DOCTORAL THESIS

Sleep duration and food intake in people with type 2 diabetes mellitus and factors affecting confectionery intake

2 型糖尿病における睡眠時間と食事摂取の関係と菓子類の摂取に与える因子について

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ORIGINAL ARTICLE

Sleep duration and food intake in people with type 2 diabetes mellitus and factors affecting confectionery intake

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ABSTRACT

Aims/Introduction: We carried out a cross-sectional study of people with type 2 diabetes mellitus to elucidate the association between sleep duration and food intake.

Materials and Methods: Overall, 2,887 participants with type 2 diabetes mellitus (mean age 63.0 years; 61.1% men; mean glycated hemoglobin level 7.5%) were included in this study. The participants' self-reported dietary habits and sleep duration were evaluated using a brief self-administered dietary history questionnaire and Pittsburgh Sleep Quality Index, respectively. The participants were categorized into the following four groups based on sleep duration: <6, 6–6.9, 7–7.9 (reference) and ≥8 h.

Results: No significant differences were observed between the groups regarding energy intake (kcal/day), absolute intake (g/day) or relative intake (% energy) of carbohydrates, total fat, proteins and fibers. However, confectionery intake was higher in the <6 h group and lower in the ≥8 h group than in the reference group after adjustment for confounding factors. In multivariate analysis, sleep durations <6 h and ≥8 h significantly correlated with increased (95% confidence interval 0.55 to 3.6; $P = 0.0078$) and decreased (95% confidence interval −4.0 to −0.32; $P = 0.021$) confectionery intake, respectively. Confectionery intake was positively correlated with female sex, glycated hemoglobin level and dyslipidemia, whereas it was negatively correlated with alcohol consumption and current smoking status.

Conclusions: Short sleep duration is associated with high confectionery intake in people with type 2 diabetes mellitus; this might disturb their glycemic control. Therefore, short sleepers with type 2 diabetes mellitus could improve their glycemic control by avoiding confectionery intake and maintaining adequate sleep duration. Confectionery intake was higher in short sleepers with type 2 diabetes mellitus than normal sleepers. Sleep duration of <6 h was associated with increased confectionery intake. Avoiding confectionery and maintaining adequate sleep duration are crucial.

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INTRODUCTION

Several observational studies have suggested that short sleep duration is a critical risk factor for weight gain in the general population and adults with impaired glucose regulation.[1,2] Reportedly, adults with short sleep duration are at high risk of developing type 2 diabetes mellitus, hypertension and dyslipidemia.[1,3–5] Furthermore, short sleep duration has been implicated in increased rates of cardiovascular diseases, stroke and all-cause mortality.[1,6] Short sleepers have shown improved metabolic factors, including blood pressure, blood glucose levels and bodyweight, after several weeks of increased sleep duration.[7,8] Based on the association between short sleep duration and adverse health effects, a sleep duration of ≥7 h has been recommended to prevent cardiovascular diseases.[9,10]

Cross-sectional studies of people with type 2 diabetes mellitus have shown that both short and long sleep durations are related to poor glycemic control.[11] Objectively measured short sleep duration has been associated with retinopathy.[12] Participants with obesity with type 2 diabetes mellitus had significantly later bedtimes and shorter sleep duration than those without obesity.[13] In addition, shorter and longer sleep durations (compared with the recommended 7 h) have been associated with increased mortality in people with type 2 diabetes mellitus.[14] Despite these established crucial associations, limited guidelines have been developed for the management of type 2 diabetes mellitus focusing on sleep duration.[15]

Previous studies have shown that sleep restriction is involved in the pathophysiology of diabetes mellitus and obesity.[16,17] Sleep loss might lead to decreased leptin levels, and increased ghrelin and evening cortisol levels, resulting in increased hunger and calorie intake.[18–20] Long waking hours are associated with increased eating time.[17] However, little is known regarding the association between night sleep duration and food intake in people with type 2 diabetes mellitus.

Therefore, to clarify this association, we carried out the Sleep and Food Registry in Kanagawa (SOREKA) study at 24 clinics and hospitals in Kanagawa Prefecture, Japan. The SOREKA study showed that people with type 2 diabetes mellitus with poorer glycemic control had higher carbohydrate-to-total energy intake ratios, poorer sleep quality and shorter sleep duration.[21,22] However, we did not examine the influence of sleep duration on food intake patterns. The present cross-sectional study aimed to investigate the association between sleep duration and food intake patterns in people with type 2 diabetes mellitus in Japan.

MATERIALS AND METHODS

Study population

Overall, 4,241 individuals of either sex with diabetes mellitus or endocrine and metabolic disorders aged 20–84 years were enrolled in this SOREKA study (UMIN000014318). The exclusion criteria were: (i) history of diabetic ketoacidosis or coma within 6 months before the commencement of this study; (ii) drug- or steroid-induced diabetes; (iii) pregnant or breast-feeding women; (iv) pre- and post-surgery patients; (v) renal replacement therapy; (vi) other fatal diseases, such as severe infection, trauma or malignancy; (vii) liver cirrhosis; or (viii) participants deemed inappropriate for the study by the attending physician. After applying the exclusion criteria, 3,511 participants with type 2 diabetes mellitus were included in the present study. Of the 3,511 participants, 512 were excluded due to their inability to complete the diet and sleep quality questionnaires. In addition, 46 participants with energy intake <500 or >4,000 kcal/day or sleep duration <3 or >11.5 h were excluded as potential outliers, as were 66 participants without data on glycated hemoglobin (HbA1c). Ultimately, 2,887 participants formed the study population.

Ethical considerations

All participants provided informed consent. This research conformed to the provisions of the Declaration of Helsinki (revised in Fortaleza, Brazil, October 2013) and was approved by the Yokohama City University Clinical Research Review Board (approval number D1405028).

Dietary assessment

As previously reported in the SOREKA study, we administered a brief-type self-administered dietary history questionnaire (BDHQ; Gender Medical Research Inc. Tokyo, Japan) in Japanese that recorded the intake frequency of 58 foods and beverages in the previous month.[22] Subsequently, we evaluated the energy-adjusted intake of each food using density methods (g/1,000 kcal).[23]

Sleep duration assessment

To evaluate sleep duration, we used the Pittsburgh Sleep Quality Index, a questionnaire used in the self-assessment of sleep quality over the previous month.[24] Question 4 of the questionnaire stated, "During the past month, how many hours of actual sleep did you get at night?" (in Japanese).

Blood sampling and biochemical analysis

Plasma glucose levels, HbA1c levels and urine albumin concentration were measured using the glucose oxidase, high-performance liquid chromatography and immunoturbidimetric methods (N-assay TIA Micro Alb System; Nittobo Medical Co, Ltd, Tokyo, Japan), respectively.

Categorization of participants and food items

Sleep duration was classified into the following four categories: <6, 6–6.9, 7–7.9 and ≥8 h. We evaluated macronutrient energy (kcal/day), relative (% energy) and absolute intakes of carbohydrates, total fat, proteins and fibers (g/day). Food groups were categorized as milk and milk products, meat, fish and shellfish, eggs, pulses, potatoes, vegetables, confectionery, fruit, cereals,

and fat and oils, which were evaluated using the density methods (g/1,000 kcal).

Statistical analysis

Continuous and categorical data are presented as mean ± standard deviation and numbers with percentages, respectively. Statistical analyses were carried out to investigate the association between sleep duration and dietary intake in people with type 2 diabetes mellitus. First, we used generalized linear regression models to compare the differences in the mean values and proportions between groups categorized by sleep duration. In this model, we used 7–7.9 h of sleep as the reference. Subsequently, multivariable linear regression analyses were carried out to adjust for factors, such as age, sex, body mass index (BMI), HbA1c level, current smoking status, alcohol consumption, hypertension and dyslipidemia. $P < 0.05$ were considered statistically significant.

Furthermore, we carried out univariate linear regression analyses to assess the association between confectionery consumption and sleep duration; variables with $P < 0.05$ were included in the multivariate regression models. We carried out statistical analyses using the JMP Pro software, version 15.0.0 (SAS Institute Inc., Cary, NC, USA).

Table 1 | Baseline characteristics

Characteristics	*n* = 2,887
Age (years)	63.0 ± 11.5
Sex (male), % (male : female)	61.1 (1,765:1,122)
Body mass index (kg/m^2)	25.3 ± 4.7
Alcohol, % (*n*/total *n*)	53.5 (1,542/2,887)
Current smoker, % (*n*/total *n*)	21.5 (622/2,887)
Hypertension, % (*n*/total *n*)	61.2 (1,768/2,887)
Dyslipidemia, % (*n*/total *n*)	74.2 (2,141/2,887)
HbA1c (%)	7.5 ± 1.6
HbA1c (mmol/mol)	58 ± 17
Treatment	
No medication, % (*n*/total *n*)	11.5 (332/2,887)
OHA only, % (*n*/total *n*)	60.0 (1,732/2,887)
Insulin or GLP-1, % (*n*/total *n*)	28.5 (823/2,887)
Complications, % (*n*/total *n*)	
Neuropathy	42.0 (1,165/2,772)
Retinopathy	23.5 (639/2,720)
Nephropathy	12.6 (357/2,831)
Macroangiopathy	18.0 (520/2887)

Data are presented as the mean ± standard deviation or percentage (%). HbA1c, glycated hemoglobin; GLP-1, glucagon-like peptide-1 receptor agonist; OHA, oral hypoglycemic agents.

RESULTS

Clinical characteristics

The mean age (±standard deviation) of the participants in this study was 63.0 ± 11.5 years, and 1,765 (61.1%) of them were men. The mean BMI and HbA1c levels were 25.3 ± 4.7 kg/m^2 and 7.5 ± 1.6% (58 ± 17 mmol/mol), respectively (Table 1). There were 749, 949, 750 and 439 individuals in the <6-h, 6–6.9-h, 7–7.9-h (set as the reference group) and ≥8-h sleep duration groups, respectively. The <6-h sleep duration group had higher proportions of younger participants, women, current smokers, and higher BMI and HbA1c levels than the 7–7.9-h sleep duration group (Table 2). In contrast, participants in the ≥8-h sleep duration group were older and had a higher rate of hypertension than those in the reference group.

Associations between dietary intake and sleep duration

The mean energy intake observed was 1,699.4 ± 588.3 kcal/day. The mean proportions of carbohydrate, total fat, protein and fiber in total energy intake were 52.3%, 26.9%, 16.3% and 0.77%, respectively.

Compared with the 7–7.9-h sleep duration group, the other groups showed no significant differences in energy intake (Table 2). Furthermore, we found no differences in absolute intake (g/day) or relative intake of carbohydrates, total fat, protein and fiber (%energy) among the groups. However, participants who slept for <6 h consumed more confectionaries and less fish and shellfish than those in the 7–7.9-h group.

After adjustment for age, sex, BMI, HbA1c level, current smoking status, alcohol consumption, hypertension and dyslipidemia, consumption of confectionaries was higher in the <6-h sleep duration group and lower in the ≥8-h sleep duration group than in the 7–7.9-h reference group (Table 3). The adjusted mean consumption of confectionaries was 29.9 g/1,000 kcal in the <6 h group (95% confidence interval [CI] 27.9–31.8; $P = 0.0059$) and 25.4 g/1,000 kcal in the ≥8 h group (95% CI 23.0–27.9; $P = 0.019$), compared with 27.3 g/1,000 kcal in the 7–7.9-h group (95% CI 25.3–29.1; Table 3). After adjustments, the difference between the <6 h group and the 7–7.9 h group regarding fish and shellfish intake was statistically insignificant.

Confectionaries were categorized into the following four groups on the BDHQ: Western sweets (such as cookies and biscuits); Japanese sweets; senbei, rice cakes and okonomiyaki; and ice cream. It was observed that the <6 h group consumed more Western sweets, senbei, rice cakes and okonomiyaki than the 7–7.9 h group. The adjusted mean consumption of Western sweets in the <6 h group was 8.8 g/1,000 kcal (95% CI 7.9–9.6), compared with 7.9 g/1,000 kcal in the 7–7.9 h group (95% CI 7.1–8.8; $P = 0.047$); consumption of senbei, rice cakes and okonomiyaki in the <6 h group was 7.9 g/1,000 kcal (95% CI 7.2–8.5), compared with 7.5 g/1,000 kcal in the 7–7.9 h group (95% CI 6.8–8.2; $P = 0.011$; Table 4). Meanwhile, the ≥8 h group consumed fewer senbei, rice cakes and okonomiyaki (the adjusted mean consumption in the ≥8 h group was 5.9 g/1,000 kcal [95% CI 5.1–6.8] compared with 7.5 g/1,000 kcal in the 7–7.9 h group [95% CI 6.8–8.2; $P < 0.001$]).

Confectionery consumption and sleep duration

As shown in Table 5, a univariate analysis of factors related to confectionery consumption (g/1,000 kcal) showed that sleep

Table 2 | Clinical characteristics and nutritional intake according to sleep duration category

Sleep duration	<6 h	6–6.9 h	7–7.9 h (Reference)	≥8 h	Total
n	749	949	750	439	2,887
Age (years)	59.1 ± 11.7 *	62.5 ± 11.4 *	64.9 ± 11.5	67.6 ± 11.1 *	63.0 ± 11.5
Male sex, % (*n*)	56.3% (422) **	59.3% (563) **	66.1% (496)	64.7% (284)	61.1%
Body mass index (kg/m^2)	26.2 ± 5.1 *	25.3 ± 4.7	24.8 ± 4.6	24.7 ± 4.2	25.3 ± 4.7
Alcohol, % (*n*)	52.2% (391)	53.5% (508)	55.5% (416)	51.9% (228)	53.5
Current smoker, % (*n*)	24.6% (184) **	21.4 (203)	19.1 (143)	21.0 (92)	21.5
Hypertension, % (*n*)	59.4% (445)	59.4% (564)	61.5% (461)	67.9% (298) **	61.2
Dyslipidemia, % (*n*)	76.1% (570)	74.2% (704)	73.1% (548)	72.7% (319)	74.2
HbA1c (%)	7.7 ± 1.8 *	7.4 ± 1.6	7.4 ± 1.5	7.5 ± 1.7	7.5 ± 1.6
HbA1c (mmol/mol)	60 ± 19	57 ± 17	57 ± 16	58 ± 18	58 ± 17
Nutritional intake					
Energy (kcal/day)	1,674.7 ± 601.9	1,698.1 ± 560.3	1,730.7 ± 591.4	1,690.9 ± 617.7	1,699.4 ± 588.3
Carbohydrate (E%)	52.9 ± 8.7	51.9 ± 9.1	52.3 ± 9.4	52.3 ± 9.3	52.3 ± 9.1
Carbohydrate (g/day)	220.7 ± 85.4	219.0 ± 79.1	225.1 ± 85.0	218.1 ± 82.4	220.9 ± 82.8
Fat (E%)	27.1 ± 6.3	27.1 ± 6.2	26.6 ± 6.5	26.4 ± 6.3	26.9 ± 6.4
Fat (g/day)	50.1 ± 20.6	51.1 ± 20.7	51.0 ± 21.5	50.1 ± 22.9	50.6 ± 21.2
Protein (E%)	16.2 ± 3.6	16.4 ± 3.6	16.3 ± 4.0	16.5 ± 3.8	16.3 ± 3.7
Protein (g/day)	66.6 ± 26.0	68.9 ± 26.4	69.8 ± 28.6	69.7 ± 31.0	68.7 ± 27.6
Fiber (E%)	0.76 ± 0.29	0.77 ± 0.28	0.76 ± 0.30	0.79 ± 0.28	0.77 ± 0.29
Fiber g/day	12.2 ± 5.4	12.7 ± 5.5	12.6 ± 5.3	13.0 ± 5.8	12.6 ± 5.5
Food group (g/1,000 kcal)					
Milk and milk products	69.2 ± 62.9	72.2 ± 65.1	72.0 ± 61.3	73.7 ± 66.0	71.6 ± 63.7
Meat	42.4 ± 24.1	40.1 ± 21.5	39.9 ± 22.3	37.9 ± 23.8	40.3 ± 22.8
Fish and shellfish	46.2 ± 27.7 *	50.4 ± 29.1	50.1 ± 30.8	51.2 ± 33.2	49.4 ± 29.8
Eggs	20.6 ± 15.6	21.0 ± 15.5	20.2 ± 15.2	21.7 ± 15.8	20.8 ± 15.5
Pulses	37.4 ± 28.7	38.3 ± 26.2	36.3 ± 26.1	37.2 ± 26.3	37.4 ± 26.9
Potatoes	22.0 ± 20.5	23.5 ± 21.0	22.7 ± 24.5	24.8 ± 24.5	23.1 ± 22.4
Vegetables	165.1 ± 112.3	169.2 ± 101.3	165.7 ± 110.2	169.4 ± 103.5	167.3 ± 106.9
Confectionaries	31.6 ± 25.8 *	29.6 ± 23.1	28.6 ± 23.9	26.8 ± 24.1	29.4 ± 24.2
Fruits	48.4 ± 49.7	50.5 ± 43.1	52.2 ± 45.8	56.8 ± 51.2	51.3 ± 46.9
Cereals	218.8 ± 77.1	208.7 ± 75.0	214.4 ± 75.6	216.3 ± 74.5	213.9 ± 75.6
Bread	23.6 ± 19.0	24.0 ± 18.9	23.2 ± 18.4	25.5 ± 22.2	23.9 ± 19.4
Noodles	45.7 ± 38.1	44.3 ± 33.8	44.0 ± 32.5	46.5 ± 34.7	44.9 ± 34.8
Rice	149.6 ± 74.9	140.4 ± 75.5	147.1 ± 77.2	144.3 ± 77.8	145.1 ± 76.1
Fat and oil	6.2 ± 3.2	6.0 ± 2.9	5.9 ± 3.1	5.6 ± 3.2	6.0 ± 3.1

Data are presented as the mean ± standard deviation or percentage (%). *$P < 0.05$, Dunnett's test was carried out for comparisons among groups (reference: 7.9 h). **$P < 0.05$, logistic regression was carried out for comparisons among groups (reference: 7.9 h). HbA1c, glycated hemoglobin; E %, a percentage of 24-h total energy intake.

duration <6 h was correlated with increased intake, whereas sleep duration ≥8 h was correlated with decreased intake, compared with the reference (7.9 h). After adjustment for factors with $P < 0.05$ in the multivariate analysis, a sleep duration of <6 h was significantly correlated with increased intake (partial regression coefficient [B] 2.1; 95% CI 0.55 to 3.6; standardized partial regression coefficient [β] = 0.062; $P = 0.0078$), whereas a sleep duration of ≥8 h was correlated with a lower consumption (B −2.2; 95% CI −4.0 to −0.32; β = −0.056; $P = 0.021$) of confectionaries. Confectionery intake was positively correlated with female sex, HbA1c level and dyslipidemia, whereas it was negatively correlated with alcohol consumption and current smoking status. No significant correlation was found between confectionery intake and BMI.

DISCUSSION

In the present study, we found that people with type 2 diabetes mellitus who slept for <6 h consumed more confectionaries, and those who slept for >8 h consumed fewer confectionaries than those who slept for 7–7.9 h. To the best of our knowledge, this is the first study to evaluate the association between sleep duration and dietary nutritional values in a large group of people with type 2 diabetes mellitus.

We found no association between sleep duration and dietary intake of macronutrients in people with type 2 diabetes

Table 3 | Multivariate adjusted mean dietary intake according to sleep duration category

Sleep duration	<6 h		6–6.9 h		7–7.9 h		≥8 h	
		95% CI		95% CI		95% CI		95% CI
Nutritional intake								
Energy (kcal/day)	1,664.6	(1,619.1, 1,710.2)	1,682.9	(1,641.7, 1,724.1)	1,689.3	(1,643.4, 1,735.2)	1,651.5	(1,594.6, 1,708.5)
Carbohydrate (E%)	53	(52.2, 53.7)	52.2	(51.5, 52.9)	52.6	(51.9, 53.4)	52.4	(51.5, 53.3)
Carbohydrate (g/day)	219.5	(213.0, 226.0)	218.4	(212.5, 224.2)	221.5	(214.9, 228.0)	213.8	(205.7, 222.0)
Fat (E%)	26.6	(26.1, 27.1)	26.7	(26.2, 27.2)	26.3	(25.8, 26.8)	26.3	(25.7, 26.9)
Fat (g/day)	49	(47.3, 50.6)	49.8	(48.3, 51.4)	49.1	(47.4, 50.8)	48.5	(46.4, 50.6)
Protein (E%)	16.4	(16.1, 16.7)	16.4	(16.1, 16.6)	16.2	(15.9, 16.5)	16.2	(15.8, 16.5)
Protein (g/day)	67.3	(65.1, 69.4)	68.1	(66.1, 70.1)	67.5	(65.3, 70.0)	66.7	(64.0, 69.4)
Fiber (E%)	0.78	(0.76, 0.80)	0.77	(0.76, 0.79)	0.76	(0.74, 0.78)	0.77	(0.75, 0.80)
Fiber (g/day)	12.6	(12.1, 13.0)	12.6	(12.3, 13.0)	12.2	(11.8, 12.7)	12.4	(11.8, 12.9)
Food group (g/1,000 kcal)								
Milk and milk products	72.2	(67.2, 77.2)	72	(67.5, 76.6)	70.2	(65.1, 75.2)	69.5	(63.2, 75.8)
Meat	40.7	(38.9, 42.5)	39.5	(37.8, 41.1)	40.2	(38.3, 42.0)	39.2	(36.9, 41.5)
Fish and shellfish	47.9	(45.6, 50.3)	50.3	(48.2, 52.4)	49	(46.6, 51.4)	48.8	(45.9, 51.8)
Eggs	21	(19.8, 22.3)	21.1	(20.0, 22.3)	20.2	(18.9, 21.5)	21.6	(20.1, 23.2)
Pulses	38.8	(36.7, 40.9)	38.5	(36.6, 40.4)	36.2	(34.0, 38.3)	36.4	(33.8, 39.1)
Potatoes	22.6	(20.8, 24.3)	23.5	(21.9, 25.1)	22.6	(20.8, 24.4)	24.3	(22.0, 26.5)
Vegetables	172.8	(164.7, 180.9)	171.3	(164.0, 178.7)	167.7	(159.5, 175.9)	168.9	(158.8, 179.1)
Confectionaries	29.9*	(27.9, 31.8)	28.1	(26.3, 29.9)	27.3	(25.3, 29.1)	25.4*	(23.0, 27.9)
Fruits	51	(47.4, 54.5)	49.3	(46.1, 52.5)	48.6	(45.0, 52.6)	50.1	(45.6, 54.5)
Cereals	219.1	(213.1, 225.1)	212.8*	(207.4, 218.2)	220	(213.9, 226.0)	222.4	(214.9, 229.9)
Bread	23.5	(22.0, 25.1)	23.5	(22.1, 24.9)	22.5	(20.9, 24.0)	24.5	(22.6, 26.5)
Noodles	44.9	(42.2, 47.7)	44.3	(41.8, 46.8)	43.8	(41.1, 46.6)	46.5	(43.0, 49.9)
Rice	150.6	(144.5, 156.7)	145*	(139.4, 150.5)	153.6	(147.5, 159.8)	151.4	(143.8, 159.0)
Fat and oil	5.8	(5.6, 6.1)	5.8	(5.6, 6.0)	5.9	(5.6, 6.1)	5.7	(5.4, 6.1)

The generalized linear model was adjusted for age, sex, body mass index, HbA1c level, current smoking status, alcohol consumption, hypertension, and dyslipidemia. *$P < 0.05$, Dunnett's test was carried out for comparisons among groups (reference: 7.9 h). 95% CI, 95% confidence interval.

Table 4 | Multivariate adjusted mean dietary intake according to sleep duration category

Sleep duration	<6 h		6–6.9 h		7–7.9 h (Reference)		≥ 8 h	
		95% CI		95% CI		95% CI		95% CI
Confectionaries (g/1,000 kcal)	29.9*	(27.9, 31.8)	28.1	(26.3, 29.9)	27.3	(25.3, 29.1)	25.4*	(23.0, 27.9)
Western sweets (cookies, biscuits)	8.8*	(7.9, 9.6)	8.2	(7.4, 9.0)	7.9	(7.1, 8.8)	7.4	(6.3, 8.5)
Japanese sweets	4.1	(3.7, 4.5)	4.2	(3.9, 4.6)	4.0	(3.6, 4.4)	3.9	(3.4, 4.5)
Senbei, rice cakes and okonomiyaki	7.9*	(7.2, 8.5)	7.2	(6.6, 7.8)	7.5	(6.8, 8.2)	5.9*	(5.1, 6.8)
Ice cream	9.1	(8.0, 10.3)	8.5	(7.4, 9.5)	7.8	(6.6, 8.9)	8.2	(6.7, 9.6)

The generalized linear model was adjusted for age, sex, body mass index, glycated hemoglobin level, current smoking status, alcohol consumption, hypertension and dyslipidemia. *$P < 0.05$, Dunnett's test was carried out for comparisons among groups (reference: 7.9 h). 95% CI, 95% confidence interval.

mellitus. Although there are many reports on the association between sleep duration and dietary intake, no definitive results have been obtained.[25,26] Several observational studies in the general population have suggested that short sleep duration is associated with increased total energy intake.[18,26] Conversely, other reports showed that energy intake did not vary with sleep duration.[27, 28] Tasali *et al*[29] carried out a randomized controlled trial and reported that prolonged objective sleep duration decreased energy intake in overweight adults in real-life. Meta-analyses of the association between decreased sleep duration and macronutrient intake reported that the absolute intake of fat, protein and carbohydrate (g/day) was higher under conditions of partial sleep loss than under normal sleep conditions.[30] However, relative fat intake (% energy) was reported to be higher, protein intake (% energy) lower and no significant difference was observed in carbohydrate intake (% energy).[31] In

Table 5 | Univariate and multivariate linear regression analyses of confectionary consumption (g/1,000 kcal)

	Unadjusted model			*P*-value	Multivariable-adjusted model			
	B	95% CI	β		B	95% CI	β	*P*-value
Sleep duration <6 h	2.5	(0.93, 4.0)	0.073	0.0016	2.1	(0.55, 3.6)	0.062	0.0078
Sleep duration 6–6.9 h	0.41	(−1.0, 1.8)	0.013	0.58	0.42	(−0.99, 1.8)	0.013	0.56
Sleep duration 7–7.9 h	Reference				Reference			
Sleep duration ≥8 h	−2.3	(−4.2, −0.46)	−0.060	0.014	−2.2	(−4.0, −0.32)	−0.056	0.021
Age (years)	0.0003	(−0.075, 0.075)	0.00018	0.99				
Female sex	2.1	(1.2, 3.0)	0.085	<0.001	1.1	(0.15, 2.1)	0.046	0.024
Body mass index (kg/m^2)	0.25	(0.059, 0.43)	0.048	0.0098	0.12	(−0.066, 0.31)	0.024	0.20
HbA1c (%)	0.82	(0.27, 1.37)	0.054	0.0036	0.80	(0.24, 1.35)	0.053	0.0048
Alcohol consumption	−1.7	(−2.5, −0.78)	−0.068	<0.001	−2.0	(−3.1, −0.94)	−0.069	<0.001
Current smoker	−2.19	(−3.27, −1.12)	−0.075	<0.001	−1.0	(−2.0, −0.089)	−0.043	0.032
Neuropathy	−0.46	(−1.38, 0.45)	−0.019	0.32				
Nephropathy	−1.3	(−2.6, 0.044)	−0.036	0.058				
Macroangiopathy	−0.082	(−1.2, 1.1)	−0.0026	0.89				
Hypertension	−0.26	(−1.2, 0.65)	−0.010	0.57				
Dyslipidemia	2.1	(1.1, 3.2)	0.078	<0.001	1.7	(0.72, 2.76)	0.063	<0.001

β, standardized partial regression coefficient; B, partial regression coefficient; CI, confidence interval; HbA1c, glycated hemoglobin.

the present study, the intake of calories along with carbohydrates, fat, protein and fiber remained unchanged based on sleep duration. A study of the validity of the BDHQ reported that the total energy intake (kcal/day) and absolute macronutrient intake (g/day) were estimated to be lower than semi-weighed dietary records.[23] Regarding the relative intake of macronutrients (% energy), BDHQ can evaluate almost equivalent to them. Several reports showed that the total energy expenditure of Japanese people with type 2 diabetes mellitus measured by doubly labeled water was from 2,113 to 2,490 kcal/day.[32, 33] Considering these results, the mean energy intake of 1,699 kcal/day might be underestimated. Therefore, we consider the result that the relative intake of macronutrients did not differ according to sleep duration to be crucial. However, we did not observe increased fat intake in short sleepers with type 2 diabetes mellitus, possibly because the patients received dietary counseling from a dietitian or self-educated themselves regarding appropriate diet.

We found that people with type 2 diabetes mellitus with short sleep duration consumed more confectionaries. Regarding confectionery intake, our findings are considered, because a correlation of 0.48 and 0.50 for men and women, respectively, was found between semi-weighed dietary records and BDHQ.[34] Several reports have suggested that adult short sleepers had increased energy intake from snacks, particularly after dinner.[28, 35–37] A cross-over study of 11 healthy individuals reported that 5.5 h sleep duration was associated with an increased amount of snacking, compared with 8.5 h sleep duration, especially between 19.00 and 07.00 h.[38] It was reported that a night of restricted sleep in women with normal weight led to increased hunger, fatigue, sleepiness, craving, and consumption of chocolate and potato chips.[39] Conversely, overweight young adults with extended sleep duration had lower overall appetite and cravings for sweet and salty foods.[40] Previous studies have not mentioned the association between confectionery consumption and sleep duration in people with type 2 diabetes mellitus. Short sleepers consumed more Western sweets, senbei, rice cakes and okonomiyaki than 7–7.9 h sleepers, whereas >8 h sleepers consumed fewer senbei, rice cakes and okonomiyaki in the present study. To the best of our knowledge, this is the first study to report that people with type 2 diabetes mellitus who consumed more confectionaries had shorter sleep duration, primarily due to Western sweets, senbei, rice cakes and okonomiyaki in Japan. Conversely, lower confectionery consumption was correlated with longer sleep duration. The present findings might suggest that insufficient sleep duration increases the consumption of confectionaries, whereas sufficient sleep duration decreases confectionery consumption.

Other factors associated with consuming confectionaries and snacks have also been mentioned. Using the BDHQ, Komada *et al*[41] found that Japanese women consumed more confectionaries (g/1,000 kcal) than men. Alcohol consumption has been reported to be associated with increased appetite, urge to snack and total calorie intake.[42] However, the difference between alcohol users and non-users regarding confectionery consumption is unknown. Nicotine use has been associated with lower calorie intake, although not specifically with confectionery and fatty food consumption.[43] In the general population, consuming confectionaries is a risk factor for metabolic syndrome, whereas consuming snacks is a risk factor for type 2 diabetes mellitus and hypercholesterolemia.[44–46] In the present study, increased consumption of confectionery was associated with higher HbA1c levels and dyslipidemia, suggesting its contribution to poor glycemic control and dyslipidemia. These

findings show that instructing people with type 2 diabetes mellitus with poor glycemic control to avoid consuming confectionaries and snacks might contribute to better glycemic control and a lower incidence of dyslipidemia. Conversely, smokers and alcohol drinkers consumed fewer confectionaries. As current smokers and alcohol drinkers consume fewer confectionaries, smoking cessation or abstaining from alcohol might lead to increased consumption. When people with type 2 diabetes mellitus stop smoking or drinking, physicians might consider informing them of the potential increased confectionery consumption. Based on the relationship between increased consuming confectionaries and short sleep duration, and higher HbA1c levels in the present study, we recommend that short sleepers with type 2 diabetes mellitus who have difficulty reducing their confectionery intake maintain adequate sleep duration, which might lead to avoiding confectionery intake and obtaining better glycemic control.

The present research had some limitations. First, the diet and sleep duration data were based on self-reported questionnaires, which were susceptible to bias, especially recall bias. In the study by Lauderdale *et al*[47], there was a 0.45 correlation between self-reported and measured sleep time. People with type 2 diabetes mellitus, people with obesity and women tended to underreport in the diet questionnaire.[48,49] Second, data on physical activity were missing. A previous report suggested that restricted sleep duration reduces physical activity.[27] In addition, data regarding shift work were missing, which has been reported to cause social jet lag and to have several effects on metabolism.[50] Essential information on obstructive sleep apnea was also missing. Compared with people with type 2 diabetes mellitus without obstructive sleep apnea, those with obstructive sleep apnea alone had an increased adjusted mean HbA1c of 0.52%–3.69% (5 mmol/mol–40 mmol/mol).[51] Third, as the present study was cross-sectional, it was impossible to determine the causality between dietary intake and sleep duration in our study population. Fourth, as participants with sleep durations of 9–9.9 h and 10–11.4 h accounted for only 2.6% (75/2887) and 1.0% (29/2887), respectively, the numbers might not be sufficient to evaluate long sleep durations.

The present study suggests that short sleepers with type 2 diabetes mellitus are associated with higher consumption of confectionaries, which contributes to poor glycemic control. Therefore, further investigations are required to evaluate the causation between sleep duration and dietary intake. An objective assessment of sleep and food intake should be carried out to accurately assess this relationship. Based on the results of this study, short sleepers with type 2 diabetes mellitus could possibly improve their glycemic control by maintaining adequate sleep duration and avoiding confectionery consumption.

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DISCLOSURE

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Approval of the research protocol: This research conformed to the provisions of the Declaration of Helsinki (revised in Fortaleza, Brazil, October 2013) and was approved by the Yokohama City University Clinical Research Review Board (approval date 22 May 2014, approval number D1405028).

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Registry and the registration no. of the study/trial: This study is registerd at UMIN Clinical Trials Registry. The registration no. is UMIN000014318.

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CLINICAL TRIAL

Effects of hybrid closed-loop system on glycemic control and psychological aspects in persons with type 1 diabetes treated with sensor-augmented pump: A prospective single-center observational study

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ABSTRACT

Aims/Introduction: This study evaluated the effects of the Medtronic MiniMed 770G hybrid closed-loop system on glycemic control and psychological aspects in persons with type 1 diabetes mellitus.

Materials and Methods: This 3-month prospective observational study included 22 participants with type 1 diabetes mellitus who used the Medtronic MiniMed 640G predictive low-glucose suspend system and were switched to the 770G system. Time in the range of 70–180 mg/dL and glycated hemoglobin levels were evaluated; satisfaction, emotional distress and quality of life were assessed using self-reported questionnaires, including the Diabetes Treatment Satisfaction Questionnaire Status, Problem Area in Diabetes and Diabetes Therapy-Related Quality of Life.

Results: Time in the range of 70–180 mg/dL increased (63.5 ± 13.4 to 73.0 ± 10.9% [mean ± standard deviation], $P = 0.0010$), and time above the range of 181–250 mg/dL decreased (26.9 ± 8.9 to 19.6 ± 7.1%, $P < 0.0005$). Glycated hemoglobin levels decreased (7.7 ± 1.0 to 7.2 ± 0.8%, $P = 0.0021$). The percentage of participants with time below the range of 54–69 mg/dL <4% of readings increased from 91% to 100% ($P < 0.0005$). No significant changes were detected in the satisfaction, emotional distress and quality of life levels, but increased sensor calibration might be related to worsened emotional distress and quality of life.

Conclusions: The hybrid closed-loop system decreased hyperglycemia and minimized hypoglycemia, but did not improve psychological aspects compared with the predictive low-glucose suspend system, probably because sensor calibration was increased.

INTRODUCTION

Type 1 diabetes mellitus is developed by the destruction of pancreatic β-cells, resulting in insulin deficiency; therefore, insulin replacement therapy is indispensable for persons with type 1 diabetes mellitus[1]. Although multiple daily insulin injection therapy is widely used for the treatment of type 1 diabetes mellitus, sensor-augmented pump (SAP) therapy, which combines continuous subcutaneous insulin infusion and continuous glucose monitoring (CGM), is an alternative treatment modality for type 1 diabetes mellitus[2]. The MiniMed 640G (Medtronic, Northridge, CA, USA) with the predictive low-glucose suspend (PLGS) system is a SAP therapy device mainly used in Japan

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until 2021. This device automatically stops basal insulin infusion when hypoglycemia is expected to occur. The PLGS system reduced the percentage of time below blood glucose range (TBR) of 70 mg/dL without increasing that of time above blood glucose range (TAR) of 180 mg/dL, predominantly in individuals of European ancestry[3]. However, in Japanese persons with type 1 diabetes mellitus, the PLGS system decreased the percentage of TBR 50 mg/dL and increased the percentage of TAR 180 mg/dL, as reported by Tsunemi *et al.*[4] Although the PLGS system had difficulty in controlling hyperglycemia, a new hybrid-closed loop (HCL) system emerged as a new technology to address these challenges. The HCL system utilizes an algorithm to adjust glucose levels to a target value, thus preventing hypoglycemia by reducing the insulin infusion rate and treating hyperglycemia by adjusting the insulin infusion rate automatically based on blood glucose levels[5]. The MiniMed 770G (Medtronic), SAP with the HCL system, was first approved in 2022 by the Japanese Pharmaceuticals and Medical Devices Agency. Previous reports carried out mainly in Western countries have shown that the HCL system improved glycemic control by preventing hypoglycemia compared with multiple daily insulin injection therapy and other SAP therapies[6–10]. However, the superiority of the new HCL system for the treatment of Japanese persons with type 1 diabetes mellitus is yet to be established.

Regarding the psychological impacts, SAP with the PLGS system has been reported to improve diabetes treatment satisfaction and reduce fear of hypoglycemia compared with blood glucose self-monitoring[11]. However, the effect of the HCL system on psychological aspects has not been fully elucidated. Therefore, this research evaluated the effects of the MiniMed 770G HCL system on both glycemic control and psychological aspects in Japanese persons with type 1 diabetes mellitus.

MATERIALS AND METHODS

Participants

The present study enrolled adults with type 1 diabetes mellitus previously treated with the MiniMed 640G PLGS system who visited Yokohama City University Medical Center. The following participants were excluded from this study: (1) with secondary diabetes or type 2 diabetes; (2) with drug-induced diabetes or current corticosteroid therapy; (3) with malignancy; (4) who refused to participate in this research; and (5) who were regarded as ineligible for the study by the attending physicians. At the beginning of the study, 23 participants were recruited, and then one participant was excluded, because she underwent simultaneous pancreas and kidney transplantation during the observational period, and weaned off the insulin pump. Thus, 22 participants completed this study.

Methods

In the present 3-month prospective observational study, all participants were switched from the PLGS system to the MiniMed 770G HCL system with Auto Mode, where the algorithm maintains sensor glucose levels at 120 mg/dL using Guardian Sensor 3 (Medtronic). For 18 participants, CIR at baseline was determined as follows: 10.5 ± 4.4 at breakfast, 13.4 ± 5.7 at lunch and 11.6 ± 5.1 at dinner, and the same CIR was continued after switching to MiniMed 770G. For four patients, CIR was not determined at baseline and was set to 10.0 when MiniMed 770G was introduced. CIR was adjusted as needed during the observational period.

We assessed standardized CGM metrics[12], glycated hemoglobin (HbA1c) levels and psychological aspects. Standardized CGM metrics included novel glucose statistics and targets, such as the percentage of time in blood glucose range (TIR) 70–180 mg/dL, the percentage of TAR (181–250 mg/dL, and >250 mg/dL); the percentage of TBR (54–69 mg/dL and <54 mg/dL); mean glucose levels (mg/dL); glucose management indicator (%); and glycemic variability. CareLink system software (Medtronic) was used to collect information directly from the MiniMed 770G HCL system and automatically analyze the data. Self-reported questionnaires were administered to the participants at baseline, and 3 months after the HCL treatment to assess their treatment satisfaction, emotional distress and quality of life (QOL) using the Diabetes Treatment Satisfaction Questionnaire Status (DTSQs), Problem Area in Diabetes Scale (PAID) and Diabetes Therapy-Related QOL (DTR-QOL) questionnaire, respectively.

DTSQs questionnaire

The DTSQs was used to assess the treatment satisfaction[13,14] encompassing eight questions, scored on a scale of 0–6. To calculate the overall score, questions 1 (satisfaction with current treatment), 4 (convenience), 5 (flexibility), 6 (satisfaction with own understanding of their diabetes), 7 (how likely to recommend the treatment) and 8 (how satisfied to continue the treatment) were summed and converted to a scale of 0–36, as previously reported. A higher score indicates greater satisfaction. Questions 2 and 3 address feelings of hyperglycemia and hypoglycemia, respectively.

PAID questionnaire

The emotional distress was assessed using PAID[15,16], which includes 20 items, scored on a scale from 1 to 5. The scores for each question were summed and converted to a scale of 0–100. A higher score indicates a higher level of emotional distress.

DTR-QOL questionnaire

The DTR-QOL questionnaire consisted of 29 questions, scored on a scale of 1–7[17]. The scores for each question were summed and converted to a scale of 0–100, with higher scores indicating higher QOL. The DTR-QOL assesses four factors; factor 1: burden on social activities and daily activities; factor 2: anxiety and dissatisfaction with treatment; factor 3: hypoglycemia; and factor 4: satisfaction with treatment.

Ethical considerations

Written informed consent was obtained from all the participants. This study was approved by the Yokohama City University Ethics Committee (approval number F211100011), and conformed to the principles of the Declaration of Helsinki (revised in Fortaleza, Brazil, October 2013).

Blood sampling and biochemical analysis

HbA1c was obtained using high-performance liquid chromatography, and urine albumin concentration was obtained using an immunoturbidimetric method (N-assay TIA Micro Alb system; Nittobo Medical Co., Ltd., Tokyo, Japan).

Statistical analysis

Continuous data are presented as the mean ± standard deviation or median (interquartile range 25–75%), and categorical data are given as numbers with percentages. The changes in CGM data and HbA1c levels at 1, 2 and 3 months after the initiation of MiniMed 770G were assessed using a two-tailed paired *t*-test and Wilcoxon signed-rank test, as needed. McNemar's test was carried out to evaluate the achievement of treatment targets at 3 months. Furthermore, Lasso regression was used to screen the factors influencing the score of the questionnaires at 3 months.

Significance was set at $P < 0.05$. Statistical analyses were carried out using the JMP Pro software, version 17.0.0 (SAS Institute Inc., Cary, NC, USA).

RESULTS

Baseline clinical characteristics

The mean age of the 22 participants was 48.2 ± 13.0 years, and five participants were men. The mean baseline body mass index and mean HbA1c levels were 24.0 ± 4.4 kg/m^2 and 7.7 ± 1.0% (60 ± 11 mmol/mol), respectively (Table 1).

Table 1 | Baseline characteristics

Characteristics	*n* = 22
Age (years)	48.2 ± 13.0
Sex (male : female)	5:17
Body mass index (kg/m^2)	24.0 ± 4.4
Duration of diabetes (years)	15 (8–23.25)
Alcohol, % (*n*)	41 (9)
Current smoker, % (*n*)	22 (5)
Hypertension, % (*n*)	32 (7)
Dyslipidemia, % (*n*)	41 (9)
Glycated hemoglobin (%)	7.7 ± 1.0
Glycated hemoglobin (mmol/mol)	60 ± 11
Treatment, % (*n*)	
Aspart	27 (6)
Lispro	73 (16)
Sodium–glucose cotransporter 2 inhibitor	18 (4)
Complications % (*n*)	
Neuropathy	23 (5)
Retinopathy	6 (27)
Nephropathy	9 (2)

Data are presented as the mean ± standard deviation, the median (interquartile range 25–75%), or percentage (%).

Glycemic outcomes

Three months after HCL system initiation, for a median of 92% (interquartile range 60.5–96%) of the time, insulin infusion was provided by the Auto Mode of MiniMed 770G. TIR 70–180 mg/dL increased from 63.5 ± 13.4 to 73.0 ± 10.9% (mean ± standard deviation; $P = 0.0010$), whereas TAR 181–250 mg/dL decreased from 26.9 ± 8.9 to 19.6 ± 7.1% ($P < 0.0005$; Table 2). One month after treatment with the HCL system, TIR 70–180 mg/dL increased from 63.5 ± 13.4 to 69.9 ± 13.4% ($P = 0.016$), and then it reached a plateau at 70.7 ± 12.2% in the next 2 months (Figure 1). In the same period, TAR 181–250 mg/dL decreased from 26.9 ± 8.9 to 21.3 ± 7.4% ($P = 0.0026$) at 1 month, and it remained at 20.9 ± 7.7% the next 2 months. Regarding TAR >250 mg/dL, TBR 54–69 mg/dL and TBR < 54 mg/dL, no significant changes were observed after 3 months of HCL system use compared with values at baseline (TAR >250 mg/dL: median [interquartile range] 3.0 [1.75–9.0] vs baseline 7.0 [2.75–12.5], $P = 0.15$; TBR 54–69 mg/dL: 1 [1, 2] vs 1 [0–2.25], $P = 0.51$; TBR <54 mg/dL: 0 [0–1] vs 0 [0–0.25], $P = 0.36$; Table 2). In regard to the percentage of the time of hypoglycemia, two participants had TBR 54–69 mg/dL ≥4% of readings 1 month before switching to the HCL system, whereas none of the participants had such readings with the HCL system ($P < 0.0005$).

Mean glucose levels decreased from 164.5 ± 20.7 to 151.4 ± 17.6 mg/dL ($P = 0.0030$), and the glucose management indicator also decreased from 7.2 ± 0.5 to 6.9 ± 0.4% ($P = 0.0072$). HbA1c levels also decreased from 7.7 ± 1.0 to 7.2 ± 0.8% ($P = 0.0021$). The basal and bolus insulin doses were not changed significantly. Sensor calibration increased from 2.7 ± 1.1 to 3.3 ± 1.6 times/day ($P = 0.023$). The number of total alarms increased from 7.5 ± 4.4 to 10.5 ± 5.6 times/day ($P < 0.0005$), and Auto-Mode related alarms were 3.4 ± 1.7 times/day at 3 months. Regarding adverse events, there were no episodes of diabetic ketoacidosis and severe hypoglycemia with the HCL system.

Psychological aspects

There were no significant changes in the DTSQs, PAID and DTR-QOL at 3 months after the treatment with the HCL system (DTSQs: 26.9 ± 5.9 vs baseline 27.1 ± 4.1, $P = 0.81$; PAID: 38.6 ± 23.4 vs 40.8 ± 21.3, $P = 0.44$; DTR-QOL: 52.2 ± 20.9 vs baseline 49.2 ± 19.5, $P = 0.38$; Table 3). Regarding the DTR-QOL, factors 1, 2, 3 and 4 did not differ significantly.

With regard to DTSQs, no significant effects were observed with any of the factors. As for question 8, "how satisfied to continue the treatment," the ratio of the participants whose score increased to those whose score decreased was 2.25 (increased participants: 41% [9/22], decreased participants: 18%

Table 2 | Glycemic outcomes at baseline and after 3 months

Outcome	Baseline	Follow up at 3 months	*P*
Median percentage of time CGM is active	87 (80.75–97)	89 (60.75–94)	0.1521
Median percentage of time in Auto Mode		92 (60.5–96)	
Mean TIR 70–180 mg/dL (%)	63.5 ± 13.4	73.0 ± 10.9	0.0010*
TIR 70–180 mg/dL >70% of readings, % (*n*/total *n*)	41 (9/22)	64 (14/22)	0.0253**
Mean TAR 181–250 mg/dL (%)	26.9 ± 8.9	19.6 ± 7.1	<0.0005*
TAR 181–250 mg/dL <25% of readings, % (*n*/total *n*)	36 (8/22)	82 (18/22)	0.0016**
Median TAR >250 mg/dL (%)	7.0 (2.75–12.5)	3.0 (1.75–9.0)	0.15
TAR >250 mg/dL <5% of readings, % (*n*/total *n*)	41 (9/22)	59 (13/22)	0.10
Median TBR 54–69 mg/dL (%)	1 (0–2.25)	1 (1–2)	0.51
TBR 54–69 mg/dL <4% of readings, % (*n*/total *n*)	91 (20/22)	100 (22/22)	<0.0005**
Median TBR < 54 mg/dL (%)	0 (0–0.25)	0 (0–1)	0.36
TBR <54 mg/dL <1% of readings, % (*n*/total *n*)	77 (17/22)	64 (14/22)	0.32
Glycated hemoglobin levels (%)	7.7 ± 1.0	7.2 ± 0.8	0.0021*
Mean glucose (mg/dL)	164.5 ± 20.7	151.4 ± 17.6	0.0030*
Glucose management indicator	7.2 ± 0.5	6.9 ± 0.4	0.0072*
Glycemic variability (%)	33.0 ± 4.9	33.3 ± 3.8	0.82
Total insulin dose (units)	39.6 ± 21.4	38.5 ± 22.7	0.27
Basal insulin dose (units)	24.5 ± 17.1	22.4 ± 16.4	0.085
Basal insulin (%)	41.0 ± 16.7	44.8 ± 15.5	0.082
Bolus insulin dose (units)	15.1 ± 7.1	16.2 ± 7.9	0.27
Bolus insulin (%)	59.0 ± 16.7	55.2 ± 15.5	0.082
CIR breakfast	10.5 ± 4.4	10.4 ± 4.1	0.31
CIR lunch	13.4 ± 5.7	13.2 ± 5.8	0.35
CIR dinner	11.6 ± 5.1	11.3 ± 4.7	0.26
Sensor calibration (times/day)	2.7 ± 1.1	3.3 ± 1.6	0.023*
Total alarms (times/day)	7.5 ± 4.4	10.5 ± 5.6	<0.0005*
Hyperglycemic alarms (times/day)	0.25 (0–1.75)	0.17 (0.05–1.33)	0.15
Hypoglycemic alarms (times/day)	2.0 (0.83–2.79)	1.1 (0.32–3.38)	0.33
Auto-mode related alarms (times/day)	–	3.4 ± 1.7	
Other alarms (times/day)	4.4 ± 2.0	3.9 ± 1.7	0.14
Bodyweight (kg)	59.8 ± 12.0	59.7 ± 12.4	0.82

Data are presented as the mean ± standard deviation and median (interquartile range 25–75%). Note that the glucose management indicator and glycemic variability represent the average of 21 participants, excluding one person, because wearing continuous glucose monitoring (CGM) was required for at least 10 days in a month to calculate; carbohydrate-to-insulin ratio (CIR) represent the average of 18 participants, excluding four people whose CIR was not determined at baseline, and set to CIR 10.0 when they started MiniMed 770G. *****$P < 0.05$, paired *t*-test and Wilcoxon signed-rank test ******$P < 0.05$, McNemar's test. TAR, time above blood glucose range; TBR, time below blood glucose range; TIR, time in blood glucose range.

[4/22]). For other questions in DTSQs, results were not shown, because the ratio was between 0.5 and 2.0.

The influence on the PAID score was analyzed by Lasso regression, and an unfavorable influence was observed with factors as follows. TBR 54–69 mg/dL at 3 months (standardized partial regression coefficient [β] 0.31; 95% confidence interval [CI] −41.91–42.52) and the change in sensor calibration from baseline to 3 months (β 0.56; 95% CI −24.70–25.82; Table 4; Figure 2). Regarding each question, (1) "Not having clear and concrete goals for your diabetes care"; (2) "Uncomfortable interactions around diabetes with family/friends"; (3) "Feeling constantly concerned about food and eating"; (4) "Feeling unsatisfied with your diabetes physician"; (5) "Feeling that friends/family are not supportive of diabetes management efforts"; and (6) "Feeling 'burned out' by the constant effort to manage diabetes," the ratios of the participants who had an increased score to those who had a decreased score were: (1) 0.33, (2) 0.44, (3) 0.43, (4) 0.25, (5) 0.20 and (6) 0.16, respectively. Conversely, regarding the question "Not accepting diabetes," the ratio was 3.0. For other questions in PAID, the ratio was between 0.5 and 2.0.

Regarding DTR-QOL score, a favorable effect on the score was found with the change in hyperglycemic alarms (β 0.44; 95% CI −6.29–7.17), whereas the unfavorable effect was observed with TBR <54 mg/dL at 3 months (β −0.077; 95% CI −17.43–17.28) and the change in sensor calibration (β −0.48; 95% CI −10.20–9.24). Regarding each factor above, with factor 1 on the DTR-QOL score, each of the three factors showed a

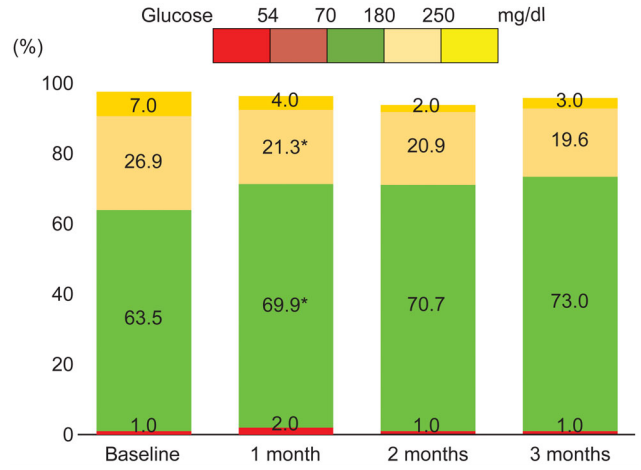


Figure 1 | Glycemic outcomes from continuous glucose monitoring data at baseline and at 1, 2 and 3 months after starting the MiniMed 770G. Time in blood glucose range 70–180 mg/dL and time above blood glucose range 180–250 mg/dL are presented as the mean, time above blood glucose range TAR >250 mg/dL, time below blood glucose range (TBR) 54–70 mg/dL and time below blood glucose range <54 mg/dL as the median. *$P < 0.05$; paired *t*-test and Wilcoxon signed-rank were used to compare glycemic outcomes in a month with those of the preceding month.

Table 3 | Psychological aspects during the baseline period and after 3 months

Outcome	Baseline	Follow up at 3 months	*P*
DTSQs score	27.1 ± 4.1	26.9 ± 5.9	0.81
PAID score	40.8 ± 21.3	38.6 ± 23.4	0.43
Total DTR-QOL score	49.2 ± 19.5	52.2 ± 20.9	0.38
Factor 1: burden on social activities and daily activities	59.4 ± 21.4	60.9 ± 22.1	0.71
Factor 2: anxiety and dissatisfaction with treatment	42.0 ± 22.6	48.1 ± 25.4	0.19
Factor 3: hypoglycemia	37.1 ± 27.7	37.3 ± 30.9	0.96
Factor 4: satisfaction with treatment	59.3 ± 18.5	63.6 ± 18.4	0.25

Data are presented as the mean ± standard deviation. A paired *t*-test was used to compare the psychological aspects at baseline and after 3 months. DTR-QOL, Diabetes Therapy-Related Quality of Life; DTSQs, Diabetes Treatment Satisfaction Questionnaire Status; PAID, Problem Area in Diabetes Scale.

similar effect (Table 4; Figure 2). For factor 2, 3 and 4, none of the factors showed a significant effect.

DISCUSSION

We showed that the MiniMed 770G HCL system could increase TIR 70–180 mg/dL and decrease TAR 181–250 mg/dL, compared with the MiniMed 640G PLGS system, without increasing hypoglycemia and affecting treatment satisfaction, emotional distress, and QOL after a 3-month period among Japanese persons with type 1 diabetes mellitus.

Table 4 | Lasso regression analysis of the factors on the score of self-reported questionnaires at 3 months

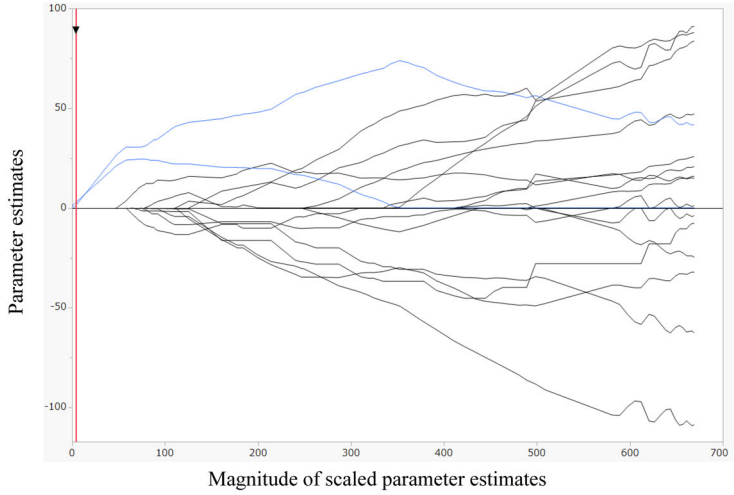
	β	95% confidence interval
DTSQs score		
Non-zero parameters were not estimated		
PAID score		
TBR 54–69 mg/dL at 3 months	0.31	−41.91–42.52
Change in sensor calibration from baseline to 3 months	0.56	−24.70–25.82
DTR-QOL score		
TBR <54 mg/dL at 3 months	−0.077	−17.43–17.28
Change in hyperglycemic alarms	0.44	−6.29–7.17
Change in sensor calibration	−0.48	−10.20–9.24
DTR-QOL score factor1: burden on social activities and daily activities		
TBR < 54 mg/dL at 3 months	−2.08	−29.81–25.66
Change in hyperglycemic alarms	1.56	−12.48–15.60
Change in sensor calibration	−1.46	−14.52–11.60
DTR-QOL score factor2, 3, 4		
Non-zero parameters were not estimated		

The variables on Lasso regression included age; sex; duration of diabetes; baseline body mass index; the percentage of time in Auto-Mode; each standardized continuous glucose monitoring metric; hyperglycemic, hypoglycemic and other alarms; Auto-Mode-related alarms; sensor calibration; glycated hemoglobin at 3 months and the change from baseline to 3 months in each standardized continuous glucose monitoring metric, hyperglycemic, hypoglycemic and other alarms, sensor calibration, and glycated hemoglobin. Only factors with non-zero regression coefficients are listed. β, partial regression coefficient; DTSQs, Diabetes Treatment Satisfaction Questionnaire Status; DTR-QOL, Diabetes Therapy-Related Quality of Life; PAID, Problem Area in Diabetes Scale; TBR, time below blood glucose range.

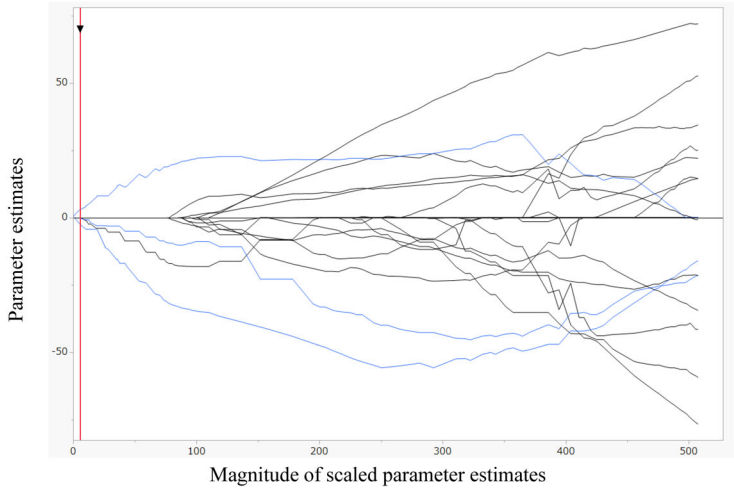
According to previous studies on glycemic control, a randomized controlled study showed that HCL systems were favored over PLGS systems on TIR 70–180 mg/dL (70.4 ± 8.1% vs 57.9 ± 11.7%, $P < 0.001$)[9]. Da Silva *et al.*[6] reported that the 3-month treatment with the MiniMed 670G HCL system was similar to MiniMed 770G in terms of glycemic control, whereby the mean TAR >250 mg/dL, TAR 181–250 mg/dL, TIR 70–180 mg/dL, TBR 54–69 mg/dL and TBR <54 mg/dL reached 5.5%, 19.6%, 72.6%, 1.8% and 0.5%, respectively, in 14 899 European users. Furthermore, among 3,141 participants in the USA, these metrics in a 3-month cohort were 5.4%, 24.6%, 73.3%, 2.1% and 0.5%, respectively[18]. In the present study, the effects of the HCL system in Japanese persons with type 1 diabetes mellitus were similar to those observed in Europeans and Americans.

The international consensus on clinical targets for CGM data of persons with type 1 diabetes mellitus recommended that target percentages of TAR >250 mg/dL, TAR 181–250 mg/dL,

(a) The variation characteristics of Lasso coefficient of variables on PAID



(b) The variation characteristics of Lasso coefficient of variables on DTR-QOL



(c) The variation characteristics of Lasso coefficient of variables on DTR-QOL factor 1

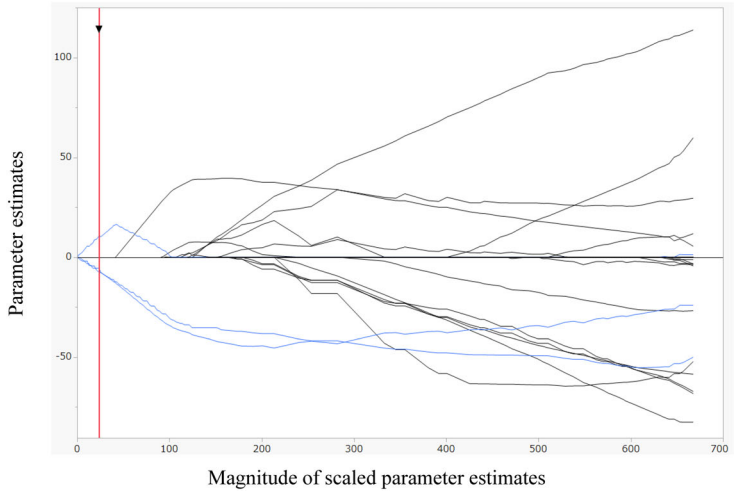


Figure 2 | The variation characteristics of Lasso coefficient of variables on each self-reported questionnaire. (a) The variation characteristics of Lasso coefficient of variables on the Problem Area in Diabetes Scale. (b) The variation characteristics of Lasso coefficient of variables on Diabetes Therapy-Related Quality of Life. (c) The variation characteristics of Lasso coefficient of variables on Diabetes Therapy-Related Quality of Life factor 1.

TIR 70–180 mg/dL, TBR 54–69 mg/dL and TBR < 54 mg/dL were <5%, <25%, >70%, <4% and <1%, respectively[12]. In the current study, the percentage of participants with TIR 70–180 mg/dL >70% of readings increased from 41% to 64%, whereas those with TAR >180 mg/dL <25% and TBR 54–69 mg/dL <4% of readings increased from 36% to 82% and from 91% to 100% after the 3-month period of time, respectively (Table 2). The present results showed that the HCL system helped achieve the target of the international consensus in Japanese persons with type 1 diabetes mellitus, decreasing hyperglycemia and hypoglycemia.

Regarding psychological aspects, a randomized crossover trial reported that the 670G HCL system improved the treatment satisfaction and sleep quality of patients compared with the PLGS system (DTSQs: HCL system 30.9 ± 0.7 vs PLGS system 27.9 ± 0.7, $P = 0.004$)[19]. McAuley *et al.*[20] reported that diabetes-specific positive well-being and QOL were better with the MiniMed 670G HCL system compared with multiple daily insulin injection therapy or insulin pump therapy without CGM, although their diabetes treatment satisfaction and diabetes distress were not changed.

The present research showed that the HCL system did not improve treatment satisfaction, emotional distress and QOL compared with the PLGS system. To the best of our knowledge, this is the first study to assess the psychological aspects between the MiniMed 770G or 670G HCL system and the 640G PLGS system in Asian populations. One of the reasons the HCL system did not improve their psychological aspects, despite improving glycemic control, might have been due to frequent alarms and the need for calibration by self-monitoring of blood glucose to maintain the Auto-Mode. These were the possible reasons reported for HCL system discontinuation[21]. Sensor calibration increased from 2.7 ± 1.1 to 3.3 ± 1.6 times/day, and the number of total alarms increased from 7.5 ± 4.4 to 10.5 ± 5.6 times/day in this study. Furthermore, our research showed that increased sensor calibration and hypoglycemia might worsen their emotional distress and QOL, especially in the burden on social activities and daily activities. However, increased hyperglycemic alarms were related to improving their QOL, possibly because they might be meant to handle the Auto-Mode, which was linked to the improvement of hyperglycemia.

Regarding each question on DTSQs and PAID, the HCL system might improve their satisfaction and distress with treatment, although the total score of these questionnaires was not changed. As a long period of time to get used to handling the HCL system is required, a 3-month period was not enough for some participants. A longer period of use might reduce self-monitoring of blood glucose and improve the psychological aspects.

The present study had several limitations. First, this was not a randomized controlled trial, but a prospective observational study without a control group. Although randomized controlled trials generally have a higher level of evidence, the results of this observational study are considered to be more reflective of actual clinical practice. Second, this was a single-center study, which restricts the generalizability of the results. Future studies, specifically multicenter randomized controlled trials, should be considered to further assess the effectiveness of HCL systems.

The novel HCL system evaluated in the present study showed good glycemic control by decreasing hyperglycemia and minimizing hypoglycemia compared with the PLGS system. Notably, the psychological aspects after the 3-month period were not improved in Japanese persons with type 1 diabetes mellitus, probably because sensor calibration was increased. However, because there is a possibility that the study period was not long enough to evaluate the psychological aspects of the participants, further investigations with a longer intervention period need to be considered.

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DISCLOSURE

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company, they obtained no current funding for this research, and this does not influence their adherence to all the journal policies on sharing data and materials. The other authors declare no conflict of interest.

Approval of the study protocol: This study conformed to the provisions of the Declaration of Helsinki (revised in Fortaleza, Brazil, October 2013), and was approved by the Yokohama City University Ethics Committee (approval date 18 January 2022, approval number F211100011).

Informed consent: Informed consent was obtained from all participants.

Approval date of Registry and the Registration No. of the research/trial: This research is registered at the UMIN Clinical Trials Registry. The registration no. is UMIN000046889 (approval date 17 February 2022).

Animal studies: N/A.

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論文目録

I.　主論文

Sleep duration and food intake in people with type 2 diabetes mellitus and factors affecting confectionary intake.

Akiyama, T., Yamakawa, T., Orime, K., Sakamoto, R., Takahashi, K., Suzuki, J., Matsuura-Shinoda, M., Shigematsu, E., Tanaka, S., Kaneshiro, M., Asakura, T., Kawata, T., Yamada, Y., Osada, U., Isozaki, T., Takahashi, A., Kadonosono, K., Terauchi, Y.

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II.　副論文

Effects of hybrid closed-loop system on glycemic control and psychological aspects in persons with type 1 diabetes treated with sensor-augmented pump: A prospective single-center observational study.

Akiyama, T., Yamakawa, T., Orime, K., Ichikawa, M, Harada, M., Netsu, T., Akamatsu, R., Nakamura, K., Shinoda, S., Terauchi, Y.

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Ⅲ. 参考論文

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