Associations of Insulin Resistance and Glycemic Control with the Risk of Kidney Stones

Yusuke Kabeya, Kiyoe Kato, Masuomi Tomita, Takeshi Katsuki, Yoichi Oikawa, Akira Shimada and Yoshihito Atsumi

Abstract

Objective  The associations of insulin resistance and glycemic control with the risk of kidney stones were explored.

Methods  Generally healthy Japanese (n=2,171) who visited Saiseikai Central Hospital (Tokyo, Japan) for a health check were included in a cross-sectional study. We calculated odds ratios (OR) of having kidney stones in terms of four measures: fasting serum insulin, homeostasis model assessment of insulin resistance (HOMA-IR), fasting plasma glucose (FPG) and glycosylated hemoglobin (HbA1c), adjusting for possible risk factors for kidney stones.

Results  Fasting serum insulin and HOMA-IR were non-significantly associated with the risk of kidney stones, whereas FPG and HbA1c were significantly associated. Compared with those with an FPG of <100 mg/dL, the ORs in those with an FPG of 100 to <126 mg/dL and ≥126 mg/dL were 1.38 (95% confidence interval [CI] =0.95-2.00) and 1.83 (95% CI =1.09-3.06) (p for trend =0.016). In relation to those with an HbA1c of <5.5%, the ORs in those with an HbA1c of 5.5 to <6.0%, 6.0% to <6.5% and ≥6.5% were 1.16 (95% CI =0.76-1.79), 1.25 (95% CI =0.70-2.23) and 1.98 (95% CI =1.11-3.52), respectively (p for trend = 0.027). The significant associations between glycemic control measures and the risk of kidney stones were preserved even after the adjustment for factors related to insulin resistance.

Conclusion  Glycemic control could be an independent risk factor for kidney stones.

Key words: kidney stone, hyperglycemia, insulin resistance, metabolic syndrome

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Introduction

Kidney stones are a common disease worldwide, which lead to a major comorbidity in industrialized countries. The prevalence of kidney stones is estimated to be approximately 6-9% in men and 3-4% in women across countries (1), which has been still increasing (2). Risk factors for kidney stones include age, gender, ethnicity, nutritional factors and genetic properties (3). Epidemiological evidence also suggests that diabetes mellitus, metabolic syndrome and obesity are associated with the risk of kidney stones. Population-based studies have demonstrated that diabetes is significantly associated with an increased risk of kidney stones (4, 5). Regarding metabolic syndrome, one study reported that the odds of having kidney stones rose among people with metabolic syndrome status (6). A dose-response relationship between body mass index (BMI) and the risk of kidney stones was also reported (7). Common pathophysiology among these conditions is insulin resistance, which is defined as an inappropriate response of peripheral tissues to circulating insulin. Several studies have reported the underlying mechanisms. Insulin resistance is associated with a reduction in renal ammonium production and low urinary pH, which could lead to the development of uric acid stones and oxalate calcium stones (8). It is reported that the compensatory hyperinsulinemia as a result of insulin resistance leads to an increase in urinary calcium excretion (9). A direct effect of hyperinsulinemia on urinary calcium excretion was also observed under the euglycemic condition (10), which
could promote the formation of kidney stones containing calcium.

Considering the findings of the epidemiological studies in combination with the basic pathophysiology, it seems to be that the risk of kidney stones may increase as insulin resistance becomes severe. A cross-sectional study (6) reported a positive relationship using a clinical assessment of insulin resistance. In the study, the odds of having kidney stones rose as the number of metabolic syndrome traits increased. However, to our knowledge, no study has explored the dose-response relationship using biochemical measures of insulin resistance such as fasting serum insulin and homeostasis model assessment of insulin resistance (HOMA-IR). The first aim of the present study was to investigate the relationship between insulin resistance and the risk of kidney stones in terms of both clinical measures (the number of metabolic syndrome traits) and biochemical measures (fasting serum insulin and HOMA-IR).

In addition, little is known about associations between glycemic control measures and the risk of kidney stones. Many studies (4, 6, 11, 12) have examined the association between hyperglycemia and the risk of kidney stones using a dichotomous category (diabetic or not). One study explored the association between fasting plasma glucose (FPG) and the risk, reporting a mild but non-significant positive relationship (5). However, no study has investigated the association of glycosylated hemoglobin (HbA1c) with the risk. The second aim was to examine the associations of glycemic control measures (FPG and HbA1c) with the risk of kidney stones.

Materials and Methods

Study subjects

We conducted a cross-sectional study in the health check unit of Saiseikai Central Hospital. The study population was composed of all participants (n=2,761) who underwent a health check focusing on metabolic syndrome from May 2008 to December 2010. These subjects generally visited the check-up unit not for symptomatic diseases but for a health check. Subjects who received insulin therapy for the treatment of diabetes were excluded from the analysis (n=40) since models for the assessment of insulin resistance were not applicable to these subjects. Four subjects were also excluded because anthropometric data, laboratory data or abdominal ultrasound results were not available. Finally, a total of 2,717 participants were included in the analysis. The study protocol was reviewed and approved by the ethics committee of Saiseikai Central Hospital.

Data collection and definitions

Information on medical history, lifestyle and health-related behaviors was obtained by a questionnaire. Anthropometric measurements were performed by trained personnel without the knowledge of the purpose of the present study. Blood samples were collected after an overnight fast and analyzed at the laboratory in the hospital.

Biochemical analyses were performed in the hospital laboratory using automated analysers. Levels of uric acid, total cholesterol, triglycerides, and high-density lipoprotein (HDL) cholesterol were measured using Hitachi LABOSPECT 008 (Hitachi High-technologies Corporation, Tokyo, Japan). Plasma glucose levels were measured using GA08 (A&T Co., Kanagawa, Japan). Insulin concentrations were measured using COBAS 6000 (Roche Diagnostics Japan, Tokyo, Japan). HbA1c levels were measured using an HPLC analyser (HLC-723G8 [ Tosoh, Tokyo, Japan]). The HbA1c data were converted to the equivalent values of National Glycohemoglobin Standardization Program according to the statement of Japanese Diabetes Society (13).

In the present study, insulin resistance was evaluated in two ways. One way was based on biochemical measurements. Fasting serum insulin levels and HOMA-IR were used as measures of insulin resistance. HOMA-IR was calculated as follows: HOMA-IR = fasting insulin (μU/mL) × FPG (mg/dL)/405. The other was based on clinical findings. Insulin resistance was evaluated by counting the total number of metabolic syndrome traits. The modified National Cholesterol Education Program—Adult Treatment Panel III criteria (14) was used in the present study. There are five abnormalities for the definition of metabolic syndrome: abdominal obesity (waist circumference ≥90 cm for males and ≥80 cm for females), glucose intolerance (FPG ≥100 mg/dL), hypertriglyceridemia (triglyceride ≥150 mg/dL), low HDL cholesterol (HDL cholesterol <40 mg/dL for males and HDL cholesterol <50 mg/dL for females) and hypertension (systolic blood pressure ≥130 mmHg and/or diastolic blood pressure ≥85 mmHg). According to the criteria (14), metabolic syndrome is diagnosed if a person has any three of the five abnormalities. Subjects who were using medications to treat an abnormality were categorized as having the abnormal condition even if the measured values were within the normal range. Regarding glycemic control measures, FPG and HbA1c were used.

A diagnosis of kidney stones was confirmed by ultrasound imaging. The ultrasound imaging was conducted by trained technicians and reviewed by radiologists, who were unaware of the results of the laboratory measurements.

Statistical analysis

Characteristics of the participants were compared between those with kidney stones and those without. Student’s unpaired t tests were used for comparing continuous variables while χ² tests were used for comparisons between categorical variables. As for variables which did not follow the Normal distribution, log-transformed values were used for comparisons between the two groups. Logistic regression analysis was performed to calculate odds ratios (OR) of having kidney stones in terms of each metabolic syndrome trait, the diagnosis of metabolic syndrome (presence of 3 or more abnormalities) and the total number of metabolic syndrome traits.
Table 1. Characteristics of Participants according to the Presence of Kidney Stones

<table>
<thead>
<tr>
<th>Characteristics</th>
<th>All subjects n = 2,717</th>
<th>Presence of kidney stones</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Yes n = 155</td>
<td>No n = 2,562</td>
<td></td>
</tr>
<tr>
<td>Age, years</td>
<td>57.7±11.9</td>
<td>58.9±10.9</td>
<td>0.169</td>
</tr>
<tr>
<td>Males, n (%)</td>
<td>1,822 (67.1)</td>
<td>126 (81.3)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Body mass index, kg/m²</td>
<td>23.1±3.2</td>
<td>23.6±3.0</td>
<td>0.045</td>
</tr>
<tr>
<td>Waist circumference</td>
<td>81.8±9.9</td>
<td>83.6±8.7</td>
<td>0.007</td>
</tr>
<tr>
<td>Blood pressure, mmHg</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Systolic</td>
<td>122.2±19.8</td>
<td>125.1±20.7</td>
<td>0.078</td>
</tr>
<tr>
<td>Diastolic</td>
<td>76.9±12.0</td>
<td>77.9±13.3</td>
<td>0.339</td>
</tr>
<tr>
<td>Uric acid, mg/dL</td>
<td>5.6±1.4</td>
<td>5.9±1.5</td>
<td>0.008</td>
</tr>
<tr>
<td>Total cholesterol, mg/dL</td>
<td>202.1±32.9</td>
<td>197.1±26.6</td>
<td>0.019</td>
</tr>
<tr>
<td>HDL cholesterol, mg/dL</td>
<td>59.9±16.1</td>
<td>57.2±14.7</td>
<td>0.020</td>
</tr>
<tr>
<td>Triglyceride, mg/dL</td>
<td>118.0±104.9</td>
<td>116.3±69.9</td>
<td>0.650</td>
</tr>
<tr>
<td>Fasting plasma glucose, mg/dL</td>
<td>103.8±20.9</td>
<td>109.1±27.1</td>
<td>0.011</td>
</tr>
<tr>
<td>HbA1c, %</td>
<td>5.8±0.7</td>
<td>5.9±0.8</td>
<td>0.008</td>
</tr>
<tr>
<td>Insulin, µU/mL</td>
<td>6.0±3.9</td>
<td>6.1±3.3</td>
<td>0.411</td>
</tr>
<tr>
<td>HOMA-IR</td>
<td>1.6±1.2</td>
<td>1.7±1.1</td>
<td>0.120</td>
</tr>
<tr>
<td>Smoking, n (%)</td>
<td></td>
<td></td>
<td>0.413</td>
</tr>
<tr>
<td>Never</td>
<td>1,620 (59.6)</td>
<td>91 (58.7)</td>
<td>1,529 (59.7)</td>
</tr>
<tr>
<td>&lt; 20 cigarettes/day</td>
<td>391 (14.4)</td>
<td>18 (11.6)</td>
<td>373 (14.6)</td>
</tr>
<tr>
<td>≥ 20 cigarettes/day</td>
<td>706 (26.0)</td>
<td>46 (29.7)</td>
<td>660 (25.8)</td>
</tr>
<tr>
<td>Medication use, n (%)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Anti-diabetic (except for insulin)</td>
<td>142 (5.2)</td>
<td>10 (6.5)</td>
<td>132 (5.2)</td>
</tr>
<tr>
<td>Anti-hypertensive</td>
<td>569 (20.9)</td>
<td>46 (29.9)</td>
<td>523 (20.4)</td>
</tr>
<tr>
<td>Anti-dyslipidemic</td>
<td>383 (14.1)</td>
<td>28 (18.1)</td>
<td>355 (13.9)</td>
</tr>
</tbody>
</table>

Values are means ± standard deviation for continuous variables and n (%) for categorical variables.
Log transformed data are used for the t-test for triglyceride, insulin and HOMA-IR.
HDL, high-density lipoprotein; HbA1c, glycosylated hemoglobin; HOMA-IR, homeostasis model assessment of insulin resistance.

Traits. Then, associations of fasting serum insulin, HOMA-IR, FPG and HbA1c with kidney stones were investigated, respectively. Regarding fasting serum insulin and HOMA-IR, participants were sorted into tertiles because of their skewed distributions and the absence of clinically important cut-off points. On the other hand, participants were categorized according to conventional cut-off points in terms of FPG (<100 mg/dL, 100-<126 mg/dL or ≥126 mg/dL) and HbA1c (<5.5%, 5.5-<6.0%, 6.0-<6.5% or ≥6.5%). Logistic regression analysis was performed to calculate ORs of having kidney stones in terms of these measures. The age- and gender-adjusted model was model 1. The multivariate models included BMI (continuous), smoking (non-smoker, <20 cigarettes/day or ≥20 cigarettes/day), uric acid (continuous), metabolic syndrome traits other than glucose intolerance (abdominal obesity [yes/no], hypertension [yes/no], hypertriglyceridemia [yes/no] and low HDL cholesterol [yes/no]) (model 2). As for the associations of FPG and HbA1c with the risk of kidney stones, the influence of further adjustment for HOMA-IR (log-transformed, continuous) (model 3a) or fasting serum insulin (log-transformed, continuous) (model 3b) were investigated. The multivariate models were tested for goodness of fit by the Hosmer-Lemeshow test and showed an acceptable fit (p>0.05). Statistical analyses were performed using STATA software (version 11; StataCorp, TX, USA). All statistical tests were two-sided, and p values less than 0.05 were considered statistically significant.

Results

Table 1 shows a summary of the characteristics of the study population. Of the 2,717 participants, 155 (5.8%) had kidney stones. Males were more prominent in the subjects with kidney stones. Significantly higher measurements for BMI, waist circumference, uric acid, FPG and HbA1c, and lower measurements for total cholesterol and HDL cholesterol were observed in those with kidney stones. Differences in age, blood pressure, triglyceride, fasting serum insulin and HOMA-IR were not significant between those with kidney stones and those without.

Table 2 shows ORs of having kidney stones in terms of metabolic syndrome traits and the diagnosis of metabolic syndrome. In the univariate analysis, the presence of hypertension and glucose intolerance significantly increased the odds of having kidney stones. The other metabolic syndrome traits modestly increased the odds but the associations were non-significant. After adjustment for age and
gender, the relationships of hypertension and glucose intolerance with kidney stones were attenuated but still significant. The diagnosis of metabolic syndrome (presence of 3 or more traits) was associated with a 1.5-fold increase in the odds of having kidney stones. It is also noteworthy that a dose-response relationship was observed between the number of metabolic syndrome traits and the odds of having kidney stones (p for trend =0.007) (Fig. 1). The presence of all 5 metabolic syndrome traits was associated with a 2.7-fold increase in the odds for kidney stones in relation to those without metabolic syndrome (presence of 0-2 traits) ([5 traits vs 0-2 traits] OR =2.67; 95% CI =1.40-5.08).

Associations of fasting serum insulin, HOMA-IR, FPG and HbA1c with kidney stones were examined using multiple logistic regression analyses (Table 3). In univariate analyses, the four measures were positively and significantly associated with kidney stones. However, after adjustment for age and gender (model 1), the associations of serum insulin and HOMA-IR with kidney stones became non-significant (serum insulin [highest tertile vs lowest tertile] OR =1.44; 95% CI =0.97-2.14, HOMA-IR [highest tertile vs lowest tertile] OR =1.33; 95% CI =0.89-1.99). On the other hand, the associations of FPG and HbA1c with kidney stones were preserved (FPG [≥126 mg/dL vs <100 mg/dL] OR =1.89; 95% CI =1.15-3.12, HbA1c [≥6.5% vs <5.5%] OR =1.97; 95% CI =1.13-3.43). Dose-response relationships were observed in the two measures (FPG, p for trend =0.009; HbA1c, p for trend =0.023). Further adjustment for BMI, metabolic syndrome traits, smoking and uric acid did not influence the results (FPG [≥126 mg/dL vs FPG<100 mg/dL], OR =1.83; 95% CI =1.09-3.06, HbA1c [≥6.5% vs HbA1c<5.5%], OR =1.98; 95% CI =1.11-3.52) (model 2). The glycemic control measures were additionally adjusted for HOMA-IR (model 3a) or fasting serum insulin (model 3b). However, the results did not change considerably.

The aim of the present was to investigate the associations of measures of insulin resistance and glycemic control with the risk of kidney stones. The number of metabolic syndrome traits, which is a clinical measure of insulin resistance, was significantly associated with the risk. On the other hand, we found modest but non-significant associations between biochemical measures of insulin resistance (fasting serum insulin and HOMA-IR) and the risk. Regarding glycemic control measures (FPG and HbA1c), strong associations were observed. Even after adjustment for various confounders, the associations were preserved.

The number of metabolic syndrome traits seems to be a useful predictor for the risk of kidney stones. The dose-response relationship shown in the present study could further confirm the association. A population-based cross-sectional study (6) including 15,000 participants reported that the presence of 4 or more traits of metabolic syndrome doubled the risk of kidney stones in relation to the absence of the traits. The present study found that the presence of all 5 traits was associated with a 2.7-fold increase in the risk of kidney stones compared with the presence of 2 or less traits. Although a direct comparison is impossible because of the difference in the categorization, the risk estimate seems to be similar in the two studies, which could validate the asso-

### Table 2. ORs of Having Kidney Stones in Terms of Metabolic Syndrome Traits and the Diagnosis of Metabolic Syndrome

<table>
<thead>
<tr>
<th>Metabolic syndrome traits</th>
<th>Presence of kidney stones</th>
<th>Crude OR (95% CI)</th>
<th>Adjusted OR a (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Yes n = 155</td>
<td>No n = 2,562</td>
<td></td>
</tr>
<tr>
<td>Abdominal obesity (Male ≥90 cm, Female ≥80 cm)</td>
<td>No 113 1,880</td>
<td>1.00</td>
<td>1.00</td>
</tr>
<tr>
<td></td>
<td>Yes 42 682</td>
<td>1.02 (0.71-1.48)</td>
<td>1.02 (0.70-1.47)</td>
</tr>
<tr>
<td>Glucose intolerance (FPG ≥100 mg/dL)</td>
<td>No 59 1,353</td>
<td>1.00</td>
<td>1.00</td>
</tr>
<tr>
<td></td>
<td>Yes 96 1,209</td>
<td>1.82 (1.30-2.54)</td>
<td>1.53 (1.08-2.17)</td>
</tr>
<tr>
<td>Hypertension (Systolic ≥130 mmHg or Diastolic ≥85 mmHg)</td>
<td>No 84 1,661</td>
<td>1.00</td>
<td>1.00</td>
</tr>
<tr>
<td></td>
<td>Yes 71 901</td>
<td>1.56 (1.12-2.16)</td>
<td>1.42 (1.01-2.01)</td>
</tr>
<tr>
<td>Hypertriglyceridemia (Triglyceride ≥150 mg/dL)</td>
<td>No 98 1,784</td>
<td>1.00</td>
<td>1.00</td>
</tr>
<tr>
<td></td>
<td>Yes 57 778</td>
<td>1.34 (0.95-1.87)</td>
<td>1.19 (0.85-1.67)</td>
</tr>
<tr>
<td>Low HDL cholesterol (Male &lt;40 mg/dL, Female &lt;50 mg/dL)</td>
<td>No 117 1,991</td>
<td>1.00</td>
<td>1.00</td>
</tr>
<tr>
<td></td>
<td>Yes 38 571</td>
<td>1.13 (0.78-1.65)</td>
<td>1.11 (0.75-1.62)</td>
</tr>
<tr>
<td>Diagnosis of metabolic syndrome</td>
<td>No (0-2 traits)</td>
<td>100 1,916</td>
<td>1.00</td>
</tr>
<tr>
<td></td>
<td>Yes (3 or more traits)</td>
<td>55 646</td>
<td>1.48 (1.04-2.10)</td>
</tr>
</tbody>
</table>

a Adjusted for age and gender.

FPG, fasting plasma glucose; HDL, high-density lipoprotein; OR, odds ratio.

### Discussion

The aim of the present was to investigate the associations of measures of insulin resistance and glycemic control with the risk of kidney stones. The number of metabolic syndrome traits, which is a clinical measure of insulin resistance, was significantly associated with the risk. On the other hand, we found modest but non-significant associations between biochemical measures of insulin resistance (fasting serum insulin and HOMA-IR) and the risk. Regarding glycemic control measures (FPG and HbA1c), strong associations were observed. Even after adjustment for various confounders, the associations were preserved.

The number of metabolic syndrome traits seems to be a useful predictor for the risk of kidney stones. The dose-response relationship shown in the present study could further confirm the association. A population-based cross-sectional study (6) including 15,000 participants reported that the presence of 4 or more traits of metabolic syndrome doubled the risk of kidney stones in relation to the absence of the traits. The present study found that the presence of all 5 traits was associated with a 2.7-fold increase in the risk of kidney stones compared with the presence of 2 or less traits. Although a direct comparison is impossible because of the difference in the categorization, the risk estimate seems to be similar in the two studies, which could validate the asso-
The dose-response relationship between the number of metabolic syndrome traits and the odds of having kidney stones is shown. The ORs were adjusted for age and gender. The presence of all 5 metabolic syndrome traits was associated with an increased risk of having kidney stones with an OR of 2.67 (95% CI = 1.40-5.08) in relation to the presence of 0-2 traits.
cause the data collection was performed without the knowledge of the study purpose. Third, the accuracy of stone diagnosis, which was confirmed by ultrasonography, minimized misclassification of the outcome. Finally, the availability of glycemic control measurements such as FPG and HbA1c is now widely available.

In conclusion, the present study shows that the number of metabolic syndrome traits is associated with the risk of kidney stones. In addition, glycemic control measures are associated with the risk. The number of metabolic syndrome traits can be easily calculated in daily medical practice and measurements of FPG and HbA1c are now widely available. From such a practical perspective, the present study provides useful information on the risk assessment of kidney stones. Moreover, glycemic control seems to have an independent effect on the risk of kidney stones. This finding may contribute to disentangle the complex etiopathogenesis of kidney stones among obesity, diabetes and metabolic syndrome.

The authors state that they have no Conflict of Interest (COI).

### References

9. Schiavi PO, Schmiedl A, Herrmann U, Wipplinger J. Postprandial hyperinsulinaemia, insulin resistance and inappropriately high

### Table 3. ORs of Having Kidney Stones in Terms of Fasting Serum Insulin, HOMA-IR, Fasting Plasma Glucose and HbA1c

<table>
<thead>
<tr>
<th>Presence of kidney stones</th>
<th>Model 1 a</th>
<th>Model 2 b</th>
<th>Model 3a c</th>
<th>Model 3b d</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>OR (95%CI)</td>
<td>OR (95% CI)</td>
<td>OR (95% CI)</td>
<td>OR (95% CI)</td>
</tr>
<tr>
<td>Fasting serum insulin</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1st tertile</td>
<td>1.00</td>
<td>1.00</td>
<td>1.00</td>
<td>1.00</td>
</tr>
<tr>
<td>2nd tertile</td>
<td>1.00</td>
<td>1.00</td>
<td>1.00</td>
<td>1.00</td>
</tr>
<tr>
<td>3rd tertile</td>
<td>1.00</td>
<td>1.00</td>
<td>1.00</td>
<td>1.00</td>
</tr>
<tr>
<td>p for trend</td>
<td>p=0.015</td>
<td>p=0.058</td>
<td>p=0.103</td>
<td></td>
</tr>
<tr>
<td>HOMA-IR</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1st tertile</td>
<td>1.00</td>
<td>1.00</td>
<td>1.00</td>
<td>1.00</td>
</tr>
<tr>
<td>2nd tertile</td>
<td>1.00</td>
<td>1.00</td>
<td>1.00</td>
<td>1.00</td>
</tr>
<tr>
<td>3rd tertile</td>
<td>1.00</td>
<td>1.00</td>
<td>1.00</td>
<td>1.00</td>
</tr>
<tr>
<td>p for trend</td>
<td>p=0.026</td>
<td>p=0.157</td>
<td>p=0.287</td>
<td></td>
</tr>
<tr>
<td>Fasting plasma glucose</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt; 100 mg/dL</td>
<td>1.00</td>
<td>1.00</td>
<td>1.00</td>
<td>1.00</td>
</tr>
<tr>
<td>100- &lt;126 mg/dL</td>
<td>1.00</td>
<td>1.00</td>
<td>1.00</td>
<td>1.00</td>
</tr>
<tr>
<td>≥ 126 mg/dL</td>
<td>1.00</td>
<td>1.00</td>
<td>1.00</td>
<td>1.00</td>
</tr>
<tr>
<td>HbA1c (%)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt; 5.5 %</td>
<td>1.00</td>
<td>1.00</td>
<td>1.00</td>
<td>1.00</td>
</tr>
<tr>
<td>5.5- &lt;6.0 %</td>
<td>1.00</td>
<td>1.00</td>
<td>1.00</td>
<td>1.00</td>
</tr>
<tr>
<td>6.0- &lt;6.5 %</td>
<td>1.00</td>
<td>1.00</td>
<td>1.00</td>
<td>1.00</td>
</tr>
<tr>
<td>≥6.5 %</td>
<td>1.00</td>
<td>1.00</td>
<td>1.00</td>
<td>1.00</td>
</tr>
<tr>
<td>p for trend</td>
<td>p=0.001</td>
<td>p=0.009</td>
<td>p=0.016</td>
<td>p=0.012</td>
</tr>
</tbody>
</table>

a Model 1: Adjusted for age and gender. b Model 2: Model 1 + adjusted for BMI, smoking, uric acid and metabolic syndrome traits (abdominal obesity, hypertension, hyperglyceridemia and low HDL-C). c Model 3a: Model 2 + adjusted for HOMA-IR. d Model 3b: Model 2 + adjusted for fasting serum insulin.

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