Relationship between underreporting of energy intake and blood ketone levels in Japanese women with obesity: A retrospective study

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Abstract. Underreporting is a problem in dietary surveys, and data on Japanese individuals with obesity are lacking. In addition, in dietary surveys of individuals with obesity, underreporting and extreme energy restrictive practices for short periods of time have been reported, and blood total ketone levels (ketone bodies) may be able to distinguish between these factors. The present study aimed to examine the relationship between underreporting [energy intake (EI)/basal metabolic rate estimate (BMR)] and ketone bodies in obese Japanese women. The participants included 91 women with obesity aged 47±9 years with a body mass index (BMI) of 29.8±3.9 kg/m² who met the exclusion criteria out of 164 individuals who participated in an institutional cohort study baseline survey between September 2006 and September 2015. The current study defined the relationship between EI/BMR, BMI and the participants' ketone body levels. EI/BMR <1.35 and ketone body level <1.0 mmol/l was defined as underreporters, while EI/BMR <1.35 and ketone body level ≥1.0 mmol/l was defined as energy-restricted reporters based on previous research. The EI/BMR of the participants was 1.44±0.32, and 25.3% had an abnormally high level of ketone bodies. Multiple regression analysis indicated that ketone bodies were explanatory variables for EI/BMR. Analysis using EI/BMR and ketone bodies estimated that 26.4% were underreporters and 12.1% were energy-restricted reporters. There were no significant differences in reported energy intake, carbohydrate intake (g/day), and percentage carbohydrate (%) between the underreporters and energy-restricted reporters. In conclusion, low EI/BMR was associated with high ketone body levels in Japanese women with obesity. The combination of EI/BMR and ketone bodies may distinguish between or screen for underreporters and energy-restricted reporters during a dietary survey.

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Introduction

In recent years, the number of individuals with obesity has increased worldwide because of changes in social environments and lifestyles, including dietary habits (1). In treating primary obesity, it is essential to understand the cause of excessive energy intake through dietary surveys and to reduce one's weight by correcting the energy balance. Since underreporting occurs in dietary surveys, it is necessary to obtain information individually (2-5). Generally, the degree of underreporting is assessed using the ratio of reported energy intake to the basal metabolic rate (EI/BMR) (2,6,7). It has been found that overweight and obese individuals, including those in Japan, have a lower EI/BMR value than individuals without obesity, and a large proportion of these are underreported (2,8-11). However, data on obese Japanese individuals are lacking. Furthermore, we have occasionally observed dietary survey data that may reflect not only mere underreporting but also extreme energy-restricted diets challenged by obese individuals for short periods of time. Therefore, some of those judged to be underreported with low EI/BMR may include those with energy deficits due to such extreme diets; distinguishing between these may be useful in accurately determining the diet that led to obesity in each patient and to provide appropriate dietary therapy based on the findings. However, there is no established way to distinguish between or screen for these factors. Because ketone bodies are evaluated in terms of energy shortage (12), it may be possible to distinguish between the two reporter types by combining EI/BMR and ketone bodies.

Accordingly, the purpose of this study was to examine the relationship between EI/BMR, body mass index (BMI), and ketone bodies in obese Japanese women to improve the quality of dietary surveys in the treatment of obesity.

Materials and methods

Participants. This institutional cohort study is an ongoing epidemiological study that began in 1994, primarily targeting women with obesity. This was a retrospective study using data previously collected for a cohort study database.

The participants of this study were those with obesity with a BMI ≥25 kg/m^2 (13) who participated in the baseline survey of the institutional cohort study between 2006 and 2015 and underwent anthropometric measurements, blood tests, and a 3-day dietary survey. All measurements were performed by a trained investigator at the research facility. Because obesity is a complex pathology related to the pre-stage of various diseases, the following exclusion criteria were set to exclude obesity-related conditions in advance, and to target as much as possible, purely obese participants: 1) age >65 years; 2) BMI less than 25 kg/m^2; 3) medication or history of hypertension, dyslipidemia, or diabetes; and 4) missing data. In addition, to exclude the effect of glucose metabolism on ketone bodies, participants with 5) fasting glucose levels of 140 mg/dl or higher or $HbA1_C$ levels of 6.5% or higher were excluded. Anthropometric measurements, blood pressure measurements, and blood tests were performed on those fasting after 22:00 on the day prior and without having had breakfast.

Anthropometric measurements. Fasting measurements of height, body weight, and abdominal circumference were conducted while lightly dressed without shoes or socks, after urinary excretion. Height and body weight measurements were recorded as 0.1 cm and 0.1 kg, respectively, and 1 kg was subtracted from the recorded body weight to adjust for the weight of clothes (14). BMI was calculated using the following formula: weight (kg)/height (m^2). The abdominal circumference was measured using a measuring tape around the navel in 0.1 cm increments, with both feet shoulder-width apart and arms hanging naturally, and with the participants lightly exhaled and relaxed (13).

Blood pressure measurement. The cuff was kept at heart level, and blood pressure was measured in a resting upright sitting position three times at 1-min intervals. The recorded blood pressure was the mean value of three consecutive measurements, with differences between measurements below 10 mmHg. It was re-evaluated if there was a difference of >10 mmHg between the three measurements (14). An upper arm-cuff sphygmomanometer (BP8800; Colin Co., Ltd.) was used for blood pressure measurements.

Blood test. Blood collection and measurement for each blood test item were sourced from SRL Co., Ltd. The inspection items used in this study were as follows. Blood cells were measured for white blood cells (automated method), red blood cells (automated method), and hemoglobin levels (automated method). Blood lipid, triglyceride, total cholesterol, and high-density lipoprotein (HDL) cholesterol levels were measured. Low-density lipoprotein cholesterol levels were calculated using the Friedewald equation (15). Glucose metabolism-related parameters were measured using fasting blood glucose (enzymatic colorimetric method), $HbA1_C$ (enzymatic colorimetric method), and insulin (chemiluminescent enzyme immunoassay) levels. Homeostasis model assessment-insulin resistance (HOMA-R) was calculated using fasting blood glucose and insulin values (16). In addition, acetoacetic acid and 3-hydroxybutyric acid were measured as organic acids in the fasting state using an enzymatic colorimetric method, and the sum was considered the level of ketone bodies in the blood. Researchers with expertise in ketones agree that a ketone body level <0.5 mmol is normal and that a ketone body level in excess of 1.0 mmol is considered hyperketonemic (17,18). In this study, those with abnormally high ketone body levels (≥1.0 mmol/l) were defined as having short-term energy deficiencies.

Dietary survey. The dietary survey was conducted on three consecutive days (one day on the weekends and on two weekdays), using a food recording method combined with photographic recording. We asked participants to be careful not to omit the recording of seasonings used, the parts of any meat consumed, favorite foods, and beverages, and to maintain a normal diet without deliberately making the meals luxurious or restricted. In addition, we asked participants to take pictures of their meals as served before eating, and when there were leftovers, we asked them to record and photograph the percentage of food left. When measurements were difficult, for example when eating out, we instructed them to record the size and quantity of foods they ate in as much detail as possible. The registered dietitian researchers carefully examined all dietary records and photographs. If any omissions or erroneous entries were suspected, the participant was contacted for face-to-face confirmation. If necessary, additions or corrections were made before energy and nutrient intakes were calculated. The energy and nutrient intakes in this study were analyzed using the Standard Tables of Food Composition in Japan (19,20) for an average of three days.

Assessment of underreporting by determining the ratio of energy intake to basal metabolic rate (EI/BMR). EI/BMR was calculated by dividing the energy intake obtained from the dietary survey via the basal metabolic rate estimated using the National Institute of Health and Nutrition formula (Ganpule's formula) (11,21,22). The Ganpule formula was developed based on the BMR values of 137 Japanese men and women aged 20-74 years (66 women) (21), and its validity was confirmed by comparison with the measured BMR values of 365 Japanese men and women aged 18-79 years (202 women, BMI range: 16.5 to 36.4 kg/m^2). Thus, compared to other estimation formulas, the BMR estimation value obtained from the Ganpule formula is less affected by age and body weight, and it has been reported that it can be applied to individuals of all ages and whose status range from thin to obese (22). The cutoff value of EI/BMR for estimating underreporting was set at 1.35 and the value is the minimum cutoff value for energy intake required to lead a normal life, as shown in previous studies using the basic principles of energy physiology (6). This cutoff value was derived from nine studies (n=207) that examined energy balance using whole-body calorimeter measurements and doubly-labelled water measurements, the gold standard of energy expenditure measurement, and is considered reliable. This cutoff value has also been used in large-scale studies investigating the relationship between underreporting and weight and lifestyle (8), as well as in a recent study of Japanese participants (23).

Thus, to accurately estimate the status of underreporters or energy-restricted reporters in this study, we defined 1) those with EI/BMR <1.35 and a ketone body level <1.0 mmol/l as underreporters, 2) those with EI/BMR <1.35 and a ketone

Table I. Participant characteristics and clinical laboratory values.

		Percentile		
Characteristic	All	25th	50th	75th
N	91			
Age (years)	47±9	40	48	53
Height (cm)	157.0±5.2	153.9	156.8	160.0
Weight (kg)	73.5±11.2	65.9	70.9	80.3
BMI (kg/m^2)	29.8±3.9	26.7	28.9	31.3
Waist circumference (cm)	97.6±8.8	91.1	96.8	103.2
Energy intake	1911±449	1,637	1,870	2,145
BMR	1336±161	1,213	1,327	1,414
EI/BMR	1.44±0.32	1.20	1.43	1.64
Systolic blood pressure (mmHg)	124±15	111	122	134
Diastolic blood pressure (mmHg)	74±10	67	74	81
White blood cell (/μl)	5,746±1,400	4,800	5,600	6,800
Red blood cell (/μl)	457±34	433	458	481
Hemoglobin (g/dl)	13.2±1.1	12.5	13.3	14.1
Total cholesterol (mg/dl)	215±41	188	210	235
LDL cholesterol (mg/dl)	136±35	112	135	156
HDL cholesterol (mg/dl)	58±12	50	56	67
Triglyceride (mg/dl)	105±56	66	94	132
Fasting blood glucose (mg/dl)	93±11	87	92	99
HbA1c (%)	5.3±0.4	5.1	5.3	5.5
Insulin (μU/ml)	10.0±5.7	6.2	9.0	12.3
HOMA-R	2.3±1.5	1.3	2.0	2.9
Ketone bodies (μmol/l)	0.98±1.50	0.40	0.63	1.04

Data expressed as mean ± SD. BMI, body mass index; BMR, basal metabolic rate; EI/BMR, the ratio of reported energy intake to basal metabolic rate; HbA1c, Hemoglobin A1c; HOMA-R, homeostasis model assessment-(insulin) resistance.

body level ≥1.0 mmol/l as energy-restricted reporters, and 3) those with EI/BMR ≥1.35 as no underreporting.

Statistical analysis. Data are shown as mean ± standard deviation. Pearson's correlation coefficient was used to determine the relationship between EI/BMR and each variable, and a stepwise multiple regression analysis was used. BMI, triglycerides, insulin, HOMA-R, and ketone bodies, which were not normally distributed, were analyzed after a log transformation. Comparisons of multiple groups were performed using one-way ANOVA variance and evaluated using Dunnett's post-hoc test with underreporters as controls, where differences were significant (vs. energy-restricted reporters and non-underreporters). Statistical Package for the Social Sciences (SPSS) v27 (IBM Institute) was used, and a two-sided p-value <0.05 was used to indicate statistical significance.

Ethical considerations. This study was approved by the ethical committee of Nakamura Gakuen University (No. Rinri-13-015) and was performed in accordance with the Declaration of Helsinki. In addition to aspects of personal information protection, the following were explained: the outline of the study, voluntary enrollment, no discrimination when refusing enrollment, freedom to withdraw from the agreement of participation with no discrimination, and that the results would be made public at scientific conferences and in the literature. Written informed consent documents were voluntarily supplied.

Results

Characteristics of the participants included in the final analysis. A total of 164 participants were enrolled in the study, and 91 were included in the final analysis. Excluded participants included 24 whose BMI was less than 25 kg/m^2; 44 who were taking medication for blood pressure, blood glucose, or serum lipids, or who had a history of hypertension, diabetes, or dyslipidemia; 3 who had missing data to be used for analysis; and 2 who had fasting blood glucose levels ≥126 mg/dl or HbA1c levels ≥6.5%. The participants were 47±9 years of age, had a BMI of 29.8±3.9 kg/m^2, and had normal mean values of blood pressure, serum blood glucose levels, and lipid levels (Table I). The mean value of the participants' ketone bodies was 0.98±1.50 mmol/l, which was within the normal range, but 25.3% of the participants exceeded 1.0 mmol/l, which was defined as the upper limit in this study. The energy intake estimated from the participants' dietary survey was 1,911±449 kcal/day, and the mean value of the BMR estimated

Table II. Multiple stepwise linear regression analysis of factors associated with EI/BMR (N=91).

Factor	Partial regression coefficient (β)	Standardized partial regression coefficient (β)	P-value
Age (years)	0.003	0.083	0.450
BMI (kg/m^2)[a]	-0.012	-0.148	0.179
Ketone bodies (μmol/l)[a]	-0.262	-0.260	0.013
R^2	0.100		
Adjusted R^2	0.069		0.026

[a]After logarithmic transformation and analyzed. The model was adjusted for age and BMI. EI/BMR, the ratio of reported energy intake to basal metabolic rate; BMI, body mass index.

using Ganpule's formula was 1,336±161 kcal/day (Table I). The mean value of EI/BMR calculated by dividing these values was 1.44±0.32, and 38.5% of the values were below the cutoff value of 1.35 (Fig. 1).

Correlation between EI/BMR and each variable. The correlations between EI/BMR and age, physical measurements, and blood test values were measured. There was a significant positive correlation between EI/BMR and log-transformed triglyceride levels (r=0.208, P=0.047) and log-transformed ketone body levels (r=-0.249, P=0.017). Multiple stepwise linear regression analysis was performed with EI/BMR as the objective variable and log-transformed triglycerides and log-transformed ketone bodies, which showed significant correlations with age and log-transformed BMI, as regulators and explanatory variables, respectively. The standard partial regression coefficients from each explanatory variable to the objective variable are shown in Table II, and only log-transformed ketone bodies are indicated as significant explanatory variables.

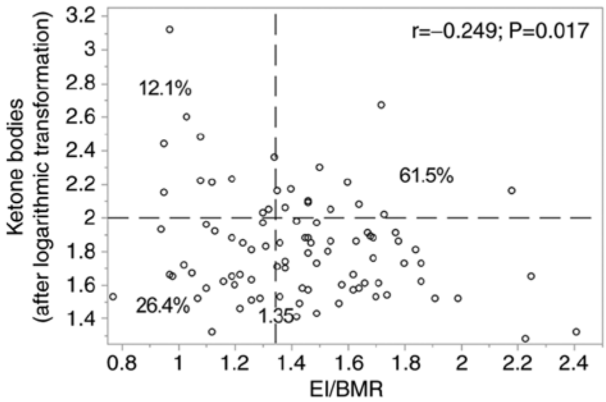

Figure 1. Estimates of underreporters or energy-restricted reporters using the participant's EI/BMR ratio and ketone body levels (n=91). There was a significant negative correlation between EI/BMR and log-transformed ketone body levels (r=-0.249; P=0.017). Underreporters (EI/BMR <1.35 and ketone body level <1.0 mmol/l) were estimated to comprise 26.4% of the participants, and energy-restricted reporters (EI/BMR <1.35 and ketone bodies ≥1.0 mmol/l) were estimated to comprise 12.1%.

Comparison of proportions and characteristics of underreporters, energy-restricted reporters and those who did not underreport (non-underreporters) estimated by EI/BMR and ketone bodies. We estimated the proportion of underreporters and energy-restricted reporters, based on the association between EI/BMR and ketone bodies. The results showed that 61.5% of the participants did not underreport (EI/BMR ≥1.35), 26.4% underreported (EI/BMR <1.35, ketone bodies <1.0 mmol/l), and 12.1% reported energy restriction (EI/BMR <1.35 and ketone bodies ≥1.0 mmol/l) (Fig. 1).

Finally, the characteristics, energy and nutrient intakes, and laboratory values were compared among the underreporter, energy-restricted reporter, and no underreporting groups. The results showed that underreporters were significantly younger and had significantly higher weights and BMI than non-underreporters. However, there were no significant differences in reported energy intake, carbohydrate intake (g/day), and % carbohydrate (%) between the underreporters and energy-restricted reporters (Table III).

Discussion

This study is the first to demonstrate a relationship between EI/BMR and ketone bodies in Japanese women with obesity and aimed to distinguish between underreporters and energy-restricted reporters to improve the quality of dietary surveys in the treatment of obesity. Dietary surveys of individuals with obesity show underreporting (2,8-11) and a lack of energy due to the extreme energy-restricted diets. EI/BMR can determine the presence and extent of underreporting, but it cannot determine energy deficiency due to extreme dietary restrictions. Conversely, ketone bodies can determine the presence of energy deficits, but provide no information about underreporting. However, the combination of the EI/BMR ratio and ketone body levels can discriminate between or screen for both, and through improved accuracy of dietary surveys, may lead to a better understanding of the original diet that led to obesity in each patient, which may lead to appropriate treatment.

The mean EI/BMR value of obese Japanese women in this study was 1.44, which is lower than the mean EI/BMR value of 1.69 for Japanese women in representative studies using data from the National Health and Nutrition Examination Survey (11). Underreporting was confirmed to be frequent, as in previous studies conducted in Japan and abroad (2,8-11).

Furthermore, 25.3% of the participants had abnormally high levels of ketone bodies, indicating that individuals with obesity undergoing dietary surveys should be assumed to have extremely deficient energy intake (12) owing to excessive

Table III. Comparison of group characteristics, clinical laboratory values and reported energy and reported energy and nutrients intake between groups by EI/BMR and ketone bodies.

Characteristic	Underreporters (n=24)	Energy-restricted reporters (n=11)	Non-underreporters (n=56)	P-value
Age (years)	43±10	49±9	48±8[a]	0.032
BMI (kg/m^2)[b]	31.3±5.0	30.7±3.1	28.9±3.3[a]	0.029
Energy (kcal/day)	1,604±293	1,469±182	2,130±398[a]	<0.001
Basal metabolic rate	1,408±189	1,315±96	1,309±150[a]	0.036
EI/BMR	1.14±0.13	1.12±0.15	1.63±0.24[a]	<0.001
Protein (g/day)	63.5±13.3	59.7±11.2	77.7±15.9[a]	<0.001
% Protein (%)	16.1±4.3	16.2±2.0	14.7±2.0	0.051
Fat (g/day)	52.4±12.2	46.9±14.2	72.3±18.1[a]	<0.001
% Fat (%)	29.5±4.7	28.3±6.2	30.5±5.0	0.385
Carbohydrate (g/day)	208.7±51.2	197.5±24.1	279.8±59.8[a]	<0.001
% Carbohydrate (%)	51.6±7.1	54.2±6.8	52.6±4.7	0.457

Data expressed as mean ± SD. [a]P<0.05 vs. underreporters; [b]After logarithmic transformation and analyzed. EI/BMR, the ratio of reported energy intake to basal metabolic rate Underreporters, EI/BMR <1.35 and ketone body level <1.0 mmol/l; Energy-restricted reporters, EI/BMR <1.35 and ketone body level ≥1.0 mmol/l; non-underreporters, EI/BMR ≥1.35.

dietary restriction. A significant negative correlation was found between EI/BMR and ketone body levels, which was also a significant variable in the multiple regression analysis. This suggests that 12.1% of those with an EI/BMR <1.35 and ketone body level ≥1.0 mmol/l included underreporters and those who reported extreme energy restriction practices at the time of the dietary survey and blood test. However, because ketone bodies are known to exhibit diurnal variation (24), further investigation is needed to determine the extent to which ketone body values in a single blood sample reflect temporary energy deficits in obese individuals. In recent years, ketone bodies have been measured simply and accurately using small devices (25). Thus, evaluation of the quality of dietary surveys combining EI/BMR and ketone bodies can be performed in real time. This method is expected to improve the quality of dietary surveys of individuals with obesity in clinical practice. In addition, an extreme lack of carbohydrate intake was not considered because there was no difference in the carbohydrate intake (g/day), and % carbohydrate (%) between the group of underreporters with ketone bodies in the normal range and the group of energy-restricted reporters with abnormal ketone bodies.

In general, EI/BMR and BMI are negatively correlated (8,10,11). In addition, EI/BMR and age were reported to be negatively related in previous studies conducted overseas (8,26) and positively related in previous studies conducted in Japan (10,11); thus, the results are conflicting. This may be because the results are affected by differences in the dietary survey methods between those used in previous studies in Japan and overseas. In particular, previous studies conducted overseas used the food intake frequency survey method (8) and 24-h recall method (26), whereas previous studies conducted in Japan used semi-weighed dietary records (10,11). In contrast, the present study was conducted with a relatively high degree of accuracy, using a three-day food recording method combined with photographic recording, as well as face-to-face confirmation of dietary content by the examiner's registered dietitian researchers. In this study, which included a special population of only obese participants, underreporters with low EI/BMR were younger and had a higher BMI than non-underreporters, consistent with the results of previous studies. However, the small number of subjects in this study makes generalization difficult and further research is needed in the future.

In previous studies, several diet quality scores, such as the Healthy Eating Index and the Mediterranean Diet Index, were significantly associated with insulin resistance and indices of inflammation (27). However, we found no association between EI/BMR and the indices of glucose metabolism or inflammation in the present study. We hypothesize this is because the Healthy Eating Index and the Mediterranean Diet Index systematically present the intake of various foods, whereas the EI/BMR only considers the ratio of reported energy intake to BMR.

This study had several limitations. First, EI/BMR affects various factors such as smoking status, educational history, recent weight changes, body composition, physical activity, self-body image, health consciousness, and social disability (2,3,8,28,29). However, in this study, these data were not sufficiently available and EI/BMR was not adjusted for various factors, which may have affected the results. Furthermore, the participants were from a relatively homogeneous population, with similar race, sex, BMI, age, and health consciousness, and we hypothesize that the results of this study provide informative results. In the future, based on the results of this study, it would be valuable to conduct studies that include several factors that may affect EI/BMR. Second, this study did not accurately evaluate physical activity levels. In addition, the target population was highly conscious of weight loss, and there seemed to be an error in the proportion of underreporters and energy-restricted reporters using the relationship between EI/BMR and ketone bodies. Third, this study targeted individuals who lived in specific areas, and the number of participants and dietary survey days were relatively small. However, few reports of careful collection and analysis of the dietary content of Japanese individuals with obesity using the food recording method combined with photographic recording exist in the literature, and the findings of the present study are therefore valuable. Fourth, there was a time lag of up to 10 years between study participants, and there may have been an error in the nutritional value due to repeated revisions of the Standard Tables of Food Composition in Japan during this period. In addition, most dietary surveys in this study were conducted between September and October, which does not allow for seasonal variations in energy intake (30). However, compared with the underreporting of energy intake, the errors in energy intake caused by food composition tables and seasonal variations are quite small and are unlikely to have a significant impact on the results of this study. Fifth, the BMR was not a measured value but an estimated one using Ganpule's formula with reference to previous studies (11). Therefore, the EI/BMR ratio calculated based on the BMR estimates may contain errors.

Furthermore, it has not been confirmed whether the EI/BMR cutoff value used in this study is suitable for the Japanese population. Therefore, the percentages of underreporters, energy-limited reporters, and non-underreporters may also contain errors. However, the combination of EI/BMR and ketone bodies is useful for screening to reduce errors included in dietary surveys, and the results of this study may lead to improvements in the quality of dietary surveys of individuals with obesity.

Despite these limitations, we hypothesize that the present study was highly significant because it showed the relationship between EI/BMR, BMI, and age in Japanese women with obesity and the possibility of estimating not only underreporting but also energy deficiency associated with energy restriction in the participants by combining EI/BMR and ketone body levels.

In conclusion, low EI/BMR was associated with high ketone body levels in obese Japanese women. The combination of EI/EMR and ketone body levels may distinguish between or screen for underreporters and energy-restricted reporters at the time of the dietary survey.

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Availability of data and materials

The datasets used and/or analyzed during the current study are available from the corresponding author on reasonable request.

Authors' contributions

KY, SN, MK and HK conceived, designed and supervised the study. KY, RM, KI, SA, MO, HU, KW, SN and HK registered subjects and collected data. IY and KY confirm the authenticity of all the raw data. IY, KY and RM analyzed and interpreted the data. RM, MO, MK and HK reviewed the manuscript. IY and KY wrote the manuscript. All authors read and approved the final manuscript.

Ethics approval and consent to participate

This study was approved by the Ethical Committee of Nakamura Gakuen University (approval no. Rinri-13-015). Written informed consent documents were provided voluntarily.

Patient consent for publication

Not applicable.

Competing interests

The authors declare that they have no competing interests.

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