

# THE ASSOCIATION BETWEEN SERUM URIC ACID AND INCIDENCE OF NON-FATAL STROKE IN THE CKD POPULATION : A LONGITUDINAL SURVEY OF A NATIONWIDE COHORT IN JAPAN

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<sup>2</sup>Steering Committee of Research on Design of the comprehensive health care system for chronic kidney disease (CKD) based on the individual risk assessment by Specific Health Checkup.



## Background & Aim

Hyperuricemia is a risk factor for cardiovascular events in the general and hypertensive populations. Some studies have shown that hyperuricemia is an independent risk factor for cardiovascular diseases including stroke. The serum uric acid level increases as a result of declining renal function, therefore the effects of uric acid for the risk of these diseases are conflicting in later chronic kidney disease (CKD) stages (III-V).

This study investigated the association between uric acid levels and non-fatal stroke in subjects with CKD.

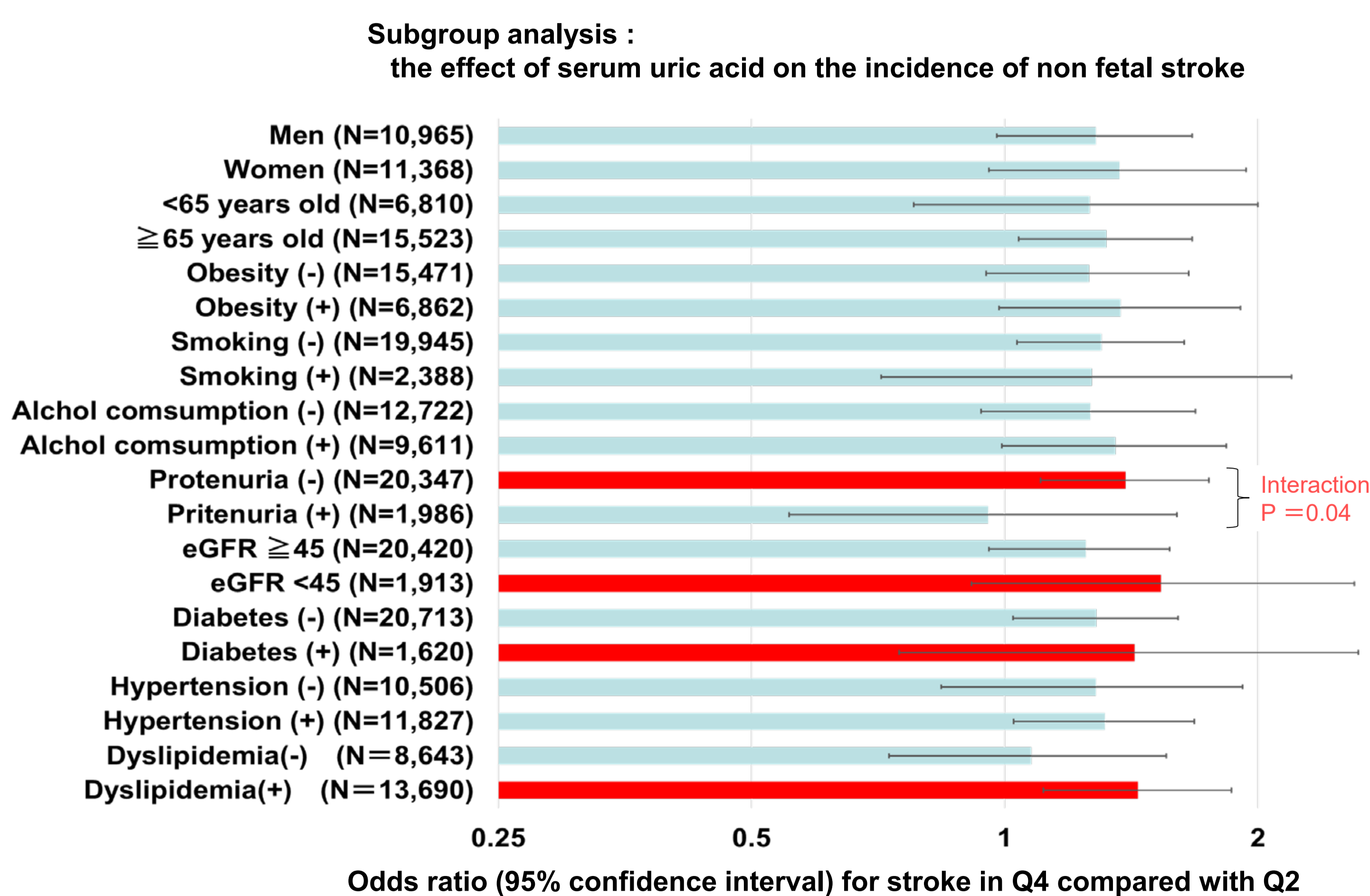
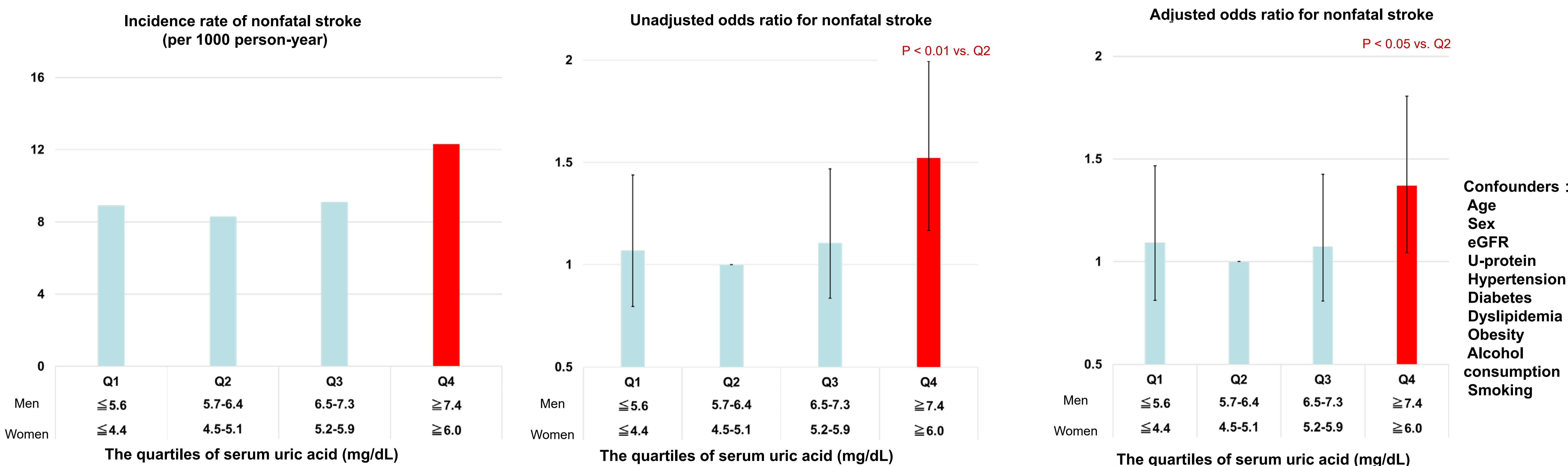
## Methods

We used a national database of 22,333 subjects with estimated glomerular filtration rate (eGFR) < 60 mL/min/1.73 m<sup>2</sup> (aged 39–73; men, 49%), who participated in an annual health checkup, "The Specific Health Check and Guidance in Japan" during 2008–2010, and examined the relationship between the gender-specific quartiles of serum uric acid levels at baseline and the 2-year incidence of non-fatal stroke.

## Results

- ◆ During the follow-up period, 432 non-fatal strokes occurred.
- ◆ The incidence rate of non-fatal stroke showed a J-shape curve with the increase in uric acid levels at baseline (the lowest [8.3 per 1,000 person-year] in the 2nd quartile of uric acid [Q2: men, 5.7–6.4 mg/dL; women, 4.5–5.1 mg/dL] and the highest [12.3] in the 4th quartile [Q4: men, ≥7.4 mg/dL; women, ≥6.0 mg/dL]).
- ◆ In the Cox proportional hazard analysis, odds ratio (OR) for the incidence of stroke was significantly increased in Q4, compared with Q2 (OR 1.49, 95% confidence interval 1.15–1.95, P < 0.01). This significant increase in OR in Q4 was preserved after adjusting for confounders including age, sex, and comorbidities.
- ◆ A significant interaction was observed between uric acid and proteinuria (P = 0.04), and the increase in the OR in Q4 was significant in subjects without proteinuria, but not in those with proteinuria. In subgroup analyses, subjects with dyslipidemia, diabetes, and eGFR < 45 mL/min/1.73 m<sup>2</sup> showed a higher OR for stroke in Q4 than subjects without these factors.

	Total subjects	Gender-specific quartiles of serum uric acid (mg/dL)				p-value
		Q1 (M ≤5.6, W ≤4.4)	Q2 (M 5.7-6.4, W 4.5-5.1)	Q3 (M 6.5-7.3, W 5.2-5.9)	Q4 (M ≥7.4, W ≥6.0)	
Number	22,333	5,067	5,438	5,993	5,835	
Age (years)	65.9 ± 5.3	65.9 ± 5.3	66.0 ± 5.2	66.0 ± 5.2	65.8 ± 5.4	0.123
Men (%)	49.1	49.5	48.8	48.9	49.3	0.858
Smoker (%)	10.7	10.1	10.3	10.9	11.4	0.121
Alcohol consumption (%)	43.0	39.3	41.8	43.6	46.8	< 0.001
Obesity (%)	30.7	22.4	26.4	31.4	41.3	< 0.001
Body mass index (kg/m <sup>2</sup> )	23.7 ± 3.2	22.9 ± 2.9	23.3 ± 3.0	23.8 ± 3.0	24.6 ± 3.3	< 0.001
Systolic BP (mmHg)	130.7 ± 17.1	128.6 ± 17.1	129.8 ± 17.1	131.1 ± 17.0	133.1 ± 17.1	< 0.001
Diastolic BP (mmHg)	77.2 ± 10.5	75.9 ± 10.4	76.8 ± 10.5	77.4 ± 10.5	78.4 ± 10.5	< 0.001
eGFR (mL/min/1.73m <sup>2</sup> )	53.3 ± 5.9	54.4 ± 4.7	54.1 ± 5.0	53.4 ± 5.4	51.3 ± 7.3	< 0.001
Triglyceride (mg/dL)	128.7 ± 79.0	114.9 ± 64.1	120.3 ± 68.0	130.0 ± 78.9	147.4 ± 95.2	< 0.001
LDL-cholesterol (mg/dL)	127.2 ± 29.8	125.2 ± 29.2	127.0 ± 28.8	127.6 ± 29.5	128.8 ± 31.3	< 0.001
HDL-cholesterol (mg/dL)	59.5 ± 15.8	61.5 ± 16.2	60.6 ± 16.0	59.2 ± 15.7	56.9 ± 15.0	< 0.001
HbA <sub>1c</sub> (%)	5.3 ± 0.6	5.3 ± 0.6	5.3 ± 0.6	5.4 ± 0.6	5.4 ± 0.5	< 0.001
Proteinuria (≥1+) (%)	8.9	7.1	8.0	8.3	11.9	< 0.001
Hypertension (%)	53.0	45.5	48.4	54.4	62.3	< 0.001
Diabetes (%)	7.3	7.6	7.2	7.1	7.2	0.727
Dyslipidemia (%)	61.3	55.7	58.8	61.9	67.9	< 0.001



## Conclusions

This study showed that serum uric acid level is significantly associated with the incidence of non-fatal stroke in the CKD population, and that this association was partially modulated by the characteristics of subjects such as proteinuria and comorbidities.

\* Disclosures:  
All the authors have declared no competing of interest.