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ORIGINAL ARTICLE

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Association between serum uric acid levels and achievement of target blood pressure among Japanese community residents with hypertension

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Abstract

The authors examined the sex-specific association between serum uric acid (SUA) levels and achievement of target blood pressure among Japanese patients with hypertension. This cross-sectional study was conducted between January 2012 and December 2015 and examined 17 113 eligible participants (6499 men; 10 614 women) with hypertension among 66 874 Japanese community residents who underwent voluntary health checkups. Multivariate analysis was used to estimate the association between high SUA level (≥7.0 mg/dL for men and ≥6.0 mg/dL for women) and "therapeutic failure" in achieving target blood pressure (BP) of 140/90 and 130/80 mmHg in both sexes. Multivariate analysis revealed that high SUA level was significantly associated with failure to achieve the 130/80 mmHg treatment goal among men (AOR = 1.24, 95% CI = 1.03–1.50, $p = .03$). Among women, high SUA level was significantly associated with failure to achieve both the 130/80 and 140/90 mmHg treatment goals (AOR = 1.33, 95% CI = 1.20–1.47, $p < .01$ and AOR = 1.17, 95% CI = 1.04–1.32, $p < .01$, respectively). Each increase in SUA quartile was positively associated with increases in systolic BP (SBP) and diastolic BP (DBP) ($p < .01$ for trend) in both sexes. SBP and DBP in each quartile (Q2–Q4) were also significantly higher compared with those of Q1 in both sexes ($p < .01$). Our data confirms the difficulties in maintain goal BP control in those with elevated SUA.

KEYWORDS
achievement rate, epidemiology, hypertension, prevention, uric acid

1 | INTRODUCTION

Hypertension is a well-recognized global health problem associated with adverse cardiovascular outcomes and represents a leading risk factor for mortality.[1–3] An analysis involving 154 countries and 8.69 million participants estimated that between 1990 and 2015, the rate of individuals with systolic blood pressure (SBP) of ≥140 mmHg increased from 17 307 to 20 526 per 100 000 persons.[4] The estimated rate of annual deaths associated with SBP ≥140 mmHg increased from 97.9 (95% UI, 87.5–108.1) to 106.3 (95% UI, 94.6–118.1).[4] Related with the increasing individuals of SBP ≥140 mmHg, loss of disability-adjusted life-years (DALYs) increased from 95.9 million (95% UI, 87.0–104.9 million) to 143.0 million (95% UI, 130.2–157.0 million).[4]

Hyperuricemia is also recognized as an important risk factor for cardiovascular disease, renal dysfunction, and gout.[5–7] In recent years, an association between elevated serum uric acid (SUA) and hypertension has also received widespread attention.[8–10] Hyperuricemia is suggested to play a role in the development of hypertension, and a causal relationship between the two has been suggested.[8] Previous studies have also reported an association between elevated SUA and cardiovascular events in patients with hypertension.[5] Potential mechanisms by which uric acid might elevate blood pressure (BP) include a reduction in nitric oxide, activation of the renin-angiotensin system, vascular smooth muscle proliferation, oxidative stress, and endothelial inflammation.[11–12] However, only a few studies have examined the impact of SUA level on the achievement of target BP among patients with hypertension. The aim of this study therefore was to determine the association between SUA level and BP among Japanese community residents with hypertension.

2 | SUBJECTS AND METHODS

The Tohoku Medical Megabank (TMM) was administered by the Tohoku Medical Megabank Organization (ToMMo), established at Tohoku University in Miyagi Prefecture, and by the Iwate Tohoku Medical Megabank Organization, established at Iwate Medical University in Iwate Prefecture, to restore medical services and the health of residents after the Great East Japan Earthquake, which spawned a devastating tsunami that damaged vast areas of the northeastern coast of Japan on March 11, 2011.[13–15] Details regarding the TMM Project were reported previously.[15]

This was a cross-sectional study that screened 66 874 Japanese community residents who underwent a voluntary health checkup conducted by the ToMMo between January 2012 and December 2015 in Miyagi and Iwate Prefectures, Japan. Among participants, 54.070 reported a confirmed medical history of hypertension according to a self-administered questionnaire. A total of 17 115 study participants were receiving treatment for hypertension, and two participants were excluded due to missing SUA concentration data. Thus, a total of 17 113 eligible participants were included in the present study (6499 men; 10 614 women).

2.1 | Variables

Height, weight, body mass index (BMI), and waist circumference (WC) were measured with participants in the standing position. BMI was calculated by dividing body weight (kg) by height in meters squared (m2). SBP and diastolic BP (DBP) were measured at the upper arm in participants who had been seated for at least 5 min. BPs were measure once or twice. First measurements were used in the analysis. Serum levels of total cholesterol (mg/dL; TC: Ultra. Violet-End [UV-End] method using cholesterol dehydrogenase), high-density-lipoprotein cholesterol (mg/dL; HDL-C: Direct method), and triglycerides (mg/dL; TGs: Enzymatic method) were also measured. LDL-C was estimated using the Friedewald equation ([TC]—[HDL-C]—[TGs/5]).[16] SUA levels were also measured using an enzymatic method (Uricase-POD). Hemoglobin A1c (HbA1c) levels were determined by latex agglutination turbidimetry. The estimated glomerular filtration rate (eGFR) was calculated using the Japanese GFR equation: eGFR (mL/min/1.73 m2) = $194 \times Cr^{-1.094} \times age^{-0.287}$ (×0.739 if female).[17] Chronic kidney disease (CKD) was diagnosed as eGFR <60 mL/min/1.73 m2 based on the Japanese guideline.

Participants were asked to complete a self-administered questionnaire that addressed healthy lifestyle characteristics (alcohol consumption, smoking behavior) and present medical history of comorbidities such as hypertension, diabetes mellitus, dyslipidemia, hyperuricemia, cardiovascular disease, cerebrovascular disease, and renal disease. Participants who answered that they had any of these comorbidities were registered as having a present medical history.

2.2 | Statistical analysis

Results are presented as mean ± standard deviation (SD) for continuous variables or prevalence (%) for categorical variables.

The primary outcome was "therapeutic failure," defined as not achieving the target BP for 140/90 and 130/80 mmHg, as the Japanese hypertension treatment guideline was revised in 2019, with target BP revised from 140/90 to 130/80 mmHg in some cases. Thus, rates of achieving both 140/90 and 130/80 mmHg were estimated in the present study.[18]

High SAU was defined as SUA ≥7.0 mg/dL for men and SUA ≥6.0 mg/dL for women, according to a previous report.[19] To estimate the association between SUA level and therapeutic failure, multivariate logistic regression analysis was performed using the following models: Model 1 was adjusted for age (years). Model 2 was adjusted for age (years), BMI (kg/m2), alcohol consumption (usual drinker), smoking behavior (current smoker), medical history of diabetes mellitus (yes), medical history of dyslipidemia (yes), and CKD (present). These cofounders, especially BMI, were chosen referring to previous reports.[9,20,21] The odds ratio (OR) and 95% confidence interval (CI) were calculated for each factor via multivariate logistic regression analysis.

In both sexes, SUA levels (mg/dL) were defined based on quartiles (Q1 < 4.1, 4.1≤ Q2 < 4.9, 4.9≤ Q3 < 5.9, 5.9≤ Q4 mg/dL). BP was compared by sex between Q1 and other quartiles using Dunnett's method. Trends in BPs across quartiles were estimated by sex using the Jonckheere–Terpstra test.

All statistical analyses were performed using the Statistical Package for Social Sciences, version 22 (SPSS Inc., Chicago, IL).

This survey was conducted in compliance with the Ethical Guidelines for Epidemiological Studies established by the Japanese Government[22] and in accordance with the Declaration of Helsinki of 1975 (revised in 2000).[23] The research protocol was reviewed and approved by the Ethics Committee of Juntendo University (no. 2020026). The research protocol was also reviewed and approved by the Council of the ToMMo (no. 2019-0079).

All study subjects included in this manuscript provided written informed consent.

3 | RESULTS

Table 1 shows the basic characteristics of eligible participants. The mean age (SD) was 62.1 (10.7) years for men and 59.6 (11.3) years for women. Mean BMI (SD) was 23.5 (3.6) kg/m2 for men and 23.6 (3.6) kg/m2 for women. Mean (SD) SBP and DBP were 126.2 (17.6) and 75.6 (10.6) mmHg, respectively, for men and 126.8 (17.5) and 75.7 (10.5) mmHg, respectively, for women. The proportions of those who were treated with antidiabetes and antilipidemia medications were 9.3% and 19.3%, respectively, for men and 8.9% and 19.1%, respectively, for women.

Table 2 shows a comparison of basic characteristics between low and high SUA levels by sex. BMI and WC were higher in those with high SUA compared to low SUA. SBP, DBP, fasting blood glucose concentration, HbA1c, and TGs were significantly higher in patients with high SUA compared to those with low SUA in both sexes. In contrast, HDL-C and eGFR were significantly lower in patients with high SUA than those with low SUA in both sexes.

Results of logistic regression analyses are shown in Table 3. The multivariate analysis revealed that SUA ≥7 mg/dL was significantly associated with failure to achieve treatment goal of 130/80 mmHg among men (AOR = 1.24, 95% CI = 1.03–1.50, $p = .03$) (Table 3). Although a significant association with failure to achieve treatment goal of 140/90 mmHg was observed in the univariate analysis (AOR = 1.47, 95% CI = 1.22–1.79, $p < .01$), there was no association in Model 2 (AOR = 1.20, 95% CI = 0.97–1.48, $p = .10$) (Table 4). Among women, SUA ≥6 mg/dL was significantly associated with failure to achieve treatment goals of both 130/80 and 140/90 mmHg (AOR = 1.33, 95% CI = 1.20–1.47, $p < 0.01$ and AOR = 1.17, 95% CI = 1.04–1.32, $p < .01$, respectively) (Tables 5 and 6). Among confounders, BMI was significantly associated with failure to achieve both treatment goals in both sexes (AOR = 1.12, 95% CI = 1.10–1.14, $p < .01$; AOR = 1.10, 95% CI = 1.08-1.12, $p < .01$; AOR = 1.13, 95% CI = 1.11–1.14, $p < .01$; AOR = 1.10, 95% CI = 1.09–1.12, $p < .01$) (Tables 3–6).

Figures 1 and 2 show the relationships between SBP/DBP and SUA quartiles in men and women, respectively. For both sexes, each increase in SUA quartile was positively associated with increases in SBP and DBP ($p < .01$ for trend). Each SBP and DPB quartile (Q2–Q4) were also significantly higher compared with Q1 of SBP and DBP in both sexes ($p < .01$).

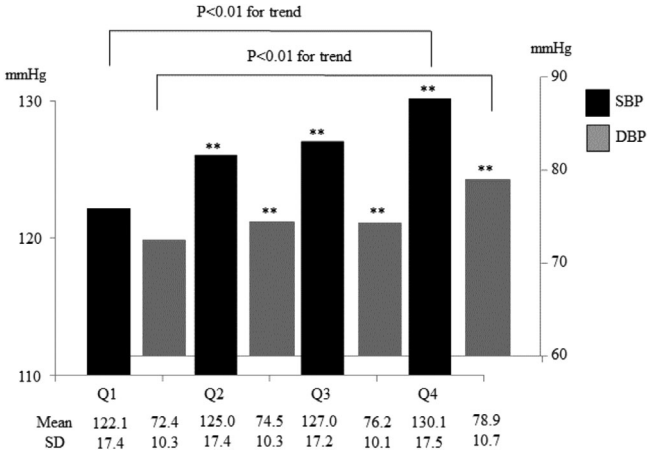

FIGURE 1 Relationship between serum uric acid quartiles and blood pressure among male participants.

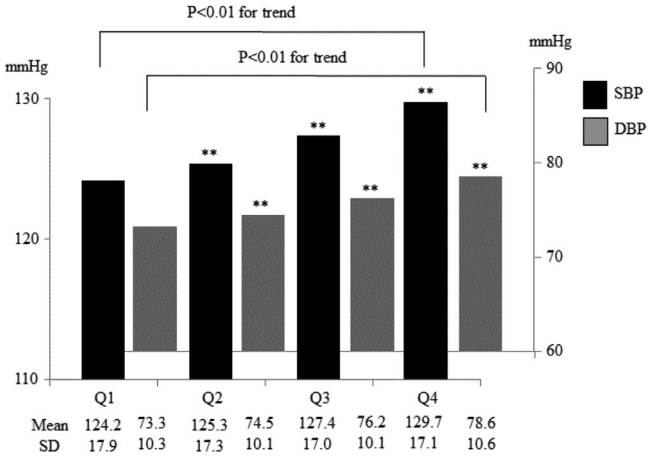

FIGURE 2 Relationship between serum uric acid quartiles and blood pressure among female participants.

4 | DISCUSSION

The present cross-sectional study examined data from a large number of community-dwelling residents who underwent a health checkup and revealed that high SUA level was significantly associated with failure to achieve treatment BP goals of 130/80 and/or 140/90 mmHg after adjusting for confounders. Moreover, SUA quartiles were also significantly associated with SBP and DBP in both sexes. To our knowledge, only a few studies have investigated the association between SUA levels and the achievement of target BP among Japanese patients with hypertension.

TABLE 1 Participant sex-specific characteristics.

	Mean (SD) or *N* (%)				
	Men (*n* = 6499)		Women (*n* = 10 614)		*p*
Age (years)	62.1	(10.7)	59.6	(11.3)	<0.01
Anthropometric measurements					
Body mass index (kg/m^2)	23.5	(3.6)	23.6	(3.6)	0.42
Waist circumference (cm)	83.0	(9.5)	83.0	(9.5)	0.91
Healthy lifestyle characteristics					
Alcohol consumption (daily drinker)	1407	(21.6)	2428	(22.9)	0.06
Smoking behavior (current smoker)	762	(11.7)	1193	(11.2)	0.33
Blood pressure measurements					
Systolic blood pressure (mmHg)	126.2	(17.6)	126.8	(17.5)	.06
Diastolic blood pressure (mmHg)	75.6	(10.6)	75.7	(10.5)	0.59
<130 (SBP) and 80 (DBP) (mmHg)	3357	(51.7)	5389	(50.8)	0.25
<140 (SBP) and 90 (DBP) (mmHg)	5145	(79.2)	8303	(78.3)	0.13
Diabetes medication (yes)	541	(9.3)	840	(8.9)	0.41
Fasting blood glucose (mg/dL)	98.9	(24.4)	99.2	(25.7)	0.39
Hemoglobin A1c (%)	5.7	(0.6)	5.7	(0.6)	0.90
Dyslipidemia medication (yes)	1145	(19.3)	1842	(19.1)	0.78
Total cholesterol (mg/dL)	208.1	(35.0)	207.8	(35.3)	0.73
High-density-lipoprotein cholesterol (mg/dL)	62.9	(16.3)	62.7	(16.2)	0.36
Low-density-lipoprotein cholesterol (mg/dL)	121.3	(30.5)	121.5	(30.8)	0.68
Triglycerides (mg/dL)	123.1	(86.3)	122.9	(81.0)	0.83
Hyperuricemia medication (yes)	337	(5.8)	540	(5.7)	0.86
Uric acid (mg/dL)	5.1	(1.3)	5.1	(1.3)	0.68
Organ damage/cardiovascular disease					
Cardiovascular disease	320	(5.4)	552	(5.7)	0.34
Cerebrovascular disease	322	(5.5)	552	(5.9)	0.39
Renal disease	61	(1.0)	116	(1.2)	0.31
CKD (eGFR < 60 mL/min/1.73 m^2)	561	(8.8)	932	(8.9)	0.73
eGFR (mL/min/1.73 m^2)	78.9	(16.2)	79.0	(16.4)	0.58

Abbreviations: CKD, chronic kidney disease; DBP, diastolic blood pressure; eGFR, estimated glomerular filtration rate; *N*, number; SBP, systolic blood pressure; SD, standard deviation.

Our multivariate logistic regression analysis data showed that SUA ≥7.0 mg/dL in men and ≥6.0 mg/dL in women were significantly associated with failure to achieve treatment goal BP of 130/80 and/or 140/90 mmHg, even after adjusting for confounders. Several previous studies have reported an association between BP control and SUA level.[20–21,24] A Chinses clinical study that analyzed 1648 inpatients with essential and uncontrolled hypertension on admission reported that hyperuricemia was associated with a 5.3-mmHg lower SBP reduction (95% CI: 3.1–7.4 mmHg, $p < .01$) in men and a 2.6-mmHg lower SBP reduction (95% CI: 0.5–4.6 mmHg, $p = .02$) in women, as determined by multiple linear regression after adjusting for confounders.[23] The Brisighella Heart Study (BHS), a prospective, population-based longi-

TABLE 2 Serum uric acid concentration–specific basic characteristics by sex.

	Men ($n = 6499$)					Women ($n = 10\,614$)				
	Mean (SD) or *N* (%)					Mean (SD) or *N* (%)				
	Serum uric acid concentration (mg/dL)					Serum uric acid concentration (mg/dL)				
	<7 ($n = 5911$)		≥7 ($n = 588$)			<6 ($n = 8079$)		≥6 ($n = 2535$)		
Age (years)	62.1	(10.8)	62.2	(10.20)	0.85	59.7	(11.3)	59.3	(11.5)	0.21
Anthropometric measurements										
Body mass index (kg/m^2)	23.3	(3.5)	25.4	(3.9)	<0.01	23.2	(3.5)	24.9	(3.5)	<0.01
Waist circumference (cm)	82.4	(9.3)	88.6	(9.6)	<0.01	81.8	(9.2)	86.8	(8.8)	<0.01
Healthy lifestyle characteristics										
Alcohol consumption (daily drinker)	1274	(21.6)	133	(22.6)	0.55	1857	(23.0)	571	(22.5)	0.63
Smoking behavior (current smoker)	693	(11.7)	69	(11.7)	0.99	906	(11.2)	287	(11.3)	0.88
Blood pressure measurements										
Systolic blood pressure (mmHg)	125.8	(17.5)	130.5	(17.6)	<0.01	125.8	(17.4)	129.8	(17.1)	<0.01
Diastolic blood pressure (mmHg)	75.2	(10.5)	79.7	(10.9)	<0.01	74.8	(10.3)	78.7	(10.6)	<0.01
<130 (SBP) and 80 (DBP) (mmHg)	3119	(52.8)	238	(40.5)	<0.01	4340	(53.7)	1049	(41.4)	<0.01
<140 (SBP) and 90 (DBP) (mmHg)	4717	(79.9)	428	(72.9)	<0.01	6435	(79.7)	1868	(73.7)	<0.01
Diabetes medication (yes)	482	(9.1)	59	(11.1)	0.14	632	(8.8)	208	(9.2)	0.59
Fasting blood glucose (mg/dL)	98.6	(24.7)	101.8	(21.5)	<0.01	98.7	(26.5)	101.0	(23.0)	<0.01
Hemoglobin A1c (%)	5.6	(0.6)	5.7	(0.6)	0.02	5.6	(0.6)	5.7	(0.5)	<0.01
Dyslipidemia medication (yes)	1037	(19.2)	108	(19.9)	0.73	1396	(19.1)	446	(19.2)	0.86
Total cholesterol (mg/dL)	208.3	(35.0)	205.9	(34.7)	0.33	208.4	(35.2)	205.5	(35.7)	0.02
High-density-lipoprotein cholesterol (mg/dL)	63.6	(16.2)	56.4	(15.1)	<0.01	64.4	(16.0)	57.5	(15.8)	<0.01
Low-density-lipoprotein cholesterol (mg/dL)	121.2	(30.4)	122.1	(31.5)	0.50	121.4	(30.5)	121.7	(31.8)	0.67
Triglycerides (mg/dL)	119.7	(81.6)	158.0	(118.8)	<0.01	114.3	(70.1)	150.2	(103.9)	<0.01
Hyperuricemia medication (yes)	300	(5.6)	37	(6.9)	0.23	414	(5.7)	126	(5.5)	0.72
Uric acid (mg/dL)	4.8	(1.0)	7.7	(0.7)	<0.01	4.5	(0.9)	6.9	(0.8)	<0.01
Organ damage (yes)										
Cardiovascular disease	287	(5.3)	33	(6.1)	0.43	424	(5.8)	128	(5.5)	062
Cerebrovascular disease	296	(5.6)	26	(4.9)	0.50	429	(6.0)	123	(5.4)	0.33
Renal disease	57	(1.0)	7	(1.3)	0.53	89	(1.2)	27	(1.2)	0.86
CKD (eGFR < 60 mL/min/1.73 m^2)	427	(7.3)	134	(23.3)	<0.01	472	(5.9)	460	(18.5)	<0.01
eGFR (mL/min/1.73 m^2)	79.7	(15.9)	70.8	(16.4)	<0.01	80.8	(15.9)	73.3	(16.8)	<0.01

Abbreviations: CKD, chronic kidney disease; DBP, diastolic blood pressure; eGFR, estimated glomerular filtration rate; SBP, systolic blood pressure; SD, standard deviation; *N*, number.

TABLE 3 Factors associated with therapeutic failure to achieve target blood pressure of 130/80 mmHg among men (logistic regression analysis).

	Univariate			Multivariate					
				Model 1[a]			Model 2[b]		
	OR	95% CI	*p*	AOR	95% CI	*p*	AOR	95% CI	*p*
Serum uric acid concentration (mg/dL)									
<7	Reference			Reference			Reference		
≥7	1.64	1.38–1.95	<0.01	1.64	0.38–1.95	<0.01	1.24	1.03–1.50	.03
Age (years)				1.00	0.99–0.01	0.86	1.00	0.99–1.01	.85
Body mass index (kg/m^2)							1.12	1.10–1.14	<.01
Alcohol consumption (usual)							1.04	0.91–1.19	.60
Smoking behavior (current)							0.95	0.80–1.13	.58
Diabetes medication (yes)							1.01	0.84–1.21	.95
Dyslipidemia medication (yes)							0.93	0.81–1.07	.30
CKD (eGFR < 60 mL/min/1.73 m^2)							1.18	0.97–1.42	.10

Abbreviations: AOR, adjusted odds ratio; CI, confidence interval; CKD, chronic kidney disease; eGFR, estimated glomerular filtration rate; OD, odds ratio.
[a]Model 1 was adjusted for age (years); [b]Model 2 was adjusted for age (years), BMI (kg/m^2), alcohol consumption status (usual), smoking behavior (current smoker), diabetes medication (yes), dyslipidemia medication (yes), and CKD (eGFR < 60 mL/min/1.73 m^2).

TABLE 4 Factors associated with therapeutic failure to achieve target blood pressure of 140/90 mmHg among men (logistic regression analysis).

	Univariate			Multivariate					
				Model 1[a]					
	OR	95% CI	*p*	AOR	95% CI	*p*	AOR	95% CI	*p*
Serum uric acid concentration (mg/dL)									
<7	Reference			Reference					
≥7	1.47	1.22–1.79	<0.01	1.47	1.22–1.79	<0.01	1.20	0.97–1.48	.10
Age (years)				1.00	0.99–1.02	0.88	1.00	0.99–1.01	.98
Body mass index (kg/m^2)							1.10	1.08–1.12	<.01
Alcohol consumption (usual)							1.05	0.89–1.24	.54
Smoking behavior (current)							0.91	0.74–1.12	.37
Diabetic medication (yes)							1.00	0.80–1.25	.99
Dyslipidemia medication (yes)							0.92	0.77–1.09	.33
CKD (eGFR < 60 mL/min/1.73 m^2)							1.12	0.91–1.41	.28

Abbreviations: AOR, adjusted odds ratio; CI, confidence interval; CKD, chronic kidney disease; eGFR, estimated glomerular filtration rate; OD, odds ratio.
[a]Model 1 was adjusted for age (years); [b]Model 2 was adjusted for age (years), BMI (kg/m^2), alcohol consumption status (usual), smoking behavior (current smoker), diabetes medication (yes), dyslipidemia medication (yes), and CKD (eGFR < 60 mL/min/1.73 m^2).

tudinal epidemiologic investigation involving 2939 randomly sampled Caucasian subjects, showed that SUA levels were essentially identical in normotensive and controlled hypertensive patients (5.1 ± 1.3 and 5.1 ± 1.2 mg/dL, respectively), whereas significantly higher values were observed in untreated and uncontrolled hypertensive patients (5.4 ± 1.3 and 5.4 ± 1.3 mg/dL, respectively; $p < .05$ vs. normotensive or controlled hypertensive patients).[20] The Blood Pressure Control Rate and Cardiovascular Risk Profile study, which examined 3206 treated hypertensive patients, reported that 25% of these patients had hyperuricemia, and SBP and 24-h SBP were significantly higher in patients with hyperuricemia compared to those with normouricemia ($p < .01$).[21] Therefore, these evidences are similar to our actual findings and high SUA level may be a risk factor for therapeutic failure to achieve goal BP, and it is thus necessary to consider the SUA level in treating hypertension in clinical settings.

In addition to the association between SUA level and failure to achieve treatment BP goals, our data showed a relationship between SUA quartiles and BP measurements in both sexes. A cross-sectional study that examined 255 adults in Bangladeshi reported that SUA level quartiles were positively correlated with BP ($p < .01$). After

TABLE 5 Factors associated with therapeutic failure to achieve target blood pressure of 130/80 mmHg among women (logistic regression analysis).

	Univariate			Multivariate					
				Model 1[a]					
	OR[a]	95% CI	*p*	AOR[c]	95% CI	*p*	AOR[c]	95% CI	*p*
Serum uric acid concentration (mg/dL)									
<6	Reference			Reference			Reference		
≥6	1.64	1.50–1.80	<0.01	1.65	1.50–1.80	<0.01	1.33	1.20–1.47	<.01
Age (years)				1.00	0.99–1.01	0.37	1.00	0.99–1.00	.98
Body mass index (kg/m^2)							1.13	1.11–1.14	<.01
Alcohol consumption (usual)							0.97	0.87–1.07	.50
Smoking behavior (current)							0.98	0.86–1.13	.80
Diabetic medication (yes)							0.96	0.83–1.11	.59
Dyslipidemia medication (yes)							0.99	0.88–1.10	.82
CKD (eGFR < 60 mL/min/1.73 m^2)							1.08	0.93–1.25	.34

Abbreviations: AOR, adjusted odds ratio; CI, confidence interval; CKD, chronic kidney disease; eGFR, estimated glomerular filtration rate; OD, odds ratio.
[a]Model 1 was adjusted for age (years); [b]Model 2 was adjusted for age (years), BMI (kg/m^2), alcohol consumption status (usual), smoking behavior (current smoker), diabetes medication (yes), dyslipidemia medication (yes), and CKD (eGFR < 60 mL/min/1.73 m^2).

TABLE 6 Factors associated with therapeutic failure to achieve target blood pressure of 140/90 mmHg among women (logistic regression analysis).

	Univariate			Multivariate					
				Model 1[a]					
	OR	95% CI	*p*	AOR	95% CI	*p*	AOR	95% CI	*p*
Serum uric acid concentration (mg/dL)									
<6	Reference			Reference			Reference		
≥6	1.40	1.26–1.55	<0.01	1.40	1.26–1.55	<0.01	1.17	1.04–1.32	<.01
Age (years)				1.00	0.99–1.00	0.99	1.00	0.99–1.00	.37
Body mass index (kg/m^2)							1.10	1.09–1.12	<.01
Alcohol consumption (usual)							0.93	0.82–1.06	.27
Smoking behavior (current)							1.08	0.92–1.27	.35
Diabetes medication (yes)							0.87	0.72–1.05	.14
Dyslipidemia medication (yes)							0.93	0.81–1.07	.31
CKD (eGFR < 60 mL/min/1.73 m^2)							1.10	0.92–1.31	.29

Abbreviations: AOR, adjusted odds ratio; CI, confidence interval; CKD, chronic kidney disease; eGFR, estimated glomerular filtration rate; OD, odds ratio.
[a]Model 1 was adjusted for age (years); [b]Model 2 was adjusted for age (years), BMI (kg/m^2), alcohol consumption status (usual), smoking behavior (current smoker), diabetes medication (yes), dyslipidemia medication (yes), and CKD (eGFR < 60 mL/min/1.73 m^2).

adjusting for baseline covariates, SUA levels were significantly associated with hypertension ($p < .01$).[25] The Iki Epidemiological Study of Atherosclerosis and Chronic Kidney Disease (ISSA-CKD) study, which was a population-based retrospective cohort study to examined the association between hyperuricemia and new-onset hypertension in the 7895 Japanese population, reported that the first quartile SUA group was set as the reference group, and the multivariable-adjusted hazard ratios (95% CI) for new-onset hypertension were 1.11 (0.90–1.36) in the second quartile, 1.25 (1.02–1.54) in the third quartile, and 1.35 (1.07–1.70) in the fourth quartile compared with those in the reference group ($p = .007$ for trend).[26] Thus, it is possible that maintaining optimal SUA levels contributes to better management of BP through these previous reports and our results.

Our study has several limitations worth noting. First, it was subject to selection bias. Participants comprised only those who underwent a voluntary health checkup in Miyagi and Iwate Prefectures, Japan. As such, these participants may be inherently more aware of health behaviors relative to residents who did not participate in the health checkup. Further analyses involving more-diverse cohorts are necessary. Second, some key data were not collected, such as detailed

information on actual medications taken for treating hypertension, diabetes mellitus, dyslipidemia and hyperuricemia, and it is limited to use these data for adjustment. Especially, the detail of anti-hypertensive therapy, including number of medications, were not collected, and it was limited to consider the disease severity. The period of the time from starting treatment were also not collect the data from the self-administered questionnaire. Further analyses collecting the detail of key data are necessary. Third, the data were collected in 2013–2015, but the draft of the JSH2019 was introduced in 2018 and published in 2019. Despite this lag, however, both thresholds of 130/80 and 140/90 mmHg were analyzed in the present study. Further studies examining data collected after 2019 will be needed. Fourth, some lifestyle-related criteria were vague because this information was collected from existing questionnaires. In addition, the information was collected using a self-administered questionnaire. Further studies using a questionnaire focused on lifestyle characteristics will be needed. Fifth, this study had a cross-sectional design, and thus causal relationships between elevated SUA and blood pressure could not be evaluated. The issue is a critical limitation of the study. Further analyses of follow-up survey data will be needed to address this issue.

5 | CONCLUSIONS

After adjusting for confounders, the present study revealed that high SUA level is significantly associated with failure to achieve treatment goal BP of 130/80 and/or 140/90 mmHg. Moreover, SUA quartiles were also significantly associated with SBP and DBP in both sexes. Our data confirms the difficulties in maintain goal BP control in those with elevated SUA.

AUTHOR CONTRIBUTIONS

Hirohide Yokokawa and Yuki Sato participated in the design of the study. Hirohide Yokokawa and Yuki Sato participated in data collection. Hirohide Yokokawa, Mai Suzuki, Nozomi Aoki, Yuki Sato, and Hirohi Fukuda wrote the manuscript. Hirohide Yokokawa, Mai Suzuki, Nozomi Aoki, Yuki Sato, Hiroshi Fukuda, Teruhiko Hisaoka T, and Toshio Naito reviewed and revised the manuscript.

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CONFLICT OF INTEREST STATEMENT

The authors have no conflict of interest to declare.

PATIENT CONSENT STATEMENT

Written informed consent was obtained from all participants.

PERMISSION TO REPRODUCE MATERIAL FROM OTHER SOURCES

That all necessary permissions have been obtained by providing the actual written permission granted by the copyright owner.

CLINICAL TRIAL REGISTRATION

The study protocol was not registered as clinical trial registration.

DATA AVAILABILITY STATEMENT

The data are under the ethical restrictions of the Ethics Committee of Juntendo University and the Council of the Tohoku Medical Megabank Organization.

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