#### Original article

# Examination of postprandial blood glucose prediction model using food nutrition component values

Shiori Uenaka<sup>1)</sup>, Mari Ogura<sup>1,2)</sup>, Masayuki Yagi<sup>1)</sup>, Wakako Takabe<sup>1,3)</sup>, Yoshikazu Yonei<sup>1)</sup>

2) Department of Food and Nutrition, Kyoto Bunkyo Junior College

 Department of Materials and Life Science, Faculty of Science and Technology, Shizuoka Institute of Science and Technology, Shizuoka, Japan

### Abstract

**Objective:** One of the methods for reducing glycative stress is to suppress postprandial hyperglycemia (PPHG). The purpose of this study is to establish a non-invasive and easy-to-implement means for suppressing PPHG. Based on the results of the past intake tests of various foods, a model formula for predicting the degree of PPHG from food contents was created.

**Methods:** A model formula was created to predict the indices for PPHG, *i.e.* iAUC (incremental area under the curve),  $\Delta$ Cmax (maximum blood glucose concentration), based on iAUC (mg/dL · min) or  $\Delta$ Cmax when ingested a standard food (*i.e.*, cocked rice, udon, and bread) and the nutritional component of the test food. The past results of the model food intake test in our laboratory were used to create the predictive model formula. We applied 18 kinds of food to the formula and verified the degree of coincidence with the actual postprandial glucose change. Then, the mean absolute relative difference (MARD) between the predicted value and the measured value was calculated for each food (n = 18) and for each subject (n = 159) in the 18 tests. In a subclass analysis, subjects were divided into three groups: top 25% (n = 42, iAUC; 7,379.9 ± 146.5), middle (n = 75, iAUC; 5,302.7 ± 73.5), and bottom 25% (n = 42, iAUC; 3,243.9 ± 61.5), based on iAUC at standard food intake. Pearson's correlation analysis was used to test the correlation between predicted and measured values, and Turkey's HSD test was used to analyze MARD.

**Results:** In the simulation of the food intake test (18 types), a highly positive correlation of r = 0.7 was observed between the predicted and measured value, and the average MARD was less than 15%. A subclass analysis showed the MARD in the top 25% group were lower than those in the bottom 25% group (p < 0.05).

**Conclusion:** A high correlation was found between the predicted value from the model formula and the measured value. Among them, the accuracy of prediction tended to be higher as the data of the subjects whose blood glucose was more likely to rise.

KEY WORDS: postprandial hyperglycemia, protein, fat, acetic acid, citric acid, dietary fiber

# Introduction

The phenomenon caused by the non-enzymatic binding of reducing sugars, *i.e.*, glucose and fructose, to proteins *in vivo* and the production and accumulation of advanced glycation end products (AGEs), which are the causative agents of age-related degeneration, is called "glycative stress". Glycative stress is one of the risk factors for aging and plays a role in the development of diseases such as skin aging and diabetic complications <sup>1, 2)</sup>. Reduction of glycative stress includes suppression of rapid postprandial hyperglycemia

Contact Address: Professor Masayuki Yagi

Medical Sciences, Doshisha University

Co-authors: Uenaka S, ctud2025@mail4.doshisha.ac.jp;

Mari O, m-ogura@po.kbu.ac.jp; Takabe W, takabe.wakako@sist.ac.jp; Yoshikazu Y, yyonei@mail.doshisha.ac.jp

<sup>1)</sup> Anti-Aging Medical Research Center/Glycative Stress Research Center, Graduate School of Life and Medical Sciences, Doshisha University, Kyoto, Japan

Anti-Aging Medical Research Center, Graduate School of Life and

<sup>1-3,</sup> Tatara Miyakodani, Kyotanabe-shi, Kyoto, 610-0321 Japan

TEL/FAX: +81-774-65-6394 e-mail: myagi@mail.doshisha.ac.jp

(PPHG), suppression of glycation reaction, and promotion of decomposition and excretion of AGEs. Of these, suppression of PPHG is a measure that can be easily incorporated into the daily diet.

The Glycemic Index (GI) was proposed by Jenkins DJ et al.<sup>3</sup> in 1981 as an index showing the degree of PPHG in foods. GI is an index developed to "qualitatively" evaluate the in vivo function of a certain amount of carbohydrates, focusing on the difference in the physiological functions of carbohydrates contained in foods. In Japan, Sugiyama et al.<sup>4)</sup> are trying to find GI in combination with a variety of foods based on cooked rice, and to incorporate the PPHG reaction in Japanese foods into nutrition education. It is concluded that these nutrition education methods are useful for disease prevention and health promotion. Furthermore, it has been reported that the GI can be lowered by combining cooked rice as a staple food with vegetable salad, vinegar, soybeans, and milk and dairy products 5,6). Therefore, the introduction of foods that reduce GI by co-ingestion with carbohydrates can be also effective in suppressing PPHG. However, Japanese food is characterized by ingesting many types of food in combination, for example, a "combination food" with a staple food, or a "composite food" with a staple food, main dish, and side dish, thus it is often difficult to apply the GI evaluated for each food. It is required to evaluate GI by ingesting multiple foods at once in a "food form".

The GI measurement is usually started to perform on the subjects from 7 to 9 a.m. without breakfast. Since the blood glucose level is measured about 7 times every 15 to 30 minutes from the start of ingestion of the test food, there are problems of multiple invasions and restraint time. Therefore, a method that does not require blood sampling is required to quickly evaluate the GI of various foods.

We have reported model foods (salad chicken, olive oil, grain vinegar, cabbage, and lemon juice), that are rich in nutritional components (protein, lipids, acetic acid, dietary fiber, and citric acid) that have been reported to reduce PPHG, was examined for its effect of suppressing the elevation in blood glucose when each food with different amounts was ingested before cooked rice<sup>7,8)</sup>. As a result, it was shown that the PPHG inhibitory effect of each nutritional component becomes stronger as the intake is increased. Additionally, when a complex food containing a part or all of each nutritional component was ingested before ingestion of cooked rice, strong suppression of PPHG was observed as compared with that of cooked rice alone. It was considered that this action was due to the fact that each nutritional component contained in the complex food worked synergistically and contributed to the PPHG suppressing effect.

In this study, we created a model formula for predicting the degree of PPHG from dietary content based on the results of intake tests of various model foods conducted in the past. Furthermore, the model formula created was applied to 18 types of food that had already been verified in the test, and the coincidence with the actual postprandial blood glucose change was analyzed, thus attempting a postprandial blood glucose simulation.

### **Methods**

# Creation of prediction model formula for postprandial blood glucose change

A model formula was created to predict indices for PPHG (iAUC,  $\Delta$ Cmax) when a test food was ingested by using the data of the incremental area under the curve (iAUC [mg/dL · min]) or maximum blood glucose concentration ( $\Delta$ Cmax [mg/dL]) and the nutritional component value of the test food. The results of the model food intake studies conducted in our laboratory were used to create the predictive model formula. Furthermore, simulation of PPHG was performed by substituting the results of the dietary intake tests of 18 cases conducted in our laboratory into the created prediction model formula.

#### Simulation of PPHG

Regarding the test food (test food + carbohydrate) and data of iAUC and  $\Delta$ Cmax used in the simulation, we used the verification results of 18 tests conducted in our laboratory from 2014 to 2020 as follows (*Table 1*)<sup>7,9-13</sup>);

- Beef bowl A (standard food: rice 230 g): (test food: beef bowl [gyudon] fixings 135 g) + rice 230 g<sup>9</sup>. Here, rice means cooked rice. The fixing consists of beef meat, onion, and sauce for gyudon.
- Beef bowl B (standard food: rice 230 g): (test food: beef bowl fixings 135 g + ginger 15 g) + rice 230 g<sup>9</sup>).
- Beef bowl C (standard food: rice 200 g): (test food: beef bowl fixings 125 g) + rice 200 g<sup>10</sup>.
- Beef bowl D (standard food: rice 200 g): (test food: beef meat 65 g) + rice 200 g<sup>10</sup>.
- Beef bowl E (standard food: rice 200 g): (test food: beef meat 65 g) + rice 200 g<sup>10</sup>).
- Breakfast A (standard food: rice 200 g): (test food: beef bowl fixings 135 g) + rice 200 g<sup>11</sup>).
- Breakfast B (standard food: rice 200 g): (test food: rice ball [onigiri] 113 g + bread 90 g)<sup>11)</sup>.
- Breakfast C (standard food: rice 200 g): (test food: 60 g of eggs, 3 wieners, 5 g of salad oil, 15 g of hashed potatoes, and 12 g of ketchup) + rice  $200 g^{11}$ .
- Vinegar rice (standard food: rice 200 g): (test food: sushi vinegar 21 g) + rice  $177 g^{7}$ .
- Fried chicken A (standard food: rice 200 g): (test food: fried chicken 135 g) + rice  $149 \text{ g}^{7}$ ).
- Fried chicken B (standard food: rice 200 g): (test food: fried chicken 135 g and lemon juice 15 g) + rice 145  $g^{7}$ ).
- Gyoza (standard food: rice 200 g): (test food: gyoza 138 g and ponzu soy sauce 15 g) + rice 129 g<sup>7</sup>). Gyoza are fried dumplings with vegetable and meat ingredients in a flour wrapper.
- Grapefruit (GF) smoothie (standard food: bread 170 g): (test food: GF smoothie 230 g) + bread 132 g<sup>12</sup>).
- Citric acid water (standard food: bread 170 g): (test food: citric acid solution 200 g) + bread 170 g<sup>12</sup>).
- Mapo eggplant bowl (standard food: 200 g of rice): (test food: eggplant with rice [mabo-don] \*) + rice 180 g<sup>13</sup>).
- Mapo eggplant udon (standard diet: udon with dietary fiber 250 g): (test diet: eggplant with dietary fiber \*) +

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	Test food	Number of subjects	Age
	Beef bowl A	4 males, 4 females	$23.3 \pm 1.3$
	Beef bowl B	4 males, 2 females	$23.0 \pm 1.3$
	Beef bowl C	3 males, 3 females	$22.2 \pm 1.0$
	Beef bowl D	3 males, 3 females	$22.2 \pm 1.0$
	Beef bowl E	3 males, 3 females	$22.2 \pm 1.0$
	Breakfast A	6 males, 8 females	$22.2 \pm 0.9$
	Breakfast B	6 males, 8 females	$22.2 \pm 0.9$
	Breakfast C	5 males, 7 females	$22.0 \pm 0.4$
	Vinegar rice	2 males, 9 females	$23.1 \pm 1.3$
	Fried chicken A	5 males, 9 females	$23.0 \pm 1.3$
	Fried chicken B	5 males, 9 females	$23.0 \pm 1.3$
	Gyoza+ponzu soy sauce	5 males, 9 females	$23.0 \pm 1.3$
	GF smoothie	3 males, 5 females	$23.1 \pm 1.2$
	Citric acid water	2 males, 3 females	$23.2 \pm 1.1$
	Mapo eggplant bowl	4 males, 4 females	$22.9 \pm 1.2$
	Mapo eggplant udon	2 males, 3 females	$22.3 \pm 1.2$
	Udon with a soft boiled egg	1 male, 2 females	$23.3 \pm 1.2$
	Salad udon	2 males, 3 females	$23.6 \pm 0.9$
Total	18	159 (65 males, 94 females)	

Table 1. The test food and subjects for the PPHG simulation.

Ages are expressed as mean  $\pm$  standard deviation. Beef bowl A, beef bowl fixings 135 g + rice 230 g; Beef bowl B, beef bowl fixings 135 g + rice 200 g; Beef bowl D, beef bowl meat only + rice 200 g; Beef bowl E, beef bowl onion only + rice 200 g; Breakfast A, beef bowl fixings 135 g + rice 200 g; Breakfast B, cooked rice balls 113 g + bread 90 g; Breakfast C, egg 60 g + three wieners + salad oil 5 g + hash browns 15 g + ketchup 12 g + rice 200 g; Vinegar rice, sushi vinegar 21 g + rice 177 g; Fried chicken A, fried chicken 135 g + porzu soy sauce 15 g + rice 129 g; Grapefruit (GF) smoothie, bread 132 g + GF smoothie 230 g; Citric acid, bread 170 g + citric acid water 200 g; Mapo eggplant bowl, mapo eggplant \* + rice 180 g; Mapo eggplant udon, mapo eggplant + sesame dressing \* + handmade udon 210 g. Rice means cooked rice. \* Intake of mapo eggplant, hot spring egg, vegetable salad, and sesame dressing is unknown.

udon with dietary fiber 230 g<sup>13</sup>). Udon is a thick white noodle made of wheat flour.

- Udon with a soft boiled egg (standard food: kake udon 270 g): (test food: a soft boiled egg \*) + udon 210 g<sup>13)</sup>.
- Salad udon (standard food: kake udon 270 g): (test food: vegetable salad \* + sesame dressing \*) + udon 210 g<sup>13</sup>).
- \* Intake of eggplant with rice, eggplant with dietary fiber, soft boiled eggs, dressing for vegetable salad + sesame is unknown.

The effective analysts adapted to this simulation were a total of 159 young men and women aged between 20 and 30 years at the time of obtaining consent to participate in the study. The measured values used for analysis were the average value for 18 kinds of food and the individual value for 159 subjects. The mean absolute relative difference (MARD) between the predicted value and the measured value was calculated according to the following formula<sup>14</sup>).

 $MARD(\%) = 100 \times | \text{(measured value)} - \text{(predicted value)} | / predicted value}$ 

MARD was calculated for the mean value (n = 18) and individual value (n = 159) of the intake group evaluated in each test. In a subclass analysis, subjects were divided into three groups: top 25% (n = 42, iAUC; 7,379.9  $\pm$  146.5) where blood glucose is likely to rise, middle (n = 75, iAUC; 5,302.7  $\pm$  73.5), and bottom 25% (n = 42, iAUC; 3,243.9  $\pm$  61.5) where blood glucose does not likely rise. Then, the MARD of each group was calculated.

#### Statistical analysis

IMB SPSS Statics 26 (IMB Japan, Minato-ku, Tokyo, Japan) was used for statistical analysis. A two-sided test determined that there was a significant difference when the risk rate was less than 5%, and the results are expressed as mean  $\pm$  standard error (SE). Pearson's correlation analysis was used to test the correlation. When comparing MARDs, the Turkey's HSD test was used.

#### Ethical standards

All 18 dietary intake tests evaluated in this study complied with the Declaration of Helsinki (revised at the 2013 WMA Fortaleza General Assembly) and the ethical guidelines for human medical research (Ministry of Education, Culture, Sports, Science and Technology, Ministry of Health, Labour and Welfare), and carried out in response to the submission of a voluntary consent form. These tests were conducted with the approval of the Ethics Review Committee on "Studies in Humans" 7,9-13).

# Results

### 1. A model formula for prediction of PPHG

# (1) Prediction formula for PPHG after intake of each nutrition

The prediction of iAUC and  $\Delta$ Cmax by ingestion of each nutrient alone is based on the result of the PPHG inhibitory effect when the subjects ate together cocked rice (200 g) and a model food having nutritional components (protein, lipids, acetic acid, dietary fiber, and citric acid), which have been reported to have an effect of alleviating PPHG<sup>7, 8)</sup>, as follows: salad chicken (A), olive oil (B), grain vinegar (C), cabbage (D), and lemon juice (E). In this model, we decided to predict iAUC and  $\Delta$ Cmax by focusing on the relationship between the collected data (iAUC,  $\Delta$ Cmax) and nutritional intake. *Table 2-a* shows an example of the relationship of the protein amount of the test food to the mean value of

iAUC for 120 minutes and  $\Delta$ Cmax. From the mean value of iAUC and  $\Delta$ Cmax after ingestion of the test food with low or high protein, we calculated the reduction value and rate of iAUC and  $\Delta$ Cmax when compared with the intake of only the standard food. Similar calculations were performed for lipids, acetic acid, dietary fiber, and citric acid (*Table 2-b, c, d, e*).

Next, a simple regression analysis was performed with the reduction rate in iAUC and  $\Delta$ Cmax after the test food ingestion as the objective variable and the amount of nutritional components contained in each model food as the explanatory variable (*Table 3*). By substituting x (nutrient component amount) into the obtained regression coefficient, y (iAUC or  $\Delta$ Cmax reduction rate) was obtained when each nutrition component was ingested with cooked rice alone.

# (2) Prediction formula for PPHG depending on the amount of carbohydrates

We created a prediction formula for how much iAUC and  $\Delta$ Cmax increase (calculation of elevated iAUC and  $\Delta$ Cmax) from the carbohydrate amount in the test food and iAUC and  $\Delta$ Cmax when ingested the standard food.

Elevated iAUC = (carbohydrate content of test food) × (iAUC at standard food intake/carbohydrate content of standard food)

Elevated  $\Delta Cmax = (carbohydrate amount of test food) \times (\Delta Cmax at standard food intake/carbohydrate amount of standard food)$ 

Table 2. Predicted values of iAUC,  $\Delta Cmax$ , and reduction rate after ingesting the model food. a)

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	Protein (g)	iAUC (mg/dL • min)	iAUC reduction rate (%)	ΔCmax (mg/dL)	∠Cmax reduction rate (%)
Standard food	0	0.0	0.0	62.7	0.0
AL	11.5	20.9	20.9	54.2	13.6
AH	23.0	35.7	35.7	46.2	26.3
b)					
	Lipids (g)	iAUC (mg/dL • min)	iAUC reduction rate (%)	ΔCmax (mg/dL)	∠Cmax reduction rate (%)
Standard food	0	4,689.8	0.0	62.7	0.0
BL	14	4,085.3	12.9	62.8	- 0.2
BH	28	3,876.7	17.3	55.9	10.9
c)					
	Acetic acid (g)	iAUC (mg/dL • min)	iAUC reduction rate (%)	$\Delta Cmax$ (mg/dL)	∠Cmax reduction rate (%)
Standard food	0	4,689.8	0.0	62.7	0.0
CL	0.6	3,780.0	19.4	54.8	12.6
СН	1.3	3.279.8	30.1	41.2	34.3

u)					
	Fiber (g)	iAUC (mg/dL ∙ min)	iAUC reduction rate (%)	ΔCmax (mg/dL)	∠Cmax reduction rate (%)
Standard food	0	4,689.8	0.0	62.7	0.0
DL	0.9	4,755.0	- 1.4	63.6	- 1.4
DH	1.8	4,478.3	4.5	61.3	2.2

#### e)

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	Citric acid (g)	iAUC (mg/dL ∙ min)	iAUC reduction rate (%)	ΔCmax (mg/dL)	∠Cmax reduction rate (%)
Standard food	0	5,031.9	0.0	71.3	0.0
EL	0.95	4,368.1	13.2	67.4	5.5
EH	1.90	3,784.4	24.8	56.8	20.3

Standard food is cooked rice 200 g in all studies. a) Comparison of protein; AL, salad chicken 55 g before cooked rice 200 g; AH, salad chicken 110 g before cooked rice 200 g, n = 10. b) Comparison of lipids; BL, olive oil 14 g before cooked rice 200 g; BH; olive oil 28 g before cooked rice 200 g, n = 10. 10. c) Comparison of acetic acid; CL, grain vinegar 15 g before cooked rice 200 g; CH, grain vinegar 30 g before cooked rice 200 g, n = 10. d) Comparison of dietary fiber; DL, cabbage 50 g before cooked rice 200 g; DH, cabbage 100 g before cooked rice 200 g, n = 10. e) Comparison of citric acid; EL, lemon juice 15 mL before cooked rice 200 g; EH; lemon juice 30 mL before cooked rice 200 g, n = 12. Results are calculated according to the below equation: iAUC reduction rate (%) = 100 × (iAUC after intake of standard food - iAUC after intake of model food)/iAUC after intake of standard food  $\Delta C$  max reduction rate (%) = 100 × ( $\Delta C$  max after intake of standard food –  $\Delta C$  max after intake of model food)/ $\Delta C$  max after intake of standard food iAUC, incremental area under the curve;  $\Delta Cmax$ , maximum blood glucose concentration.

#### Table 3. Regression analysis between the measured and predicted values.

#### a) iAUC

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	Regression coefficient	Standard error	t-value	p-value	
Protein	1.6054	0.0736	21.826	0.002	
Lipids	0.6795	0.0853	7.9679	0.015	
Acetic acid	25.248	1.9601	12.881	0.006	
Fiber	1.6952	1.1459	1.4793	0.277	
Citric acid	12.555	0.2248	55.839	< 0.001	

#### **b)** ∆Cmax

	Regression coefficient	Standard error	t-value	p-value	
Protein	1.1511	0.0098	117.38	< 0.001	
Lipids	0.3081	0.1130	2.7276	0.112	
Acetic acid	25.771	2.0407	12.629	0.006	
Fiber	0.6734	0.8020	0.8397	0.490	
Citric acid	9.2290	1.3217	6.9827	0.020	

a) Results of simple regression analysis with iAUC reduction rate as the objective variable and the amount of nutrients contained in each model food as the explanatory variable. **b**) Results of simple regression analysis with  $\Delta$ Cmax reduction rate as the objective variable and the amount of nutrients contained in each model food as the explanatory variable. See Table 2 for substitution values; iAUC, incremental area under the curve;  $\Delta Cmax$ , maximum blood glucose concentration.

#### (3) Calculation of predicted iAUC and $\Delta Cmax$

By combining the evaluation methods described in (1) and (2), a predictive model formula for iAUC and  $\Delta Cmax$  was created from the food content. The predicted value of iAUC after ingestion was defined as predicted iAUC, and the predicted value of  $\Delta Cmax$  after ingestion was defined as predicted as predicted  $\Delta Cmax$ .

Predicted iAUC = Elevated iAUC ×  $\{1 - (1.6054 a / 100)\}$  ×  $\{1 - (0.6795 b / 100)\}$  ×  $\{1 - (25.248 c / 100)\}$  ×  $\{1 - (1.6952 d / 100)\}$  ×  $\{1 - (12.555 e / 100)\}$ 

Predicted  $\Delta Cmax = \text{Elevated } \Delta Cmax \times \{1 - (1.1511 a / 100)\} \times \{1 - (0.3081 b / 100)\} \times \{1 - (25.771 c / 100)\} \times \{1 - (0.6734 d / 100)\} \times \{1 - (9.229 e / 100)\}$ 

**a**: protein content, **b**: lipid content, **c**: acetic acid content, **d**: dietary fiber content, and **e**: citric acid content of the test food.

#### 2. Simulation of PPHG

#### (1) PPHG simulation from measured values for each food

PPHG simulation was performed by substituting the verification results of the past 18 tests into the above prediction formula. The predicted iAUC was calculated by substituting the nutritional content and elevated iAUC of the test food of each test into the formula. However, since the nutritional component values of beef bowl D and beef bowl E were unknown, we used the nutritional component values of 65 g of beef (ribs: raw with fat) and 25 g of onion stalk (boiled) listed in Food Composition Table<sup>15</sup> as a reference value. *Figure 1-a* shows the correlation between the measured value and the predicted value. A high positive correlation was found between them; correlation coefficient, r = 0.72; MARD,  $11.7 \pm 2.0\%$ . The food with the smallest MARD was beef bowl D (0.8%), while the food with the highest MARD was beef bowl B (30.8%).

Similarly, the amount of nutritional components and the elevation in  $\Delta$ Cmax of the test food in each test were applied to the prediction formula, and the predicted  $\Delta$ Cmax was calculated. *Figure 1-b* shows the correlation between the measured value and the predicted value. A high positive correlation was found between the measured and predicted value; correlation coefficient, r = 0.70, MARD, 13.7 ± 1.9%. The food with the smallest MARD was udon with a soft boiled egg (0.5%), while the food with the highest MARD was beef bowl D (27.6%).

# (2) PPHG simulation from measured values for each subject

The predicted iAUC was calculated by substituting the nutritional component amount and elevated iAUC of the test foods of 159 subjects in the 18 tests into the prediction model formula. *Figure 2-a* shows the correlation between the measured value and the predicted value. A positive correlation was found between them; correlation coefficient, r = 0.53; MARD,  $32.4 \pm 2.0\%$ . A subclass analysis, in which the subjects (n = 159) was divided into three groups according to the ease with which the blood glucose rose, showed 25.5

 $\pm$  2.3% in the top 25% group (n = 42), and 31.7  $\pm$  2.8% in the middle group (n = 75), and 40.4  $\pm$  5.1% in the bottom 25% group (n = 42) (*Fig. 3-a*). The MARD in the bottom 25% group was significantly higher than that in the top 25% group (p < 0.05).

Similarly, the amount of nutritional components and the elevated  $\Delta$ Cmax were applied to the formula to calculate the predicted  $\Delta$ Cmax. *Figure 2-b* shows the correlation between the measured value and the predicted value. A positive correlation was found between the measured value x of each test and the predicted value; correlation coefficient, r = 0.57; MARD, 24.5 \pm 1.5\%. The subclass analysis showed 21.7  $\pm$  2.4% in the top 25% group, 23.6  $\pm$  2.0% in the middle group, and 28.7  $\pm$  3.4% in the bottom 25% group (*Fig. 3-b*). There was no significant difference between three groups.

### Discussion

Focusing on the PPHG simulation results that evaluated in the standard food group of 18 tests, the MARD between the predicted iAUC/ $\Delta$ Cmax and the measured value was approximated within 15% on average (*Fig.1*). In contrast in the test food group, there was a large difference in the MARD value. This difference may be due to the fact that the nutritional component values of the test foods substituted into the model formula were not accurate, and that the sample size evaluated in each test was biased.

From the simulation results when the individual values of each test were evaluated, it was suggested that the smaller the value of the elevated iAUC at the time of standard food intake, the larger the deviation from the subsequent simulation value of test food intake (*Fig. 3*). In the intake tests evaluated in this study, bread and udon were used in addition to cooked rice as the standard food. Since the GI value of bread and udon is lower than that of cooked rice, it is considered that there was a difference in the ease with which the blood glucose level rose even if the carbohydrate content was the same. Therefore, when one individual uses this prediction formula as a means for preventing PPHG, it is necessary in advance to measure iAUC at the time of ingestion of the standard food, followed by verification of the elevation in blood glucose level.

Additionally in this study, we focused only on the amount of nutritional components in each test food and predicted the association of PPHG. However, since the types of proteins and lipids composed of foods differ greatly, it is considered that there are differences in glucose changes depending on the composition of foods, even with the same nutrient ratio. For example, when grilled beef or boiled mackerel is ingested before rice as a food consisting of protein and lipid, the effects of promoting GLP-1 secretion and prolonging the gastric emptying time are equivalent, while there is a difference in GIP secretion between two types of test foods<sup>16</sup>. It is thought that this is because even if the energy and nutrient ratios of both are the same, the composition of amino acids and lipids are significantly different between beef and blue-backed fish, i.e. mackerel, sardine, and saury. Therefore, in order to apply this prediction

a)



Measured iAUC (mg/dL · min)

b)



#### *Fig.1.* Simulation results from measured values for each food.

**a)** Correlation between the measured iAUC of the simulation target (average value of each intake group) and the predicted iAUC obtained by applying the measured value of the simulation target to the prediction model.

**b**) Correlation between the measured  $\Delta Cmax$  of the simulation target (average value of each intake group) and the predicted  $\Delta Cmax$  obtained by applying the measured value of the simulation target to the prediction model. Results are expressed as mean  $\pm$  SE, n = 18. MARD, mean absolute relative difference; iAUC, incremental area under the curve;  $\Delta Cmax$ , maximum blood glucose concentration; SE, standard error.





#### Fig.2. Simulation results from measured values for each food.

a) Correlation between measured iAUC of simulated target (individual value of each intake group) and predicted iAUC obtained by applying measured value of simulated target to the prediction model.

**b**) Correlation between measured  $\Delta$ Cmax of simulated target (individual value of each intake group) and predicted  $\Delta$ Cmax obtained by applying measured value of simulated target to the prediction model. Results are expressed as mean  $\pm$  SE, n = 159. MARD, mean absolute relative difference; iAUC, incremental area under the curve;  $\Delta$ Cmax, maximum blood glucose concentration; SE, standard error.



#### Fig.3. Box plot of MARD (%) to the measured value and predicted value of each subject.

a) Box Plot of MARD (%) to the measured iAUC and predicted iAUC of each subject.

**b)** Box Plot of MARD (%) to the measured  $\Delta$ Cmax and predicted  $\Delta$ Cmax of each subject. Subjects (n = 159) were divided into three groups by iAUC values; Group A, top 25% (n = 42); Group B, middle (n = 75); Group C, bottom 25% (n = 42). \* p < 0.05, Tukey's HSD (honestly significant difference) test. MARD, mean absolute relative difference; iAUC, incremental area under the curve;  $\Delta$ Cmax, maximum blood glucose concentration.

model from various angles in the future, it is necessary to consider the influence of the amino acid composition and the type of lipids of the food material constituting the test food.

This simulation used data from a food intake test targeting healthy young individuals without impaired glucose tolerance. Currently, the number of patients with lifestylerelated diseases is increasing in Japan, and the number of diabetic patients is increasing remarkably. According to the National Health and Nutrition Survey in 2016<sup>17</sup>, one in five to six people in the population are with diabetes or its reserves. The onset of diabetes is mainly after middle age; however, it is important to control the blood glucose from a young age, because it develops due to the accumulation of lifestyle habits for many years. Therefore, it is expected that this prediction model will be further applied in the future as a non-invasive and easy-to-implement means for young people in selecting a food menu useful for PPHG control from the daily eating habits.

# **Research limitation**

The subjects of this study are all university students or post-graduate students in their 20s. Their living environment is similar. Subjects of other ages are expected to be different in glucose tolerance, frequencies and degrees of PPHG, or gastric emptying time. The simulation model formula proposed this time is mainly applied to subjects in their twenties. The simulation model formula obtained this time is mainly applied to subjects in their twenties. MARD may increase further when applying subjects of other ages.

# Conclusion

In this paper, based on the results of the intake test of model foods, we investigated the prediction of iAUC and  $\Delta$ Cmax as indices for PPHG in subjects with age of twenties from the dietary content. Predictive simulation was performed by applying the created predictive formula to 18 tests that had been conducted in the past. As a result, a high correlation was found between the predicted and the measured value. Among them, the accuracy of the prediction formula tended to be higher as the data of the subjects whose blood glucose level was more likely to rise.

## Conflict of interest declaration

There are no conflicts of interest in carrying out this research.

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