	Reference	Reference	Reference
Yes	23885	125	5.2	1.41 (1.13, 1.77)	1.11 (0.88, 1.38)	1.07 (0.85, 1.39)
Hypertriglyceridemia, %						
No	67251	195	2.9	Reference	Reference	Reference
Yes	14070	85	6.0	1.78 (1.38, 2.31)	1.17 (0.90, 1.52)	1.14 (0.85, 1.46)

Abbreviations: HR, hazard ratios CI, confidence intervals

1) Multivariable analysis adjusted further for drinking status, smoking status, body mass index, eGFR, hypertension, diabetes, hypercholesterolemia, hypertrigliceridemia, and menopause (women only) at baseline.

2) Because few women had a smoking status of ≥ 20 cigarettes/day or drinking status ≥ 46g ethanol/day, smoking and drinking status among women were classfied into never, former, and current.

Taiwanese study demonstrated that high blood pressure (>130/85 mmHg) was associated with a 19% higher risk of gout in men but not in women[18]. It should be noted that these previous studies did not adjust for baseline uric acid levels.

Insulin resistance and high insulin concentrations due to increased BMI have been reported to be associated with decreased uric acid clearance and renal excretion[31]. A cross-sectional study investigated the relationship between visceral fat measured *via* abdominal computed tomography and uric acid excretion. That study demonstrated that visceral fat in men was positively correlated with uric acid levels[32] and inversely with uric acid clearance[33]. However, the present study found no association between BMI and risk of hyperuricemia or gout in either men or women after adjustment for baseline uric acid levels. The association between high BMI and hyperuricemia or gout was observed in previous studies[14-18], but such studies did not adjust for uric acid levels at baseline. A study that investigated risk factors for hyperuricemia in Japanese working men followed up for 8 years reported that a 2.64-kg/m^2 increase in BMI even after adjustment for baseline uric acid levels was associated with a 19% higher risk of hyperuricemia[16].

Regarding alcohol consumption, the results of the present study in men were similar to those of the previous ones[13, 14, 16, 17, 34]. In the Framingham study, heavy drinking of ≥ 7 ounces per week (≥ 28-g ethanol/day) was found to be positively associated with gout incidence compared with abstinence or light drinking of 0–1 ounce per week (0–4-g ethanol/day)[17]. However, no such association was observed among women in the present study. A small amount of alcohol consumed in women in our study, approximately 12-g ethanol/day, may have obscured the association. Alcohol consumption increases urinary oxypurine, a precursor of uric acid[35]. Another mechanism may be that an increase in blood lactate concentration due to ethanol intake promotes uric acid reabsorption in the proximal tubules *via* urate transporter 1, resulting in decreased uric acid excretion[36].

The association between current smoking status and risk of hyperuricemia or gout was observed only in women. Previous studies have shown inconsistent results regarding the association between smoking and the risk of hyperuricemia or gout. In cohort studies among Korean[14] and Japanese[16] men, there was no association between current smoking status at baseline and the risk of hyperuricemia or gout. On the other hand, in the Singapore Chinese Health Study, which investigated the association between smoking and risk of gout, the risk was lower among current smokers (HR=0.77 [0.64–0.91]) compared with never smokers in men, but no association was observed in women[37].

This study was a long-term, community-based, prospective study, and to the best of our knowledge, there have been no prospective studies investigating the risk factors for hyperuricemia or gout in Japanese women. Another strength was the evaluation of risk factors adjusted for baseline uric acid levels, which has not been performed in previous studies. Several limitations need to be considered when interpreting the results. First, there was no information on dietary habits. Dietary habits that have been reported to cause hyperuricemia or gout include excessive consumption of foods such as red meat, seafood, and fructose[38, 39]. Second, information on the specific type of drug, including diuretics, was lacking. The Framingham study demonstrated that diuretic use was positively associated with the development of gout in both men and women (HR=2.39 [1.53–3.74] in women, HR=3.41 [2.38–4.89] in men)[16]. Although calcium channel blocker was commonly prescribed for hypertension in Japan at the baseline of the 1980s[40], it was possible that diuretics may have impacted the association between hypertension and hyperuricemia or gout. Third, we used information on the treatment for hyperuricemia or gout obtained from the face-to-face interview. However, its validity was not investigated.

Conclusion

Hypertension and alcohol drinking were associated with the risk of hyperuricemia or gout among men and smoking among women.

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Conflict of Interest

The authors have no conflicts of interest to declare for this study.

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