

Significance and association of serum uric acid (UA) levels with components of metabolic syndrome (MS) in the elderly

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ABSTRACT

Information concerning the association of serum UA levels and the development of MS in the Chinese aging population is limited. The aims of this study were to investigate age-related metabolic disorders and analyze the relationship between serum UA levels and the components of MS in the elderly. This cross-sectional observational study was performed in subjects from the Department of Health Examination, including 1182 subjects aged ≥ 65 years; among these subjects, 528 were women (mean age, 70.7 ± 4.8 years) and 654 were men (mean age, 71.4 ± 5.3 years). All the subjects underwent three-dimensional (3-D) whole-body scanning for accurate anthropometric measurements. Data analyses were performed using SPSS software. **Results:** MS, hyperuricemia, hypertension, and diabetes mellitus (DM) were present in 53.9%, 40.6%, 33.1%, and 30.1% of the subjects, respectively. Univariate statistical analysis showed that age, blood pressure, blood sugar levels, high-density lipoprotein levels, triglyceride levels, WBC count, and related anthropometric indices differed significantly in subjects categorized according to serum UA levels. In conclusion, our study showed that a high percentage of elderly subjects had hyperuricemia. The results showed an association between serum UA levels and cardiovascular risk factors, and this finding warrants concern with regard to the aging population.

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1. Introduction

Recent studies have shown that UA has strong antioxidant properties that might afford protection against several age-related physiological changes, oxidative stress, and bone health in elderly men (Lippi et al., 2008; Nabipour et al., 2011). However, hyperuricemia is an important risk factor for the development of several age-related degenerative diseases (Lee et al., 2005). Higher levels of UA in the elderly are associated with increased cardiovascular risk factors despite the observed protective effect on muscular strength (Macchi et al., 2008). A recent epidemiological study on MS showed that serum UA levels were significantly correlated with the body mass index (BMI), waist circumference, and dyslipidemia (Rho et al., 2008). However, data are needed to confirm the association of serum UA levels with metabolic disorders and with MS in the aging population. In this regard, the association of serum UA levels with type 2 DM, leukocyte count, and cardiovascular events has been illustrated in recent studies (Kocaman et al., 2009; Causevic et al., 2010).

3-D whole-body scanning is a potentially powerful tool because it is a noninvasive, inexpensive method to capture the proportions, composition, and size of the human body. In a previous study, we showed that the health index (HI), BMI, and waist-to-hip ratio (WHR) were significantly related to laboratory markers of MS (Lin et al., 2002). The objective of this study was to explore the relationship between serum UA levels and DM, hypertension, and the risk of MS in the elderly. We found that several age-associated components of MS correlated with the serum UA levels.

2. Materials and methods

The study was performed in 1182 consecutive subjects selected from the Department of Health Examination, Chang Gung Memorial Hospital, Linkou, Taiwan. The selected subjects were ≥ 65 years old. Blood tests, 3-D whole-body scanning, and anthropometric evaluations were performed on all the subjects. Subjects with a past history of DM, hypertension, cancer, or congenital disorders were excluded from the study. All the examinations were conducted using standardized protocols, and the data were collected by trained staff. The subjects were instructed to fast for 12–14 h before testing, and compliance to this instruction was verified via an interview taken on the morning of the examination.

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Height (to the nearest 0.1 cm) and weight (to the nearest 0.1 kg) were measured by using specified protocols (Berenson et al., 1980; Laurier et al., 1992). Blood pressure measurements were taken from the right arm with the subjects seated and relaxed. The mean values of 3 replicate mercury readings of systolic blood pressure (SBP) and diastolic blood pressure (DBP) obtained by 2 randomly assigned and trained nurses were used for the assessments. Blood pressure levels were determined according to the 1999 WHO-International Society of Hypertension guidelines (Berenson et al., 1980). Hypertension was defined as a SBP of at least 140 mm Hg, and/or a DBP of at least 90 mm Hg.

2.1. Measurements

To measure serum UA levels, venous blood was sampled after overnight fasting and centrifuged at 3000 rpm for 30 min at 4 °C. UA was detected in the blood samples by using a colorimetric enzymatic method. Hyperuricemia was defined as a UA concentration of >7.7 mg/dL in men and >6.6 mg/dL in women (Laurier et al., 1992). Hypertriglyceridemia was defined as a triglyceride concentration of >150 mg/dL (1.695 mmol/L). Low serum high-density lipoprotein cholesterol (HDL-C) levels of <40 mg/dL in men and <50 mg/dL in women were considered abnormally low. DM was defined as a fasting glucose level of ≥ 126 mg/dL or a postprandial glucose level of ≥ 200 mg/dL. To define MS, we used a modified adult treatment panel definition issued in 2004 by the Bureau of Health Promotion, Department of Health, ROC (Taiwan). The subjects who met 3 or more of the following criteria were considered to have MS: central obesity with a waist circumference of >90 cm (men) or >80 cm in (women) and/or BMI ≥ 27 kg/m²; hypertriglyceridemia (triglyceride levels ≥ 150 mg/dL [1.695 mmol/L]); HDL-C level of <40 mg/dL (1.036 mmol/L) (men) and <50 mg/dL (1.295 mmol/L) (women); blood pressure $\geq 130/85$ mm Hg; and, fasting glucose level ≥ 110 mg/dL (6.1 mmol/L). The study was approved by the Institutional Review Board of Chang Gung Memorial Hospital.

2.2. Anthropometric measurements

Anthropometric measurements using the 3D scanner were performed to determine the BMI, WHR, and waist-height ratio (WHR). HI was calculated using the following equation: $HI = [\text{body weight} \times 2 \times \text{waist area}] / [\text{body height}^2 \times (\text{breast}$

area + hip area)], as described previously (Lin et al., 2002). Data were entered into a computer. The 3-D whole-body laser scanner can scan a cylindrical volume with a height of 190 cm and diameter of 100 cm. These dimensions accommodate the majority of human subjects. A platform supports the subject and provides alignment for the towers. The system is built to withstand shipping and repeated use without re-alignment or adjustment. The standard scanning apparel for both men and women was light-gray cotton biker shorts. Women wore gray sports bras. The laser scans the body from head to toe in the co-horizontal plane. A whole-body scan requires 7.5 s for a body height of 180 cm when the Gemini 10085 scanner is set up for a 0.4-cm vertical scanning resolution. If the scanner is configured at a vertical scanning resolution of 0.25 cm, whole-body scanning requires 12 s. About 280 measurements were calculated from the scanned data. More than 30 of these were new anthropometric parameters that are not obtained by traditional measurements. Subjects were also asked to provide demographic data such as age, ethnicity, gender, area of residence, education, and present occupation. Related available hospital health and clinical records were obtained for each subject. Subjects who had an obvious disease or body weight change $\geq 10\%$ during the last 6 months were excluded from this study.

2.3. Data management

All data analyses were performed using the SPSS software (v16.0; SPSS Inc., Chicago, IL, USA) (Levesque, 2007). Separate statistical analyses were performed for male and female subjects and for different age groups. The age and biochemical and anthropometric parameters of subjects of both genders were compared using the independent *t*-test. The different age groups and serum UA quintiles and the risk factors for MS were compared using one-way analysis of variance (ANOVA). Associations between metabolic factors and serum UA levels were examined using Pearson's correlation coefficients. Statistical significance was set at a probability level of 0.05.

3. Results

Table 1 lists the clinical characteristics and anthropometric measurements of the 1182 subjects including 528 women (mean age, 70.7 ± 4.8 years) and 654 men (mean age, 71.4 ± 5.3 years).

Table 1
Anthropometric measurements and clinical features of 1182 aging subjects.

	Female	Male	<i>p</i> value	65–69 years	70–74 years	75–79 years	>80 years	<i>p</i> value
Number	528 (45%)	654 (55%)	–	540 (46%)	382 (32%)	179 (15%)	81 (7%)	–
Age (years)	70.7 ± 4.8	71.4 ± 5.3	0.025					
UA (mg/dL)	5.87 ± 1.59	6.81 ± 1.81	<0.0001	6.27 ± 1.66	6.46 ± 1.80	6.60 ± 2.00	6.38 ± 1.88	0.14
SBP (mm Hg)	130.7 ± 19.1	126.4 ± 18.1	<0.0001	127.7 ± 18.8	128.5 ± 19.0	129.9 ± 18.7	128.7 ± 16.3	0.58
DBP (mm Hg)	77.1 ± 10.8	76.2 ± 10.5	0.14	77.5 ± 10.9	76.5 ± 10.2	75.5 ± 10.7	74.1 ± 10.2	0.019
Fasting glucose (mg/dL)	109.5 ± 39.8	106.2 ± 34.3	0.12	108.1 ± 38.5	106.8 ± 37.4	107.3 ± 30.9	110.3 ± 36.2	0.88
Postprandial glucose (mg/dL)	132.5 ± 69.9	125.5 ± 64.2	0.073	125.9 ± 68.3	127.8 ± 65.2	133.9 ± 62.5	139.8 ± 73.8	0.23
Total cholesterol (mg/dL)	208.4 ± 38.3	195.3 ± 37.8	<0.0001	204.9 ± 39.5	199.1 ± 38.0	194.2 ± 36.1	202.1 ± 37.9	0.0073
LDL-C (mg/dL)	123.8 ± 33.7	120.3 ± 33.5	0.075	125.4 ± 34.3	119.7 ± 33.6	116.2 ± 29.7	121.3 ± 35.0	0.0050
HDL-C (mg/dL)	54.8 ± 14.0	48.1 ± 13.1	<0.0001	50.7 ± 13.6	51.4 ± 14.0	50.4 ± 13.6	53.7 ± 15.7	0.27
Triglyceride (mg/dL)	152.0 ± 95.6	136.6 ± 91.1	0.0047	146.8 ± 93.5	142.6 ± 99.7	139.8 ± 86.4	134.2 ± 76.2	0.62
WBC ($10^3/\mu\text{L}$)	6.16 ± 1.66	6.43 ± 1.92	0.010	6.11 ± 1.66	6.41 ± 1.94	6.53 ± 1.76	6.64 ± 2.09	0.0049
TSH ($\mu\text{IU/mL}$)	1.79 ± 3.58	1.53 ± 2.54	0.15	1.77 ± 3.75	1.46 ± 1.76	1.48 ± 1.44	2.03 ± 4.72	0.27
Waist circumference (cm)	92.0 ± 11.8	91.2 ± 9.7	0.22	90.8 ± 9.9	92.0 ± 10.7	93.2 ± 11.5	90.8 ± 13.1	0.047
BMI (kg/m ²)	25.8 ± 3.6	25.1 ± 3.2	0.0003	25.5 ± 3.2	25.5 ± 3.4	25.2 ± 3.5	24.4 ± 3.9	0.042
HI	33.2 ± 8.3	33.6 ± 7.8	0.38	32.9 ± 7.5	33.9 ± 7.9	34.7 ± 8.9	32.7 ± 9.7	0.029
WHR	0.94 ± 0.09	0.94 ± 0.07	0.22	0.93 ± 0.07	0.94 ± 0.08	0.96 ± 0.09	0.94 ± 0.09	0.0020
WHR	0.61 ± 0.08	0.56 ± 0.06	<0.0001	0.58 ± 0.07	0.59 ± 0.07	0.59 ± 0.08	0.58 ± 0.09	0.13
MS	331 (62.7%)	306 (46.8%)	<0.0001	280 (51.9%)	217 (56.8%)	100 (55.9%)	40 (49.4%)	0.37
Hyperuricemia	215 (40.7%)	265 (40.5%)	0.94	213 (39.4%)	157 (41.1%)	78 (43.6%)	32 (39.5%)	0.79
Hypertension	199 (37.7%)	192 (29.4%)	0.0025	180 (33.3%)	120 (31.4%)	63 (35.2%)	28 (34.6%)	0.82
DM	170 (32.2%)	186 (28.4%)	0.16	151 (28.0%)	124 (32.5%)	48 (26.8%)	33 (40.7%)	0.059

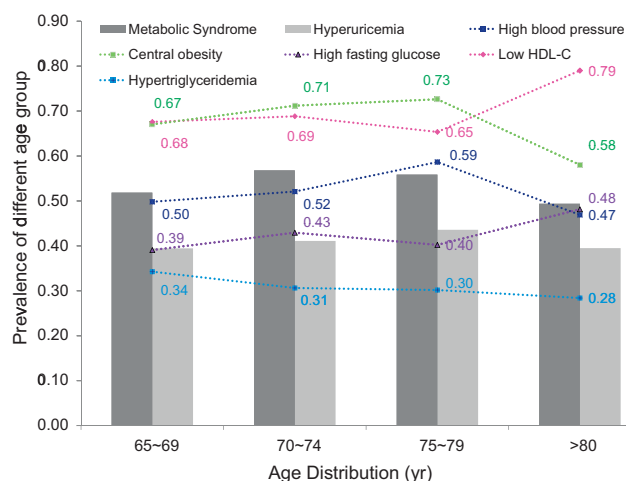


Fig. 1. The number and percentage of subjects with DM, hypertension, hyperuricemia, central obesity, and MS stratified according to age.

Among these subjects, 53.9% had the MS; 40.6% hyperuricemia; 33.1% hypertension; and 30.1% DM. The prevalence of hypertension and SBP in women was greater than that in men. The lipid profile data showed that women had higher total cholesterol levels, triglyceride levels and HDL-C levels, while the WBC count was higher in men. The BMI and WHtR were higher in women than in men. However, waist circumference, WHR, and HI did not differ with gender. There were significant differences in the DBP, total cholesterol levels, low-density lipoprotein cholesterol (LDL-C) levels, WBC count, waist circumference, BMI, HI, and WHR among subjects in the 4 age groups. The mean values for the 4 age groups showed that UA levels, SBP, waist circumference, HI, WHR, WHtR, incidence of hypertension, and hyperuricemia reached a plateau and the lowest HDL-C levels were seen in the age group of 75–79 years.

Fig. 1 shows the prevalence of MS, hyperuricemia, and the 5 components of MS in subjects stratified according to age. In comparison with their prevalence in other age groups, the prevalence of MS (56.8%) and hyperuricemia (43.6%) was slightly higher in the age groups of 70–74 years and 75–79 years, respectively ($p > 0.05$). The incidence of low HDL-C levels and high fasting glucose levels increased with age, from 67.6% to 79.0% and from 39.1% to 48.2%, respectively. Among the 480 subjects with

hyperuricemia, 152 (31.7%) had DM and 179 (37.3%), hypertension. The prevalence of hypertension was significantly higher in subjects with hyperuricemia than in subjects with normal UA levels groups ($p < 0.05$). The prevalence of DM was slightly higher in subjects with hyperuricemia than in subjects with normal UA levels ($p > 0.05$).

Subjects were categorized according to serum UA concentration as follows: 2.3–4.8 mg/dL (137–286 $\mu\text{mol/L}$), 4.9–5.7 mg/dL (291–339 $\mu\text{mol/L}$), 5.8–6.6 mg/dL (345–393 $\mu\text{mol/L}$), 6.7–7.7 mg/dL (399–458 $\mu\text{mol/L}$), and 7.8–16.1 mg/dL (464–958 $\mu\text{mol/L}$) (Table 2). Univariate statistical analyses were performed using the data from UA groups and the risk factors for MS. The UA groups showed statistically significant differences in gender, blood pressure, blood sugar levels, HDL-C levels, triglyceride levels, WBC count, waist circumference, BMI, HI, WHR, and WHtR. The percentage of subjects with MS in the 4.9–5.7 mg/dL UA group was 47.7%, whereas the percentage increased to 60.7% for subjects in the 7.8–16.1 mg/dL UA group. In contrast, age, total cholesterol levels, LDL-C levels, and thyroid stimulating hormone (TSH) levels did not differ between the UA groups. Among the subjects with hyperuricemia, 60.4% (280/480) were diagnosed with MS. In contrast, only 50.3% (349/702) of subjects with normal UA concentrations had the syndrome.

Fig. 2 shows the correlation of serum UA levels with SBP, fasting glucose levels, HDL-C levels, triglyceride levels, WBC count, waist circumference, BMI, HI, and WHR. All these findings showed statistically significant correlation. Fig. 3 shows the mean serum UA levels in the elderly subjects categorized according to the number of components that met the defined criteria for the diagnosis of MS. Subjects with hyperuricemia had significantly higher levels of SBP, DBP, postprandial blood sugar levels, total cholesterol levels, and triglyceride levels. HDL-C levels were lower in subjects with hyperuricemia than in subjects with normal UA concentrations.

4. Discussion

The association between hyperuricemia and various MS components is well established in different populations but this is the first study in an elderly population. In this study, we investigated the main components of MS in the aging population and their potential associations with serum UA levels.

Table 2
Characteristics of aging subjects categorized in different serum UA quintiles.

	UA (quintile category)					p value
	2.3–4.8 (n = 229)	4.9–5.7 (n = 237)	5.8–6.6 (n = 238)	6.7–7.7 (n = 244)	7.8–16.1 (n = 234)	
Gender (F/M)	151/78	124/113	102/136	84/160	67/167	<0.0001
Age (years)	71.2 \pm 5.4	70.9 \pm 5.2	71.0 \pm 4.9	71.2 \pm 4.8	71.4 \pm 5.1	0.88
SBP (mm Hg)	124.9 \pm 18.9	126.3 \pm 17.6	129.3 \pm 18.3	130.5 \pm 18.7	130.6 \pm 19.4	0.0014
DBP (mm Hg)	74.7 \pm 10.9	76.1 \pm 10.5	77.7 \pm 10.9	77.5 \pm 11.1	77.0 \pm 9.7	0.012
Fasting glucose (mg/dL)	117.7 \pm 52.6	106.5 \pm 34.1	102.5 \pm 25.4	105.9 \pm 34.3	106.3 \pm 31.7	0.0001
Postprandial glucose (mg/dL)	148.9 \pm 92.0	124.4 \pm 61.7	120.4 \pm 53.3	124.3 \pm 64.0	126.1 \pm 53.5	<0.0001
Total cholesterol (mg/dL)	201.3 \pm 34.7	195.9 \pm 35.4	204.1 \pm 38.8	203.1 \pm 43.2	201.5 \pm 39.7	0.17
LDL-C (mg/dL)	121.6 \pm 30.8	118.2 \pm 30.6	125.8 \pm 34.6	122.8 \pm 38.3	120.8 \pm 32.7	0.16
HDL-C (mg/dL)	54.8 \pm 15.3	53.0 \pm 14.3	51.5 \pm 12.3	49.2 \pm 13.1	47.0 \pm 13.1	<0.0001
Triglyceride (mg/dL)	125.4 \pm 64.0	124.9 \pm 76.2	135.2 \pm 75.4	156.8 \pm 97.8	174.6 \pm 129.3	<0.0001
WBC ($10^3/\mu\text{L}$)	6.16 \pm 1.96	6.07 \pm 1.96	6.11 \pm 1.62	6.53 \pm 1.67	6.66 \pm 1.76	<0.0001
TSH ($\mu\text{IU/mL}$)	1.34 \pm 1.07	1.80 \pm 3.26	1.82 \pm 4.50	1.58 \pm 2.79	1.67 \pm 2.54	0.43
Waist circumference (cm)	89.4 \pm 12.1	88.8 \pm 9.5	90.3 \pm 9.4	93.3 \pm 9.8	95.8 \pm 11.1	<0.0001
BMI (kg/m^2)	24.5 \pm 3.5	24.8 \pm 3.3	25.2 \pm 3.1	25.9 \pm 3.3	26.5 \pm 3.5	<0.0001
HI	31.5 \pm 8.4	31.5 \pm 7.3	32.6 \pm 7.4	35.0 \pm 8.0	36.7 \pm 7.9	<0.0001
WHR	0.93 \pm 0.09	0.92 \pm 0.07	0.93 \pm 0.08	0.95 \pm 0.07	0.97 \pm 0.08	<0.0001
WHtR	0.58 \pm 0.08	0.57 \pm 0.07	0.58 \pm 0.07	0.59 \pm 0.07	0.60 \pm 0.08	<0.0001
MS	115 (50.2%)	113 (47.7%)	127 (53.4%)	140 (57.4%)	142 (60.7%)	0.033
Hypertension	60 (26.2%)	76 (32.1%)	77 (32.4%)	97 (39.8%)	81 (34.6%)	0.037
DM	80 (34.9%)	69 (29.1%)	52 (21.8%)	76 (31.1%)	79 (33.8%)	0.018

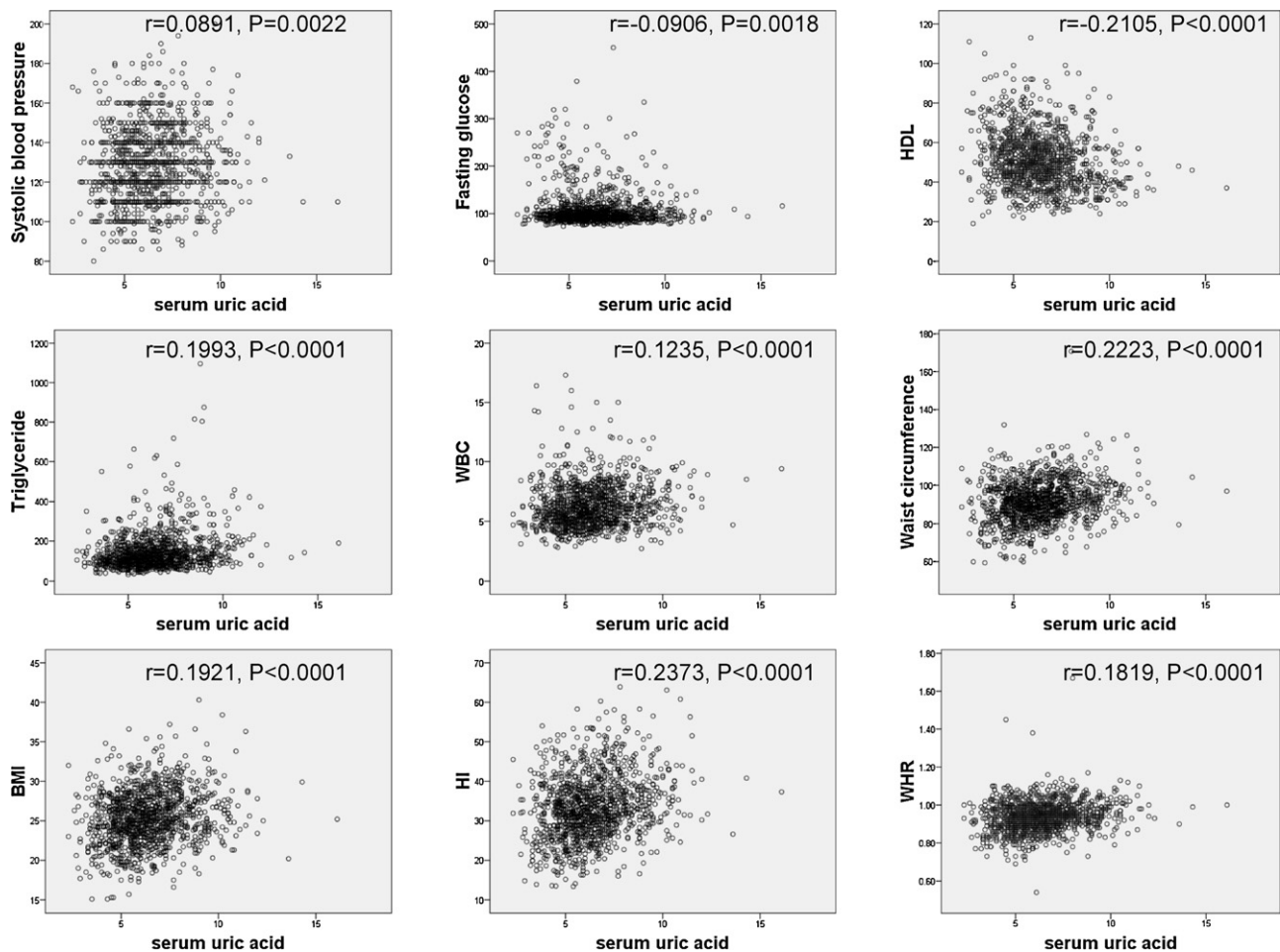


Fig. 2. Correlation of serum UA with other metabolic factors.

Serum UA concentrations are related to the renal handling of UA excretion and cellular metabolism in the body. Age, gender, genetic constitution, and diet also influence the UA concentrations. Young men usually have higher serum UA levels than women. With age, the influence of declining sex hormone and the concomitant decline in renal function may hamper UA excretion (Nabipour et al., 2011). Elevated serum UA levels had been known to be associated with MS. However, data concerning this association in the aging population were lacking. In this study, male subjects had

higher mean serum UA levels, and the gender-related difference (6.81 ± 1.81 mg/dL and 5.87 ± 1.59 mg/dL for male and female subjects, respectively) was less prominent than that seen in the younger population. There was no statistical difference in the incidence of hyperuricemia between the male and female subjects in this study. Recent epidemiological and clinical evidence suggests that hyperuricemia is a risk factor for cardiovascular disease (Perlstein et al., 2006; Lin et al., 2007).

Most studies have shown that in the aging population, blood pressure, central obesity, and low HDL-C levels are the main components of MS (Paccaud et al., 2000; Lin et al., 2002; Alexander et al., 2008). In our study, only HDL-C levels, which are beneficial to health and survival, differed between the elderly male and female subjects. Recent studies have shown that high HDL-C levels are associated with better survival in aging subjects (Landi et al., 2007, 2008). The protective effects of HDL-C may explain the higher life expectancy in elderly women. HDL-C is an independent factor for cardiovascular complications in different conditions (Chien et al., 2007; Cordero et al., 2008). Despite clinical evidence for the protective effects of high HDL-C levels, further studies comparing the protective effects of endogenous and exogenous HDL-C are needed (Tardif et al., 2007; Nieuwdorp et al., 2008).

Elevated serum UA level was a predictor of incident hypertension and elevated blood pressure in age- and gender-based studies (Sundström et al., 2005; Krishnan et al., 2007). A prospective, longitudinal study showed that elevated serum UA levels are a major risk factor for the development of hypertension (Perlstein et al., 2006). A link between serum UA levels and blood pressure in elderly subjects has not been established. In this study, we showed

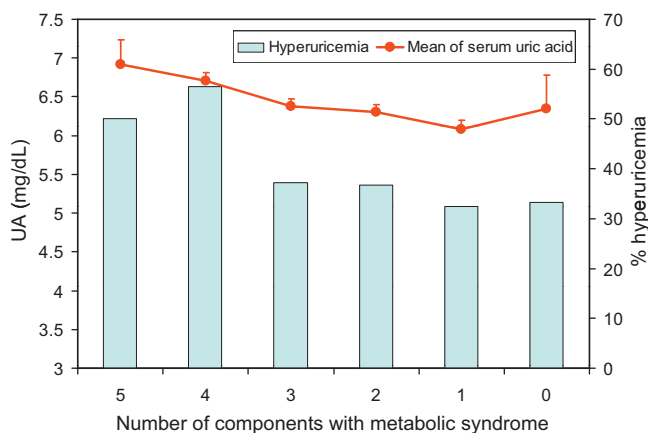


Fig. 3. Mean serum UA levels in different groups of aging subjects who were categorized according to the number of components that met the defined criteria for the diagnosis of MS.

that high SBP and DBP as well as hypertension were significantly more prevalent in elderly subjects with hyperuricemia. Hyperuricemia-induced endothelial dysfunction is the likely mechanism whereby UA causes hypertension and vascular disease (Khosla et al., 2005). There are limitations to our study. The enrolled subjects were selected from 1 institute. In addition, the elderly subjects were in good health with better economic conditions than the general population in Taiwan. The study subjects are not representative of this age group for epidemiological data. However, our results do present the relationship of serum UA levels and components of MS.

In conclusion, this cohort of elderly subjects had a high prevalence of hyperuricemia. Serum UA levels were closely associated with the components of MS. The effectiveness of therapeutic interventions that target hyperuricemia and their ability to reduce the incidence of MS in the elderly is yet to be investigated.

Conflict of interest

There is no conflict of interest existing with this paper.

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