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Characteristics of the glycometabolic categories based on the oral glucose tolerance test results in Japanese adults without diabetes

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Abstract. – OBJECTIVE: We aimed to classify Japanese adults without diabetes into different categories based on the oral glucose tolerance test (OGTT) and characterize their insulin sensitivity and insulin secretion.

PATIENTS AND METHODS: The OGTT was performed on 1,085 Japanese individuals without diabetes (aged 20–64 years); blood glucose and insulin levels were measured at 0, 30-, 60-, 90-, and 120-min. Fasting blood chemistry, hematology, and urine were analyzed. The participants were classified into four categories based on the following: (A) 30 min post-load plasma glucose levels < 157 mg/dL and/or (B) 120 min post-load plasma glucose levels < 126 mg/dL and Matsuda index > 4.97. Category 1 satisfied both conditions, category 2 satisfied condition A but not B, category 3 satisfied condition B but not A, and category 4 satisfied neither condition.

RESULTS: Overall, 46%, 21%, 13%, and 20% of the participants were classified into categories 1, 2, 3, and 4, respectively. Compared with category 1, the characteristics of the other categories were: 2, low insulin sensitivity and high blood glucose levels during the later period; 3, low insulin secretion and a rapid increase in blood glucose levels; and 4, combined characteristics of categories 2 and 3. Most blood test values besides glucose metabolism in category 4 were also worse than those in category 1. Categories 1 and 2 had a high proportion of females, whereas categories 3 and 4 had a low proportion.

CONCLUSIONS: Japanese adults without diabetes are classified into four categories with different insulin sensitivities and insulin secretion using OGTT results. Each category has different characteristics of age and sex distribution and clinical values besides glucose metabolism.

Key Words:
Diabetes mellitus, Glucose tolerance test, Prediabetic state.

Introduction

Early prediabetes detection and lifestyle improvement are essential for diabetes prevention[1-4]. For this reason, it is crucial to monitor the state of glucose metabolism in individuals. The oral glucose tolerance test (OGTT) is important to evaluate the state of glucose metabolism and diagnose a prediabetic state and diabetes[5]. However, this test is typically performed in patients either already diagnosed with diabetes or suspected of having diabetes and is rarely performed in those who are healthy. Accordingly, the glucose metabolism profile of the population without diabetes remains unclear.

Impaired glucose tolerance (IGT) and impaired fasting glycaemia (IFG) refer to metabolic states intermediate between normal glucose metabolism and diabetes[5] and are established risk categories for diabetes[6,7]. IGT and IFG present overlapping pathophysiology and both states exhibit decreased insulin sensitivity and secretion. The contribution of these factors to diabetes is different among various ethnic populations. Therefore, other categories to clearly distinguish between decreased insulin sensitivity and secretion may be helpful for characterizing glucose metabolism in the population without diabetes.

In this study, we aimed to elucidate the glucose metabolism in a population without diabe-

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tes. For this purpose, we recruited Japanese participants aged 20-64 years without diabetes to undergo the OGTT and classified them into four glycometabolic categories based on the results. We investigated the different characteristics of their glucose metabolism, the characteristics of age and sex distribution, and clinical values in addition to glucose metabolism. The reference values for the classification were 30 min post-load plasma glucose (30 mPG), 120 min post-load plasma glucose (120 mPG), and the Matsuda index (whole-body insulin sensitivity index). The 120-mPG value during the OGTT is used to diagnose IGT[5] and is a predictor of diabetes[8]. Other plasma glucose levels during the OGTT are also risk factors for diabetes[9-14]. A 30 mPG is also a risk factor for diabetes independent of fasting blood glucose and 120 mPG values[15,16]. These values are associated with insulin sensitivity and insulin secretion. Wang et al[17] reported that a glucose peak time during OGTT in patients with diabetes reflects their insulin sensitivity and insulin secretion. The Matsuda index is derived from the measured insulin and glucose levels during the OGTT and reflects a composite of both hepatic and peripheral insulin sensitivity, thus being strongly correlated with the hyperinsulinemic-euglycemic clamp[18].

Patients and Methods

Study Design and Participants

This cross-sectional study involved 1,085 Japanese adults (543 men and 542 women) without diabetes. The selection criteria were as follows: (1) participants aged between 20 and 64 years and (2) those who provided written informed consent. The exclusion criteria were as follows: (1) females who were pregnant, lactating, or planned to become pregnant during the study; (2) individuals who participated in other clinical studies within the past 4 weeks; (3) individuals with current heart, liver, or kidney disorders; or (4) individuals with diabetes. Diabetes was defined as a fasting plasma glucose level ≥ 126 mg/dL, a 120 mPG value ≥ 200 mg/dL, and/or the use of anti-diabetic medications[5]. The participants fasted overnight before undergoing urine collection, anthropometry, and venous blood sampling. Blood samples were used for hematological and biochemical examinations and fasting glucose and insulin level measurements. The participants then drank a 75 g glucose solution, following which venous blood was collected after 30, 60, 90, and 120 min. These blood samples were used for glucose and insulin levels measurements.

Physical, Hematological, and Biological Assessments

Physical factors including height and weight were measured. The body mass index (BMI) was calculated as the weight divided by height squared (kg/m^2). Systolic blood pressure (SBP) and diastolic blood pressure (DBP) were also measured.

The blood collected from the participants after overnight fasting was used for examining the counts/levels of the following: white blood cells (WBC), red blood cells (RBC), hemoglobin (Hb), platelets (Plt), and hematocrit (Ht).

The following biological factors were examined: liver function [total protein (TP), albumin (ALB), aspartate aminotransferase (AST), alanine aminotransferase (ALT), total bilirubin (T-Bil), and gamma-glutamyl trance peptide (γ-GTP)]; renal function [blood urea nitrogen (BUN), creatinine (CRE), and uric acid (UA)]; lipid metabolism profile [triglyceride (TG), total cholesterol (T-cho), low-density lipoprotein cholesterol (LDL-cho), and high-density lipoprotein cholesterol (HDL-cho)]; glycometabolism profile [glucose, insulin, hemoglobin A1c (HbA1c), glycoalbumin (GA), and 1,5-anhydroglucitol (1,5-AG)]; and other profiles [alkaline phosphatase (ALP), lactate dehydrogenase (LDH), creatine phosphokinase (CPK), calcium (Ca), sodium (Na), potassium (K), chlorine (Cl), and iron (Fe)].

Urine samples were collected, and urobilinogen, glucose, and protein levels were quantified. The Matsuda index was calculated as follows to reflect insulin sensitivity: 10,000/[square root of (fasting glucose × fasting insulin) × (mean glucose × mean insulin during the OGTT)]. Homeostatic model assessment–insulin resistance (HOMA-IR) was used as another indicator of insulin sensitivity. HOMA of β cell function (HOMA-β) was used as an index to reflect the insulin secretion. The insulinogenic index was calculated as follows to reflect the initial insulin secretion after glucose loading: (30 min post-load plasma insulin − fasting blood insulin)/(30 min post-load plasma glucose − fasting plasma glucose)[19]. The disposition index was calculated as follows to assess β cell function: insulinogenic index/HOMA-IR[20].

Classification of Glycometabolic Category

Plasma glucose concentrations during the OGTT and the Matsuda index were used to dif-

ferentiate the participants in categories based on the following: condition A, 30 mPG < 157 mg/dL; condition B, 120 mPG < 126 mg/dL, and Matsuda index > 4.97. Category 1 satisfied conditions A and B; category 2 satisfied condition A but not condition B; category 3 satisfied condition B but not condition A, and category 4 satisfied neither condition A nor condition B.

The rationale for determining these specific boundary values was as follows. The threshold of 30 mPG was selected based on the findings of Hirakawa et al[16], who divided 30 mPG levels into four groups by quartiles in a Japanese cohort study; a significant increase in the risk of type 2 diabetes was observed in the third quartile (30 mPG = 157-177 mg/dL), compared to the one in the first quartile (30 mPG ≤ 135 mg/dL). The 120 mPG threshold is widely used for the diagnosis of prediabetes[5]. IGT was defined as a 120-mPG value between 140 and 199 mg/dL. However, we set the lower limit of 120 mPG at 126 mg/dL. This limit was derived from a fasting blood glucose level of 126 mg/dL, which is the diagnostic criterion for diabetes. Although the blood glucose level in the OGTT reflects the state of glucose metabolism, a more accurate classification may be achieved by observing the insulin level. The Matsuda index is an index of systemic insulin sensitivity derived from insulin and glucose levels during the OGTT[18]. Yoshinari et al[21] reported a cut-off value of the Matsuda index of 4.97 for its optimal discriminatory ability for assessing the risk of incident diabetes in a Japanese cohort study; therefore, this value was selected for the present study. We set these limits for the glycometabolic categories more strictly than those for prediabetes because we considered that detecting a decline in glucose metabolism at an early stage is clinically important.

Statistical Analysis

The data are presented as the mean and 95% confidence interval (CI). The characteristics of each glycometabolic category and the OGTT values were compared using the analysis of variance (ANOVA) with Dunnett's test for multiple comparisons. Category 1 served as the reference for the analyses. For the insulinogenic index and disposition index, outliers were excluded using the Smirnov-Grubbs test. Statistical analyses were performed using R ver. 4.1.0 (R Foundation for Statistical Computing, Vienna, Austria). A p-value of < 0.05 was considered to indicate statistical significance.

Results

Characteristics of Each Glycometabolic Category

Of the 1,085 participants, 12 dropped out and 32 were diagnosed with diabetes during the OGTT and were therefore excluded from the study. The remaining 1,041 participants were classified into the four glycometabolic categories. Table I shows the characteristics of the participants in each category. The mean BMI, SBP, and DBP values of participants in categories 2 and 4 were higher than those of participants in category 1. The mean HbA1c levels for participants in categories 2, 3, and 4 were significantly higher than those for participants in category 1. The mean values of most of the blood tests were the worst for participants in category 4. The following values showed significant differences between participants in categories 4 and 1: WBC, RBC, Hb, and Ht (hematological examination); TP, AST, ALT, and γ-GTP (liver function); UA (renal function); TG, T-cho, and LDL-cho (lipid metabolism profiles); and ALP, LDH, and Cl (other profiles) (Table I and **Supplementary Table I**). In contrast, only UA, LDH, Hb, and Ht values showed significant differences between participants in categories 3 and 1. The mean age of participants in categories 3 and 4 was significantly higher than that of participants in category 1. Categories 1 and 2 had a higher proportion of females than categories 3 and 4.

Blood Glucose and Insulin Levels of Each Glycometabolic Category Based on the OGTT Results

Figure 1 shows the mean blood glucose and insulin levels of each glycometabolic category obtained in the OGTTs. The 120 mPG values of participants in category 2 remained higher than those of participants in category 1. The insulin levels of participants in category 2 were higher than those of participants in category 1 at all time points. The blood glucose levels of participants in category 3 sharply increased immediately after the glucose load compared with those of participants in category 1 but returned near to the fasting blood glucose level within 2 hours. In contrast, despite the high 30 mPG values, the insulin levels of participants in category 3 were not significantly different from those of participants in category 1 at any time point. The blood glucose level of participants

Table I. Characteristics of the participants in each glycometabolic category.

Values	Category 1	Category 2	Category 3	Category 4
n	482	217	139	203
Proportion of women (%)	53.1	55.8	38.8	45.3
Age (years)	41.9 (40.9-42.9)	43.6 (42.1-45.1)	46.3 (44.3-48.2)*	48.4 (46.9-49.9)*
Physical measurements				
BMI (kg/m^2)	21.4 (21.1-21.6)	23.6 (23.1-24.0)*	21.6 (21.2-22.0)	23.3 (22.8-23.7)*
SBP (mmHg)	116 (114.7-117.3)	121.8 (120-123.7)*	118.6 (116.1-121.1)	123.8 (121.5-126.1)*
DBP (mmHg)	72.4 (71.5-73.3)	77.7 (76.2-79.3)*	74.2 (72.4-76)	79.8 (78.3-81.2)*
Glycometabolic values				
1,5-AG (μg/mL)	22 (21.3-22.6)	21.2 (20.2-22.2)	20.9 (19.6-22.2)	19.5 (18.5-20.4)*
GA (%)	13.9 (13.8-14.0)	13.6 (13.4-13.7)*	13.9 (13.7-14.1)	13.7 (13.6-13.9)
HbA1c (%)	5.2 (5.2-5.2)	5.3 (5.3-5.3)*	5.3 (5.3-5.4)*	5.4 (5.4-5.5)*
Blood biochemical values				
TP (g/dL)	7.3 (7.2-7.3)	7.4 (7.3-7.4)*	7.3 (7.2-7.4)	7.4 (7.3-7.4)*
ALB (g/dL)	4.4 (4.4-4.4)	4.4 (4.4-4.5)	4.4 (4.4-4.5)	4.4 (4.4-4.5)
AST (U/L)	20.7 (20.1-21.2)	22.0 (20.8-23.2)	22.3 (21.3-23.3)	24.0 (22.9-25.2)*
ALT (U/L)	17.7 (16.9-18.5)	24.2 (21.5-27)*	19.4 (17.9-20.9)	25.8 (23.3-28.3)*
T-Bil (mg/dL)	0.7 (0.7-0.8)	0.7 (0.7-0.7)	0.7 (0.7-0.8)	0.7 (0.7-0.8)
γ-GTP (U/L)	23.6 (21.8-25.3)	34.5 (29.3-39.7)*	27.1 (23.3-30.9)	40.1 (34.6-45.6)*
BUN (mg/dL)	12.8 (12.5-13.0)	12.5 (12.1-12.9)	13.4 (12.9-14.0)	13.2 (12.7-13.6)
CRE (mg/dL)	0.7 (0.7-0.7)	0.7 (0.7-0.7)	0.8 (0.7-0.8)	0.8 (0.7-0.8)
UA (mg/dL)	4.9 (4.8-5.1)	5.4 (5.2-5.6)*	5.4 (5.1-5.6)*	5.7 (5.5-5.9)*
TG (mg/dL)	75.1 (71.8-78.5)	113.4 (102.2-124.7)*	82.3 (73.9-90.8)	117.9 (104.4-131.4)*
T–Cho (mg/dL)	198.2 (195.1-201.2)	205.6 (200.7-210.4)*	203.1 (196.9-209.3)	212.0 (207.3-216.7)*
LDL–cho (mg/dL)	119 (116.4-121.7)	127.4 (123.0-131.7)*	121.9 (116.6-127.2)	128.4 (123.7-133.1)*
HDL–cho (mg/dL)	69.8 (68.4-71.1)	63.4 (61.4-65.5)*	71.1 (68.5-73.7)	67.8 (65.2-70.3)
ALP (U/L)	187.3 (182.5-192.1)	191.5 (184.7-198.4)	197.2 (187.5-206.9)	207.1 (197.5-216.7)*
LDH (U/L)	175.3 (172.5-178.1)	179.4 (175.3-183.4)	183.1 (177.7-188.5)*	183.6 (179.5-187.7)*
CPK (U/L)	119.6 (107.0-132.3)	103.0 (95.6-110.4)	137.9 (107.5-168.2)	124.9 (109.5-140.4)
Hematological values				
WBC (/μL)	5090.2 (4967.7-5212.8)	5685.2 (5473.1-5897.2)*	5339.6 (5070.9-5608.2)	5665.5 (5478.3-5852.7)*
RBC (104/μL)	465.1 (461.0-469.2)	475.0 (468.9-481.1)*	468.3 (460.8-475.8)	477.3 (470.6-484.1)*
Hb (g/dL)	13.8 (13.6-13.9)	14.1 (13.9-14.3)*	14.1 (13.9-14.4)*	14.3 (14.1-14.5)*
Ht (%)	43.8 (43.5-44.2)	44.8 (44.2-45.3)*	44.8 (44.2-45.5)*	45.4 (44.8-45.9)*
Plt (104/μL)	25.2 (24.7-25.7)	26.1 (25.4-26.8)	25.5 (24.7-26.3)	26.3 (25.5-27.1)

Data are presented as mean (95% confidence interval (CI)), percentage, or number of individuals. *$p < 0.05$ *vs.* category 1. *Abbreviations:* BMI, body mass index; SBP, systolic blood pressure; DBP, diastolic blood pressure; 1.5-AG, 1.5-anhydroglucitol; GA, glycoalbumin; HbA1c, Hemoglobin A1c; TP, total protein; ALB, albumin; AST, aspartate aminotransferase; ALT, alanine aminotransferase; T-Bil, total bilirubin; γ-GTP, gamma-glutamyl trans peptide; BUN, blood urea nitrogen; CRE, creatinine; UA, uric acid; TG, triglyceride; T-cho, total cholesterol; LDL-cho, low-density lipoprotein cholesterol; HDL-cho, high-density lipoprotein cholesterol; ALP, alkaline phosphatase; LDH, lactate dehydrogenase; CPK, creatine phosphokinase; WBC, white blood cells; RBC, red blood cells; Hb, hemoglobin; Ht, hematocrit; Plt, platelet count.

in category 4 sharply increased immediately after glucose loading and remained high even after 120 min. In addition, the insulin level peaked slowly, and a high amount of insulin was secreted during the later period. Statistical analysis showed that, if compared to category 1, significant differences were observed at all time points of glucose and insulin levels except in the insulin levels and 120 mPG values of participants in category 3.

Indices of Insulin Resistance and Secretion for Each Glycometabolic Category

Figure 2 shows the indices of insulin resistance and secretion for each category. The mean HOMA-IR values of participants in categories 2 and 4 were higher than those of participants in category 1, whereas the mean HOMA-IR value of participants in category 3 was not significantly different from that of the participants in category 1. The mean values of the Matsuda index

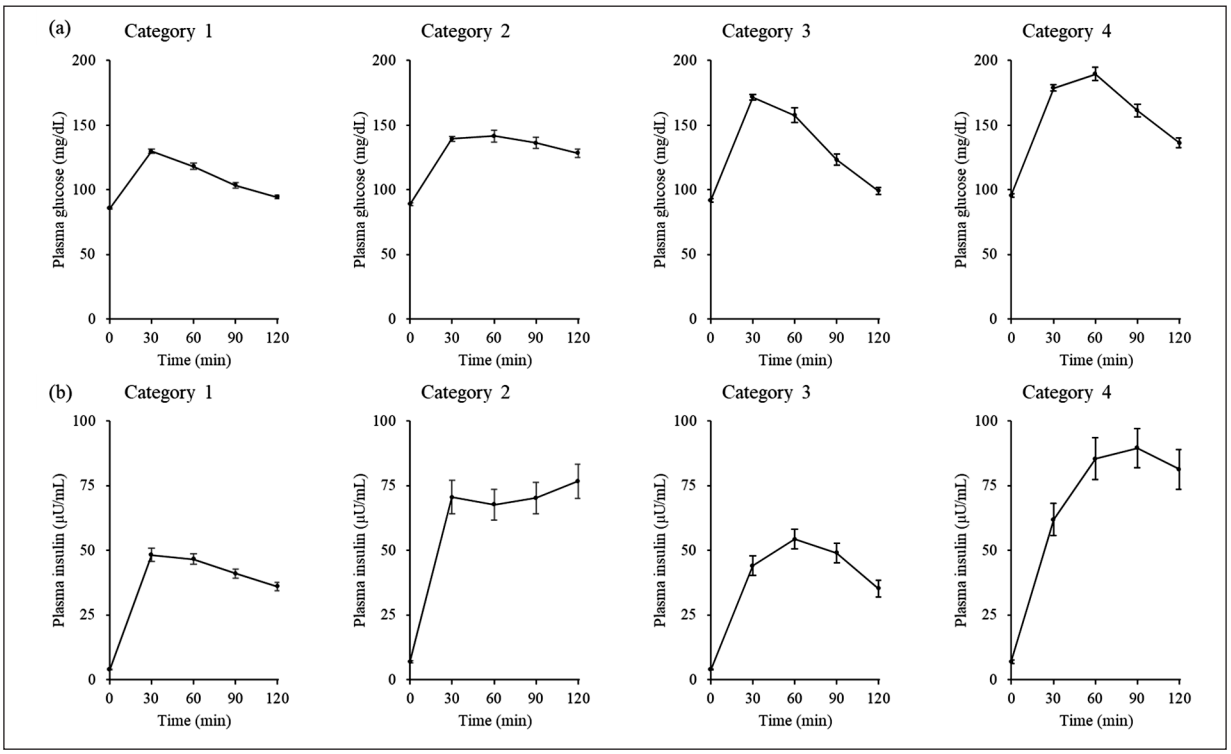

Figure 1. Mean blood glucose and insulin levels of participants in each glycometabolic category in the oral glucose tolerance test (OGTT). Data are presented as mean ± 95% confidence interval. **(a)** Plasma glucose and **(b)** plasma insulin concentration patterns of each glycometabolic category.

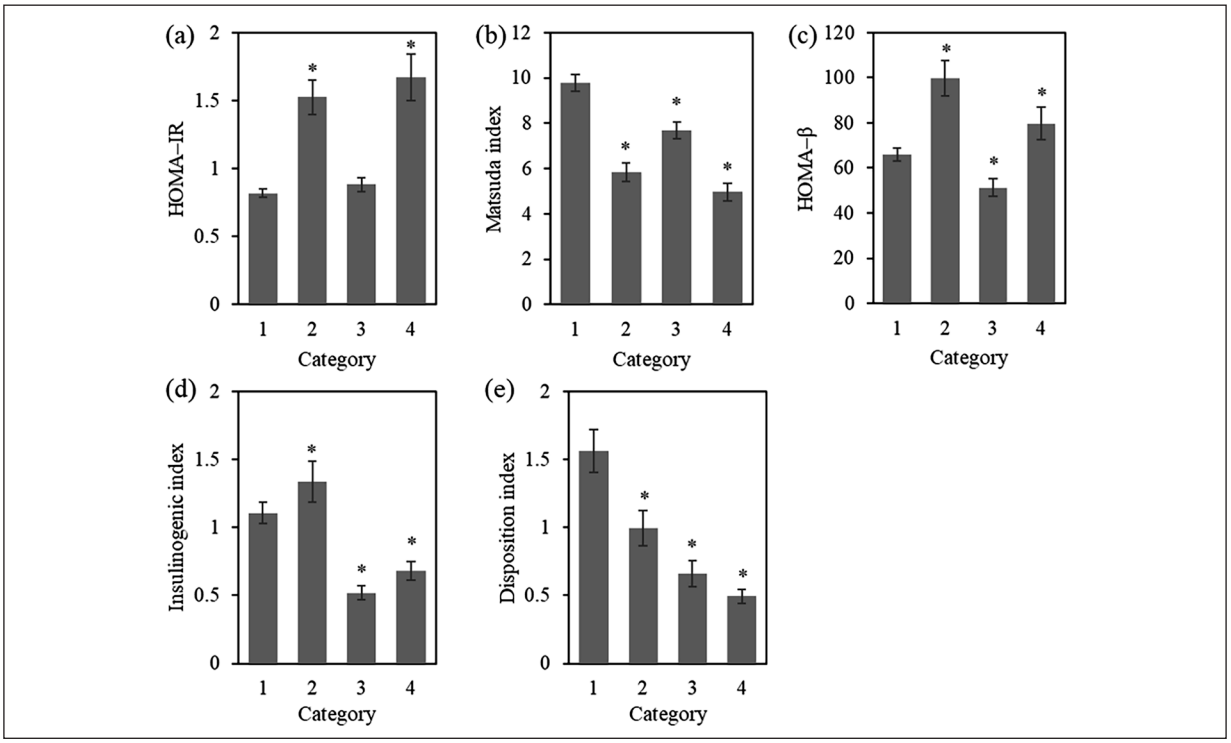

Figure 2. Indices of insulin resistance and secretion in each glycometabolic category. Data are presented as mean ± 95% confidence interval. *$p < 0.05$ *vs.* category 1. **(a)** Homeostatic model assessment–insulin resistance (HOMA-IR); **(b)** HOMA-β, HOMA of β cell function; **(c)** Matsuda index; **(d)** insulinogenic index; and **(e)** disposition index.

for participants in categories 2, 3, and 4 were significantly lower than those of participants in category 1. The mean HOMA-β value of participants in category 3 was significantly lower than that of participants in category 1. The mean values of the insulinogenic index of participants in categories 3 and 4 were significantly lower than those of participants in category 1. The mean values of the disposition index of participants in categories 2, 3, and 4 were significantly lower than those of participants in category 1.

Distribution of Glycometabolic Categories by Age Group and Sex

Table II shows the distribution of glycometabolic categories by age group and sex. Participants in category 4 were older than those in category 1. The proportion of participants in their 20s, 30s, 40s, and 50s, in category 2 was higher than that in category 3, whereas the proportion of participants in their 60s in category 3 was higher than that in category 2. Category 3 had a higher proportion of males than females, whereas category 2 had a higher proportion of females than males in all age groups except for those in their 50s.

Discussion

In this study, we performed the OGTT on Japanese individuals without a prior diagnosis of diabetes or suspected diabetes and classified them into four categories according to their glucose metabolism. The proportion of participants with any extent of glucose metabolism defects (i.e., glycometabolic categories 2, 3, and 4) was 54%, at 21%, 13%, and 20% in categories 2, 3, and 4, respectively. Considering the glucose and insulin concentration patterns in the OGTT, both 120 mPG values and the insulin levels of participants in category 2 were higher than those of participants in category 1. Therefore, participants classified into category 2 may have low insulin sensitivity. The participants in category 3 had a high 30 mPG value but low insulin level 30 min after the glucose load. Therefore, category 3 may be associated with low insulin secretion. The participants in category 4 showed a high blood glucose level immediately after glucose loading, which lasted 120 min. The insulin level peaked slowly with a substantial quantity of secretion in the later period. Therefore, category 4 may be characterized by weak insulin secretion and poor insulin sensitivity. In addition, the impairment in the HOMA-IR and Matsuda index values among participants in categories 2 and 4 confirmed the characteristics of these categories. Similarly, the decrease in the HOMA-β value, insulinogenic index, and disposition index among the participants in categories 3 and 4 confirmed the characteristics of these categories.

Regarding the distribution of glycometabolic categories in each age group, the proportion of participants in their 20s to 50s was higher in category 2 than that in category 3, while this pattern was reversed for participants in their 60s. Additionally, the mean age of the participants in categories 3 and 4 was significantly higher than that of participants in category 1.

Table II. Distribution of glycometabolic categories by age group and sex.

	Age	n	Category 1	Category 2	Category 3	Category 4
Total	20s	144	60% (87)	19% (28)	10% (14)	10% (15)
	30s	239	52% (124)	23% (54)	12% (29)	13% (32)
	40s	226	50% (114)	23% (53)	11% (25)	15% (34)
	50s	338	38% (128)	20% (67)	15% (51)	27% (92)
	60s	94	31% (29)	16% (15)	21% (20)	32% (30)
Men	20s	74	64% (47)	14% (10)	12% (9)	11% (8)
	30s	116	53% (62)	21% (24)	17% (20)	9% (10)
	40s	106	42% (45)	20% (21)	17% (18)	21% (22)
	50s	174	31% (54)	21% (36)	16% (27)	33% (57)
	60s	48	38% (18)	10% (5)	23% (11)	29% (14)
Women	20s	70	57% (40)	26% (18)	7% (5)	10% (7)
	30s	123	50% (62)	24% (30)	7% (9)	18% (22)
	40s	120	58% (69)	27% (32)	6% (7)	10% (12)
	50s	164	45% (74)	19% (31)	15% (24)	21% (35)
	60s	46	24% (11)	22% (10)	20% (9)	35% (16)

Data are presented as the percentage (n) of each category in each age group.

Insulin secretion from β cells decreases with age[22,23]. These results suggest that aging is one of the primary factors that drives the transition to categories 3 and 4. The mean BMI value of participants in category 3 was not significantly different from that of participants in category 1. Asians are more likely to develop type 2 diabetes, even if they are not overweight, due to their lower insulin secretion compared to other ethnic groups[24,25]. Therefore, the genetic background may be another factor that influences the transition to category 3.

Insulin resistance is known to increase with obesity[26-28]; in fact, the mean BMI values of participants in categories 2 and 4 were higher than those of participants in category 1. However, the BMI histogram of women in category 2 was bimodal **(Supplementary Figure 1)**. This indicates that Japanese women may be at a risk of insulin resistance even if they are not overweight. Sato et al[29] reported that underweight young Japanese women had a higher proportion of IGT and showed a higher tendency of insulin resistance than normal-weight young Japanese women. Although the reasons for these observations are not clear, one explanation is that underweight Japanese women have a higher percentage of body fat than their counterparts from other ethnicities (Americans and African Americans)[30] and consequently a lower muscle mass to metabolize glucose. The ratio of the participants of each age group in category 2 did not increase linearly with increasing age. Additionally, the mean age of the participants in category 2 was not significantly different from that of participants in category 1. These results suggest that the transition from category 1 to 2 depends more on weight gain and low muscle mass than on ageing.

The blood test values besides glucose metabolism had different characteristics in each category. Only four blood test values of category 3 participants were significantly different from those of category 1 participants. Conversely, many blood test values of participants in categories 2 and 4 from hematological examination, liver function, renal function, lipid metabolism profiles, and other profiles were significantly worse than those of category 1. Low insulin sensitivity is associated with various molecular mechanisms, such as inflammation, lipotoxicity, and mitochondrial dysfunction[31,32]. These results suggest that the category with low insulin sensitivity rather than low insulin secretion has a poorer general condition. A total of 16% of the participants met the World Health Organization (WHO) diagnostic criteria for prediabetes; 15% of the participants had IGT, 1% had IFG, and 1% had combined glucose intolerance (CGI) **(Supplementary Table II)**. All groups of patients with prediabetes had overlapping pathophysiology, with both decreased insulin sensitivity and decreased insulin secretion **(Supplementary Figure 2)**. Therefore, the classification of prediabetes cannot separate the characteristics of the glucose metabolism in this population. We also tried to classify the four categories using only 30 and 120 mPG values **(Supplementary Table III)**. However, categories 2 and 3 had similar levels of insulin sensitivity. In addition, the insulinogenic index value was low in both categories 2 and 3 **(Supplementary Figure 3)**. Therefore, the glycometabolic categories using Matsuda index were needed to clearly explain the insulin sensitivity and insulin secretion in the participants.

This study has some limitations. First, the study was conducted only on Japanese individuals; therefore, whether these characteristics also exist in other ethnicities remains to be elucidated. Second, as this was a cross-sectional study, the prognosis of each glycometabolic category remains unclear. Impaired β cell function and insulin resistance, especially the combination of both, contribute to the development of type 2 diabetes in Japanese communities[21]; therefore, the glycometabolic categories may differ not only in current glucose metabolism characteristics but also in the risk of developing diabetes in the future. Follow-up studies for these populations may reveal a relationship between each glycometabolic category and the risk of developing diabetes and other diseases.

Conclusions

In this study, we classified Japanese adults without diabetes into four glycometabolic categories using OGTT results. Each category had different characteristics of insulin sensitivity and insulin secretion. In addition, the age and sex distribution and clinical values besides glucose metabolism showed different characteristics in the participants of each category. Further research is needed to better understand how these categories in individuals without diabetes are related to the risk of developing diabetes and other diseases.

Conflict of Interest

H.K. is an employee of Suntory Beverage and Food Limited. The funders had no role in the design of the study; in the collection, analyses, or interpretation of data; in the writing of the manuscript; or in the decision to publish the results.

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Approval of the research protocol: This study was conducted in accordance with the guidelines laid down in the Helsinki Declaration (as revised by the Fortaleza General Meeting of the World Medical Association, Brazil, 2013), and all procedures involving human participants were approved by the Ethics Committee of Suntory Holdings Limited. This study complied with the Ethical Guidelines for Medical Research Involving Human Subjects (2014 Ministry of Education, Culture, Sports, Science and Technology and the Ministry of Health, Government of Japan, Labor and Welfare Ministerial notification No. 3). All participants provided written informed consent.

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Authors' Contribution

Contributors are as follows. Conceptualization, T.U., T.T., S.F., Y.N., and N.M.; investigation, T.U., T.T., and H.K.; formal analysis, T.U. and T.T.; writing and original draft preparation, T.U. and T.T.; supervision, M.S. All authors have read and agreed to the published version of the manuscript.

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