JDI Journal of Diabetes Investigation Open access
Official Journal of the Asian Association for the Study of Diabetes

ORIGINAL ARTICLE

Year-long effects of COVID-19 restrictions on glycemic control and body composition in patients with glucose intolerance in Japan: A single-center retrospective study

Ryo Tsukaguchi[1†], Takaaki Murakami[1†], Satoshi Yoshiji[1], Kenichiro Shide[2], Yoshihito Fujita[1], Masahito Ogura[1], Nobuya Inagaki[1*]

[1]Department of Diabetes, Endocrinology, and Nutrition, Graduate School of Medicine, Kyoto University, Kyoto, Japan, and [2]Department of Metabolism and Clinical Nutrition, Kyoto University Hospital, Kyoto, Japan

Keywords
Body composition, COVID-19, Social restrictions

***Correspondence**
Nobuya Inagaki
Tel.: +81-75-751-3560
Fax: +81-75-751-4244
E-mail address:
inagaki@kuhp.kyoto-u.ac.jp

J Diabetes Investig 2022; 13: 2063–2072

doi: 10.1111/jdi.13893

ABSTRACT

Aims/Instruction: During the coronavirus disease 2019 (COVID-19) pandemic, the lockdowns in Europe raised concerns about negative effects on glycemic control and body composition in patients with diabetes. In Japan, voluntary-based restrictions were imposed as the declaration of a state of emergency (DSE), whose metabolic consequences have not been fully investigated. We carried out a single-center retrospective study to evaluate changes in glycemic control and body composition in outpatients with glucose intolerance after the DSE.

Materials and Methods: We enrolled outpatients with glucose intolerance: (i) for whom longitudinal data about body composition were available; (ii) who participated in dietary follow up with nutritionists; and (iii) whose laboratory data included glycated hemoglobin (HbA1c) levels before and after the DSE.

Results: Among 415 patients, we found no significant changes in HbA1c overall after the DSE. Bodyweight and fat mass increased significantly, whereas skeletal mass decreased significantly. HbA1c changes after the DSE were significantly correlated with changes in bodyweight and fat mass. In 128 patients whose HbA1c levels increased ≥0.3%, changes in bodyweight and fat mass were significantly larger than those in the other 287 patients. With regard to lifestyle changes, increased snacking was likely to worsen glycemic control (odds ratio 1.76, P = 0.036).

Conclusions: COVID-19 restrictions in Japan had unfavorable metabolic consequences for patients with glucose intolerance, highlighted by increased bodyweight and body fat, and decreased skeletal muscle. In addition, lifestyle changes, such as increased snacking, might worsen glycemic control. Clinical attention and interventions are required to prevent such metabolic changes.

INTRODUCTION

Coronavirus disease 2019 (COVID-19) has spread all over the world[1]. Several countries, especially in Europe, implemented city lockdowns to prevent further spread of the infection, whereas Japan issued a declaration of a state of emergency (DSE) instead of implementing lockdowns[2].

In the lockdowns, strict social restrictions, such as stay-at-home orders, were imposed. For patients with diabetes, the dramatic social changes have raised concerns about negative effects on glycemic control and body composition through increased mental stress and lifestyle changes[2–4]. Several studies about how the lockdowns affected glycemic control in patients with glucose intolerance (GI) including diabetes mellitus have been carried out, but the reported results have varied[3–8]. In contrast, the state of emergency (SoE) in Japan entailed less strict

†These authors contributed equally to this work.

Received 4 May 2022; revised 25 July 2022; accepted 2 August 2022

restrictions; people were requested to stay at home, and the use of public transportation and facilities was restricted[2]. Although a SoE is a request-based measure, and the rate of compliance and its actual influence on individual daily activities are uncertain, similar concerns about metabolic influences should be raised, because the interdependent character of Japanese populations might cause equivalent metabolic consequences through lifestyle changes[9]. In fact, an approximately 50% reduction in the flow of people in several commercial districts 2 weeks after the DSE was reported[10]. Some reports showed altered lifestyles and metabolic influences in patients with diabetes, mainly during the initial 1–2 months after the DSE[2,11–13]. However, the SoE was first declared for the areas including Kyoto, on 7 April 2020; then it expanded to include the whole nation on 16 April 2020, and lasted throughout the nation until 31 May 2021, with intermittent lifting. Furthermore, most of the studies were carried out only with questionnaires about lifestyles; only one study with a small number of elderly participants provided data about body composition[14]. Thus, the year-long metabolic consequences of the prolonged SoE in Japan, including body composition, have not been fully investigated.

We carried out a single-center retrospective study of metabolic changes, including bioelectrical impedance analysis (BIA)-derived body composition, in Japanese outpatients with GI after the initial 2 months of the SoE. In addition, we studied interview records evaluated by registered dietitians to evaluate the influence of the SoE on aspects of metabolic status, such as glycemic control, bodyweight and body composition, as well as the influence of lifestyles, including dietary habits and physical activity. To clarify the risk factors for changes in glycemic control during COVID-19 pandemic-related social restrictions, we also investigated the association between these factors and glycemic control.

MATERIALS AND METHODS

Study design

The present single-center retrospective observational study was carried out in the diabetes outpatient clinic of Kyoto University Hospital (Kyoto City, Japan). We defined the period before the DSE as 1 January 2019 to 31 December 2019 (period 2019), and the period after the DSE as 1 June 2020 to 31 May 2021 (period 2020–2021) as the main study periods, and the main comparisons were carried out between the two periods. The 2020–2021 time period was set to start in June of 2020 to exclude early effects of the SoE, which were previously investigated focusing on the initial 1–2 months after the DSE[2,11–13]. We additionally collected the clinical data for enrolled patients that had been obtained from 1 January 2018 to 31 December 2018 (period 2018), for further validation of unique changes during the SoE. This was an opt-out study. The protocol of this study was approved by the Kyoto University Graduate School and Faculty of Medicine, Ethics Committee (registry no. R2377), and conformed to the provisions of the Declaration of Helsinki.

Study population

We enrolled patients with GI: (i) who received a body composition examination at least once during period 2019 and period 2020–2021, respectively; (ii) whose dietary follow-up records were evaluated by registered dietitians at least once during each period; and (iii) whose laboratory data included levels of glycated hemoglobin (HbA1c) that were obtained in the same month as body composition acquisition and nutritional guidance during each period. We excluded those who had been hospitalized, who underwent surgical operations after fasting, who took prescription corticosteroids or in whom late-stage cancers were diagnosed during the study period.

Data collection and measurements

All data used in the present study were collected retrospectively from the patients' electronic medical records. The laboratory data and clinical information included dietary records documented by registered dietitians obtained in the same month that body composition was measured. The clinical information also included sex, age, types and estimated duration of diabetes, laboratory data, therapeutic agents, presence of diabetic retinopathy and nephropathy, and medical history. For analysis of participants who were tested more than once during a period, the latest data were regarded as eligible. GI was defined as borderline GI, including impaired fasting glucose (IFG) and/or impaired glucose tolerance and diabetes mellitus, which were diagnosed in accordance with the report of the committee on the classification and diagnostic criteria of diabetes mellitus[15]. In the present study, we included the patients with impaired fasting glucose/impaired glucose tolerance, as little is known about the social restriction-induced metabolic consequences of such patients, although their glycemic control and body compositions might readily be expected to be affected by SoE in a manner similar to that of diabetes mellitus. During their regular nutritional guidance, registered dietitians collected exercise-related information, such as exercise frequency, in addition to dietary records, which included snack intake. To evaluate body composition, BIA was used (InBody 720; InBody Japan, Tokyo, Japan), as previously reported[16]. In the present study, the patients whose HbA1c levels increased $\geq$0.3% between period 2019 and period 2020–2021 were considered to have worsening glycemic control, whereas those whose HbA1c levels increased <0.3% were considered to have non-worsening glycemic control, in accordance with previous reports[13,17].

Statistical analysis

JMP Pro®, version 16 (SAS Institute, Cary, NC, USA) was used to carry out the statistical analyses. Continuous variables with normal distribution and those changes were presented as the mean ± standard deviation and mean ± standard error, respectively. In the case of non-normal distribution, medians with interquartile ranges were used. A paired or unpaired t-test, Wilcoxon sign-rank sum test, Mann–Whitney U-test or χ^2-test was applied appropriately. Correlations were evaluated with

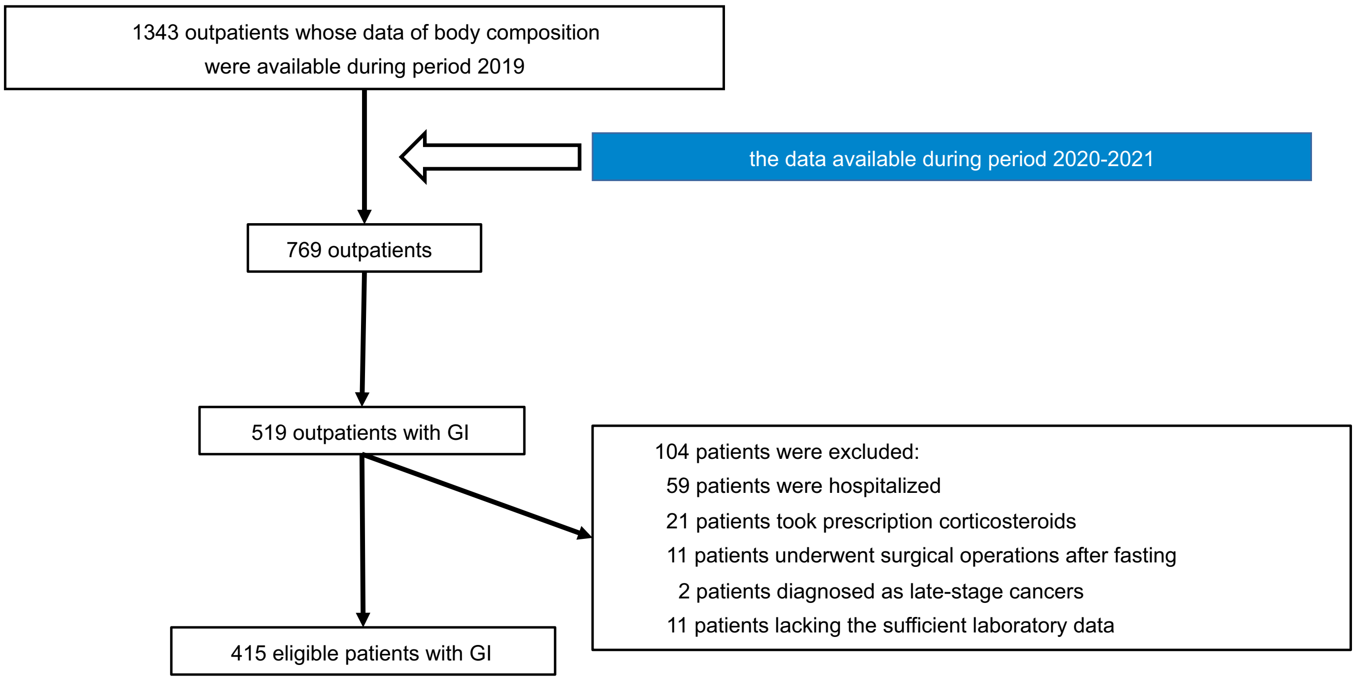

Figure 1 | The number of outpatients enrolled in the present study. There were 1,343 outpatients whose data of body composition were available during period 2019, and 769 outpatients whose data of body composition were also available during period 2020–2021. Among them, 519 outpatients had glucose intolerance (GI). A total of 104 patients were excluded for various reasons, and finally, we identified 415 eligible patients with GI in this study.

Spearman's rank correlation coefficient. A *P*-value of <0.05 was considered statistically significant, and 95% confidence intervals (CIs) are reported as appropriate.

RESULTS

Clinical characteristics of enrolled patients and changes during SoE

We identified 415 eligible patients (248 men, 167 women) with GI (Figure 1). The clinical characteristics of all the enrolled patients are shown in Table 1. Between periods 2019 and 2020–2021, body composition was assessed at intervals of, on average, 453.1 ± 78.7 days. During period 2019 (before the DSE), patients' age was 64.8 ± 12.4 years, HbA1c level was 7.33 ± 1.15%, bodyweight was 70.0 ± 16.5 kg and body mass index (BMI) was 26.1 ± 4.9 kg/m^2. In terms of body composition assessment by BIA, the skeletal muscle mass was 26.2 ± 5.9 kg; skeletal muscle percentage was 37.7% ± 4.9%; skeletal muscle index (SMI) was 9.7 ± 1.4 kg/m^2; body fat mass was 22.1 ± 10.2 kg; body fat percentage was 30.8% ± 8.4%; and lean body mass was 47.9 ± 9.9 kg. Between periods 2019 and 2020–2021 (during SoE), the HbA1c level did not change significantly ($P = 0.197$); however, the bodyweight increased significantly (to 70.3 ± 17.0 kg; $P = 0.034$), as did BMI (to 26.2 ± 5.2 kg/m^2; $P = 0.018$).

In terms of body composition during period 2020–2021, the skeletal muscle mass was 26.1 ± 6.0 kg, skeletal muscle percentage was 37.4 ± 4.9% and SMI was 9.7 ± 1.4 kg/m^2. These levels had decreased significantly since period 2019: skeletal muscle mass decreased by 0.12 ± 0.05 kg ($P = 0.016$); skeletal muscle percentage by 0.32% ± 0.08% ($P < 0.001$); and SMI by 0.04 ± 0.02 kg/m^2 ($P = 0.032$). In addition, during period 2020–2021, the body fat mass was 22.6 ± 10.7 kg and body fat percentage was 31.2 ± 8.4%. These measurements had increased significantly since period 2019: body fat mass increased by 0.45 ± 0.14 kg ($P = 0.001$) and body fat percentage by 0.47 ± 0.14% ($P = 0.001$). The clinical profiles and body composition measurements by BIA during period 2018 were available for 353 of the enrolled patients (Table 1). These body composition measurements, as well as HbA1c levels, bodyweight and BMI, did not differ significantly between periods 2018 and 2019. In analyses of only the populations whose data during period 2018 were available, the consistent trends, such as the insignificant change of HbA1c levels ($P = 0.130$), significantly increased BMI and body fat mass ($P = 0.039$ and $P = 0.001$, respectively), and decreased skeletal muscle mass and SMI ($P = 0.006$ and $P = 0.015$, respectively), were observed.

Associations between changes in body composition and status of glycemic control during SoE

We investigated whether changes in body composition were associated with glycemic control during the SoE. The

Table 1 | Clinical characteristics of enrolled patients and profile changes in 2018–2020/2021

	2018	2019	2020–2021	Change from 2018 to 2019	*P*-value (2018 vs 2019)	Change from 2019 to 2020–2021	*P*-value (2019 vs 2020–2021)
n (men/women)	353 (209/144)	415 (248/167)					
Age (years)	65.1 ± 12.3	64.8 ± 12.4					
Type of diabetes (BGI/type 2/type 1/other)	27/310/9/7	31/364/12/8					
Diabetes duration (years)		9 (3,15)					
eGFR (mL/min/1.73 m^2)	68.2 ± 18.3	66.5 ± 18.1	66.2 ± 18.9	−1.68 ± 6.79	<0.001*	−0.38 ± 0.38	0.556
HbA1c (%)	7.27 ± 1.10	7.33 ± 1.15	7.38 ± 1.18	0.06 ± 0.65	0.069	0.05 ± 0.04	0.197
Bodyweight (kg)	70.2 ± 16.5	70.0 ± 16.5	70.3 ± 17.0	−0.22 ± 2.75	0.127	0.32 ± 0.15	0.034*
BMI (kg/m^2)	26.2 ± 5.0	26.1 ± 4.9	26.2 ± 5.2	−0.09 ± 1.02	0.089	0.13 ± 0.05	0.018*
Skeletal muscle mass (kg)	26.3 ± 6.0	26.2 ± 5.9	26.1 ± 6.0	−0.08 ± 0.84	0.093	−0.12 ± 0.05	0.016*
Skeletal muscle percentage (%)	37.7 ± 4.9	37.7 ± 4.9	37.4 ± 4.9	0.04 ± 1.56	0.635	−0.32 ± 0.08	<0.001*
SMI (kg/m^2)	9.7 ± 1.4	9.7 ± 1.4	9.7 ± 1.4	−0.03 ± 0.31	0.112	−0.04 ± 0.02	0.032*
Body fat mass (kg)	22.2 ± 10.2	22.1 ± 10.2	22.6 ± 10.7	−0.13 ± 2.72	0.356	0.45 ± 0.14	0.001*
Body fat percentage (%)	30.8 ± 8.4	30.8 ± 8.4	31.2 ± 8.4	−0.15 ± 2.72	0.317	0.47 ± 0.14	0.001*
Lean body mass (kg)	48.0 ± 10.0	47.9 ± 9.9	47.8 ± 10.0	−0.09 ± 1.43	0.243	−0.14 ± 0.08	0.108
No. visiting hospital (times/year)		6 (4, 7)	5 (4, 6)			−0.53 ± 0.10	<0.001*
No. nutritional guidance (times/year)		5 (4, 6)	4 (3, 5)			−1.02 ± 2.10	0.017*
Comorbidities							
Dyslipidemia		354 (85.5%)					
Hypertension		274 (66.0%)					
Nephropathy (stage ≥2)		159 (39.6%)					
Retinopathy		103 (30.7%)					
Cardiovascular disease		77 (18.6%)					
Antidiabetic drugs							
DPP-4 inhibitor		196 (47.2%)	197 (47.5%)				0.945
Sulfonylurea		82 (19.8%)	83 (20.0%)				0.931
Glinide		23 (5.5%)	26 (6.3%)				0.659
Metformin		156 (37.6%)	169 (40.7%)				0.355
Thiazolidine		9 (2.2%)	9 (2.2%)				1.000
SGLT2 inhibitor		78 (18.8%)	87 (21.0%)				0.434
α-Glucosidase inhibitor		25 (6.0%)	24 (5.8%)				0.883
GLP-1 receptor agonist		25 (6.0%)	31 (7.5%)				0.406
Insulin		84 (20.2%)	85 (20.5%)				0.931

Data are presented as mean ± standard deviation, median (1st, 3rd) or *n* (%), except for changes from 2019 to 2020–2021 presented as mean ± standard error. The data at period 2018, 2019 and 2020–2021 were obtained from 1 January 2018 to 31 December 2018, from 1 January 2019 to 31 December 2019, and from 1 June 2020 to 31 May 2021, respectively. **P*-value <0.05. BGI, borderline glucose intolerance; BMI, body mass index; DPP-4, dipeptidyl peptidase-4; eGFR, estimated glomerular filtration rate; GLP-1, glucagon-like peptide-1; HbA1c, glycated hemoglobin; SGLT2, sodium–glucose cotransporter 2; SMI, skeletal muscle index.

Table 2 | Association of body composition changes with glycemic control during declaration of a state of emergency

	ΔHbA1c (%)
ΔBodyweight (kg)	0.37 (<0.001*)
ΔBMI (kg/m^2)	0.36 (<0.001*)
ΔSkeletal muscle mass (kg)	–0.02 (0.732)
ΔSkeletal muscle percentage (%)	–0.32 (<0.001*)
ΔSMI (kg/m^2)	–0.02 (0.747)
ΔBody fat mass (kg)	0.41 (<0.001*)
ΔBody fat percentage (%)	0.35 (<0.001*)
ΔLean body mass (kg)	–0.03 (0.550)

Data are presented as correlation coefficient (*P* value). **P* value <0.05. BMI, body mass index; SMI, skeletal muscle index.

correlations between body composition and HbA1c changes are shown in Table 2. We found significant correlations between changes in HbA1c from period 2019 to period 2020–2021, and changes in bodyweight ($r = 0.37$, $P < 0.001$) and in BMI ($r = 0.36$, $P < 0.001$). Furthermore, changes in HbA1c levels were correlated significantly with changes in skeletal muscle percentage ($r = –0.32$, $P < 0.001$), body fat mass ($r = 0.41$, $P < 0.001$) and body fat percentage ($r = 0.35$, $P < 0.001$), whereas changes in HbA1c were not correlated significantly with changes in skeletal muscle mass ($r = –0.02$, $P = 0.732$), SMI ($r = –0.02$, $P = 0.747$) or lean body mass ($r = –0.03$, $P = 0.550$).

Changes in body composition between the patients with and without worsening of glycemic control during SoE

We identified 128 individuals whose HbA1c levels increased by ≥0.3% during the SoE (the "worsening" group); the remaining patients did not show such worsening of glycemic control (the "non-worsening" group; Table S1, Table 3). In both groups, HbA1c did not differ significantly during periods 2018 and 2019 (Figure 2). Then we carried out a subgroup analysis of the worsening and non-worsening groups to clarify the clinical factors associated with worsening of glycemic control during

Table 3 | Changes in glycated hemoglobin and body compositions between the worsening group and the non-worsening group

	Worsening group (*n* = 128)	Non-worsening group (*n* = 287)	*P*-value
ΔHbA1c (%)	0.82 ± 0.05	–0.30 ± 0.03	<0.001*
ΔBody weight (kg)	1.76 ± 0.29	–0.33 ± 0.16	<0.001*
ΔBMI (kg/m^2)	0.66 ± 0.11	–0.11 ± 0.06	<0.001*
ΔSkeletal muscle mass (kg)	–0.12 ± 0.09	–0.12 ± 0.06	0.994
ΔSkeletal muscle percentage (%)	–0.99 ± 0.12	–0.03 ± 0.10	<0.001*
ΔSMI (kg/m^2)	–0.04 ± 0.03	–0.04 ± 0.02	0.989
ΔBody fat mass (kg)	1.92 ± 0.23	–0.20 ± 0.16	<0.001*
ΔBody fat percentage (%)	1.71 ± 0.21	–0.08 ± 0.17	<0.001*
ΔLean body mass (kg)	–0.16 ± 0.15	–0.13 ± 0.10	0.846
ΔNo. hospital visits (times/year)	–0.59 ± 0.17	–0.50 ± 0.11	0.701

The worsening group and non-worsening is defined as the patients with increase of HbA1c level by 0.3% or more and those without, respectively. The data are presented as mean ± standard error. **P* value <0.05. BMI, body mass index; HbA1c, glycated hemoglobin; SMI, skeletal muscle index.

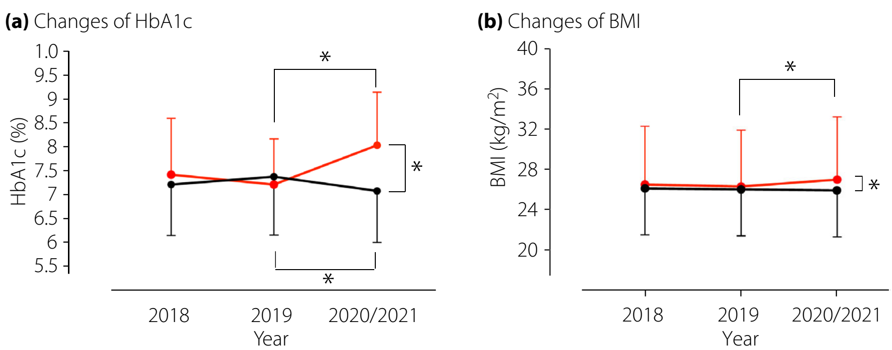

Figure 2 | Changes in glycated hemoglobin (HbA1c) and body mass index from 2018 to the period 2020–2021 in the patients with and without worsening of glycemic control during the state of emergency. (a) Changes in HbA1c. (b) Changes in body mass index (BMI). The worsening group (red line) comprised the patients whose HbA1c levels increased by ≥0.3% o during the state of emergency, and the non-worsening group (black line) comprised the patients whose HbA1c level increased by <0.3%. The data during period 2018 were obtained from 1 January 2018 to 31 December 2018 (109 patients in the worsening group, 244 in the non-worsening group); the data during period 2019, from 1 January 2019 to 31 December 2019 (128 and 287 patients, respectively); and data during period 2020–2021, from 1 June 2020 to 31 May 2021 (128 and 287 patients, respectively). Each parameter is shown as the mean ± standard deviation. **P* < 0.05.

the SoE in patients with GI. Clinical characteristics of the two groups are listed in Table S1. During period 2019, HbA1c levels and BMI did not differ significantly between the two groups. However, in the worsening group, HbA1c levels increased significantly from period 2019 to period 2020–2021 ($P < 0.001$), as did BMI ($P < 0.001$; Figure 2), and during period 2020–2021, the worsening group had significantly higher HbA1c levels ($P < 0.001$) and BMIs ($P < 0.001$) than the non-worsening group. From period 2019 to period 2020–2021, those changes were also significantly larger in the worsening group than in the non-worsening group (changes in HbA1c: $P < 0.001$, changes in BMI: $P < 0.001$; Table 3). Additionally, in analyses of only the populations whose data during period 2018 were available, the same trends in changes in HbA1c levels and BMI were also confirmed (Figure S1).

In terms of body composition, the worsening group showed significant increases from period 2019 to period 2020–2021 in body fat mass ($P < 0.001$) and body fat percentage ($P < 0.001$), but no significant changes in skeletal muscle mass and lean body mass (Figure 3). The body fat mass and body fat percentage in the worsening group during period 2020–2021 were significantly higher than in the non-worsening group ($P < 0.001$ and $P < 0.001$, respectively). Changes in body fat mass and body fat percentage from period 2019 to period 2020–2021 were also significantly larger in the worsening group than in the non-worsening group, whereas skeletal muscle mass, SMI and lean body mass did not differ significantly between the two groups (Table 3). Additionally, the analyses of only the populations whose data during period 2018 were available corroborated the body composition findings found after the SoE (Figure S2).

Associations of lifestyle changes with changes in glycemic control during SoE

The dietary records were obtained in the same month as body composition assessment and laboratory examinations in both periods before and after the DSE in 320 (77.1%) of the 415 patients: 102 (79.7%) of the 128 patients in the worsening group and 218 (76.0%) of the 287 patients in the non-worsening group. Overall, increased snack intake during the SoE was reported by 77 patients: 32 (31.4%) of the 102 patients in the worsening group and 45 (20.6%) of the 218 patients in the non-worsening group. Increased frequency of exercise was reported by 77 patients: 24 (19.6%) in the worsening group

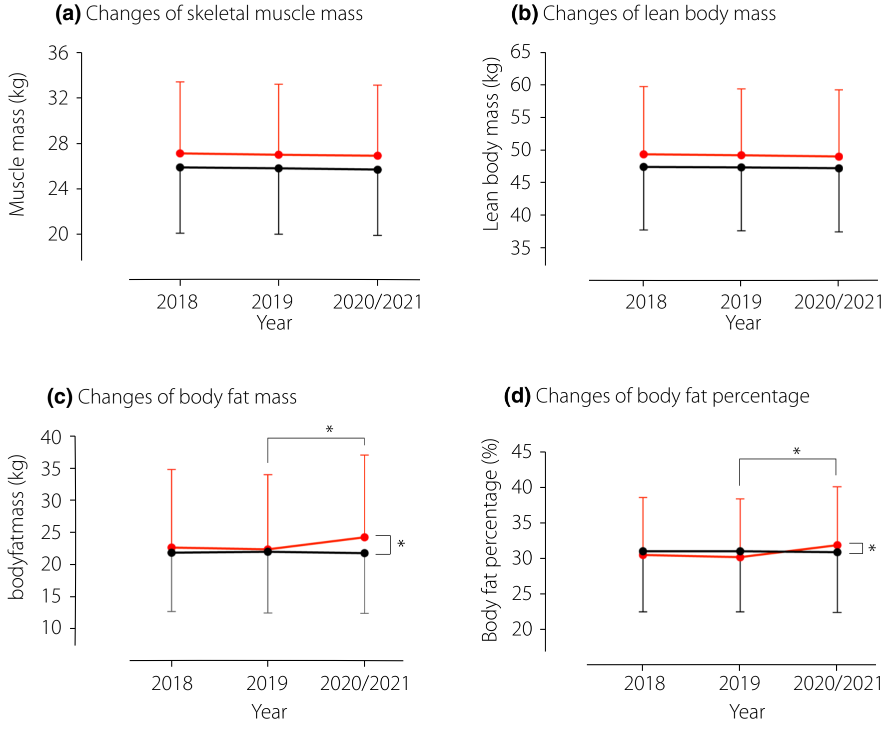

Figure 3 | Changes in body composition from period 2018 to period 2020–2021 in patients with and without worsening of glycemic control during the state of emergency. (a) Changes in skeletal muscle mass. (b) Changes in lean body mass. (c) Changes in body fat mass. (d) Changes in body fat percentage. Patients whose glycated hemoglobin (HbA1c) levels increased by ≥0.3% during the state of emergency were classified as the worsening group (red line), and those without such an increase, as the non-worsening group (black line). The data during period 2018 were obtained from 1 January 2018 to 31 December 2018 (109 patients in the worsening group, 244 in the non-worsening group); during period 2019, from 1 January 2019 to 31 December 2019 (128 and 287 patients, respectively); and during period 2020–2021, from 1 June 2020 to 31 May 2021 (128 and 287 patients, respectively). Each parameter is shown as the mean ± standard deviation. *$P < 0.05$.

and 53 (24.3%) in the non-worsening group. Snack intake was significantly more increased in the worsening group (odds ratio 1.76, 95% CI 1.03–2.99, $P = 0.036$), whereas the changes in exercise frequency did not differ significantly between the two groups (odds ratio 0.96, 95% CI 0.55–1.66, $P = 0.880$).

Comparisons of body composition and lifestyle changes between older and younger patients with worsening of glycemic control during SoE

According to a previous report of lifestyle changes very soon after the DSE in patients with diabetes, changes in body composition and lifestyle might be age dependent[2]. We therefore carried out a subgroup analysis of individuals in the worsening group, comparing 71 patients aged ≥65 years (the elderly group) and 57 patients aged <65 years (the younger group) according to the previous report[2]. Clinical characteristics of the two groups are listed in Table S1. The HbA1c levels of the two groups were comparable ($P = 0.612$), whereas the elderly group showed significantly lower bodyweight and BMI than did the younger group ($P < 0.001$ and $P < 0.001$, respectively). The changes in HbA1c levels and BMI from period 2019 to period 2020–2021 did not differ significantly between the two groups (Table 4). In terms of body composition, body fat mass and body fat percentage were significantly higher in both groups during period 2020–2021 than during period 2019 (Table S2), whereas changes in body fat mass and body fat percentage did not differ significantly in the two groups (Table 4). In addition, from period 2019 to period 2020–2021, both groups showed no significant changes in skeletal muscle mass, SMI or lean body mass, and changes in skeletal muscle mass, SMI and lean body mass did not differ significantly between the two groups (Table 4). With regard to lifestyle changes, snack intake and exercise frequency increased after the DSE in similar percentages of the patients in both groups (Table 4).

DISCUSSION

The present study showed year-long unfavorable metabolic consequences of the prolonged COVID-19 restrictions in Japanese patients with GI, which were highlighted by changes in body composition. Although HbA1c levels did not significantly change after the DSE in such patients, the longitudinal assessment of body composition by BIA showed significant increases in bodyweight and body fat, and significant decreases in skeletal muscle. Furthermore, the changes in glycemic control after the DSE were significantly associated with changes in bodyweight, body fat mass and body fat percentage during the SoE, whereas they were not with changes in skeletal muscle mass or SMI. The changes in bodyweight, body fat mass and body fat percentage were significantly larger, and increased snack intake was more common in the patients with worsening glycemic control than in those whose glycemic control was maintained or improved.

In European nations and other countries, studies have shown varying degrees of the influence of lockdowns on glycemic control status in patients with GI, probably because of characteristics of the countries or regions, study periods or study populations[3–8,18–21]. The present study was carried out in Japan, where only request-based restrictions, such as the SoE, were imposed instead of lockdowns, and we observed no significant changes in HbA1c levels during the SoE in the patients with GI (Table 1). Although our study covered the late period of the SoE, this result is consistent with that of one of the earlier reports, in which the HbA1c levels soon after DSE (1 June 2020 to 31 August 2020) were analyzed[22]. In previous reports of the early effects of the SoE on glycemic control, the results varied, as in cases of lockdowns; with regard to HbA1c levels, some studies showed an increase after DSE[11,23], another showed insignificant changes[21], and others showed a decrease[2,24]. This variation might have resulted from insufficient adaptation to

Table 4 | Changes in body composition and lifestyle between the elderly and younger patients with worsening of glycemic control during the declaration of a state of emergency

	Elderly group (n = 71)	Younger group (n = 57)	P-value
ΔHbA1c (%)	0.76 ± 0.06	0.91 ± 0.09	0.172
ΔBodyweight (kg)	1.44 ± 0.28	2.16 ± 0.55	0.220
ΔBMI (kg/m^2)	0.56 ± 0.10	0.78 ± 0.20	0.297
ΔSkeletal muscle mass (kg)	−0.13 ± 0.10	−0.10 ± 0.16	0.876
ΔSkeletal muscle percentage (%)	−0.99 ± 0.19	−0.98 ± 0.15	0.976
ΔSMI (kg/m^2)	−0.04 ± 0.04	−0.03 ± 0.06	0.831
ΔBody fat mass (kg)	1.56 ± 0.27	2.37 ± 0.39	0.082
ΔBody fat percentage (%)	1.64 ± 0.30	1.81 ± 0.28	0.690
ΔLean body mass (kg)	−0.12 ± 0.16	−0.21 ± 0.26	0.755
ΔHospital visits (times/year)	−0.55 ± 0.24	−0.65 ± 0.24	0.465
Increased snack intake (n)	19 (31.67%)	13 (21.67%)	0.939
Exercise frequency changes (n)	15 (25.00%)	9 (21.43%)	0.676

The elderly group and younger group are defined as the patients whose ages were ≥65 years, and those who were aged ≤65 years, respectively. Changes of glycated hemoglobin (HbA1c), body compositions and the number of visiting a hospital are presented as the mean ± standard error. *P-value <0.050. BMI, body mass index; SMI, skeletal muscle index.

the SoE, which was implemented suddenly, as well as from the heterogeneity of the individual attitudes and the patterns of lifestyle changes in response to the SoE.

We actually found distinct patterns of glycemic control changes among the enrolled patients; the patients in whom HbA1c levels increased ≥0.3% during the SoE (the worsening group) showed significant HbA1c changes in comparison with those whose HbA1c levels increased <0.3% (the non-worsening group), although the HbA1c levels of the two groups did not differ significantly during period 2019 (Table 3, Figure 2a). Therefore, the present results might suggest that changes in glycemic control status reflect year-long metabolic influences with lifestyle adjustment in response to a prolonged SoE in Japanese patients with GI. Surprisingly, the non-worsening group showed a rather significant improvement of glycemic control during the SoE (Figure 2a). Such different patterns of lifestyle changes during lockdowns among patients with overweight/obesity and diabetes were also reported[25], suggesting that some patients used the lockdowns as an opportunity to improve their lifestyles and glycemic control, whereas other patients did not. Thus, any factors responsible for worsening glycemic control during a SoE should be identified to establish effective interventions in clinical practice.

Body composition can be affected by social isolation and lifestyle changes, as shown during the COVID-19 outbreak and the lockdowns[25–27]. Weight gain resulting from increased fat, as well as decreased skeletal muscle, can cause a reduction in glucose tolerance, especially in Asian populations, including Japanese people; however, little information about changes in body composition during the SoE is available[28,29]. To address this deficiency, the present study provided longitudinal data about body composition as evaluated by BIA during a prolonged SoE in 415 patients with GI. In this study, bodyweight, BMI, body fat mass and body fat percentage increased significantly after the DSE; at the same time, skeletal muscle mass and SMI decreased significantly (Figure 2, Table 1). Of importance is that the changes of bodyweight and BMI were significantly associated with glycemic control changes (Table 2), as previously reported[2]. Furthermore, our finding of a loss of skeletal muscle was consistent with results of a previous study of elderly Japanese patients with diabetes (mean age 75.2 ± 7.1 years) after the first 2 months of the SoE, in which a significant decrease in SMI was also found[13].

The present findings highlight the significant influence of changes in body fat mass on glycemic control during a prolonged SoE. The changes in body fat mass and body fat percentage were significantly and positively correlated with those in HbA1c levels (Table 2). Furthermore, in the comparison between the patients with and without worsening of glycemic control during the SoE, body fat mass and body fat percentage increased significantly in the worsening group, whereas the changes in skeletal muscle mass and SMI did not differ significantly between the two groups (Figure 3, Table 3). Although the previous report in the limited number of elderly patients during the early period of SoE showed no increase in fat mass during the SoE[14], the present study accounted for changes in body composition of younger and larger-scale participants, and also focused on longer-term outcomes after the start of the SoE. In addition, the longitudinal assessment of dietary records suggested that snack intake might contribute to the increase of body fat mass and bodyweight in the worsening group, as a lifestyle change after the DSE. Increased snack intake and its relationship with higher bodyweight and HbA1c levels were also observed in other Japanese cohorts[2,13]; thus, controlling snack intake can be effective in the achievement and maintenance of glycemic control during social restrictions, such as a SoE, in patients with diabetes.

We also investigated the possibility that changes in body composition and lifestyle were age-dependent in patients with worsening glycemic control during the SoE. A previous study carried out very soon after the DSE suggested that an increase in snack intake affected bodyweight and HbA1c levels in younger patients with diabetes, and a reduction in exercise frequency led to weight gain in elderly patients with diabetes[2]. However, that investigation was a questionnaire-based study, and body composition was not assessed. In the present study, the ages of the enrolled patients were comparable with those in the previous study, and we used the same ages to classify elderly and younger patients. However, skeletal muscle mass and SMI decreased, and body fat mass and body fat percentage increased in both the younger and elderly groups (Table 4), although the insignificantly increased use of metformin and sodium–glucose cotransporter 2 inhibitors in the younger group with worsening of glycemic control might mask the change in their body composition (Table S2). Furthermore, snack intake also increased in both groups. These findings might suggest the common contribution of increased body fat mass and snack intake to glycemic control, and their clinical importance during a prolonged SoE in both younger and elderly patients with GI.

The present study had several limitations. First, it was a single-center retrospective investigation. Further large-scale multicenter investigations in different regions in Japan are warranted to confirm the reproducibility of our findings. We did not include patients who had no clinic visits or follow up with laboratory examination and body composition assessment, which might have led to selection bias. Furthermore, we did not show that the COVID-19 outbreak and SoE had causal relationships with the changes that we observed, although the clinical characteristics and body compositions were comparable between the periods 2018 and 2019 in this study. Second, the latest data during each period were regarded as eligible in this study, as the longitudinal acquisition of the data on the same day in the same population was impractical in a retrospective study. Thus, the possible influence of seasonal biases should be considered for the interpretation of the results, although no significant seasonal differences between the eligible data of period 2019 and 2020–2021, as well as between the worsening group and non-worsening group during period 2020–2021 were observed. Third, information about patient lifestyle was obtained from dietary records evaluated by registered dietitians who, although they followed up the same patient, quantified the changes in exercise and snack frequency only as increased or decreased, as in most of the previous studies, which were based on self-reported questionnaire. Further analyses based on objective continuous variables are warranted. Fourth, the duration of data collection varied among the study participants, and data collection was dependent on the individual hospital visits, as in the previous studies, although the intervals between acquisitions of data about body composition were longer than those in previous reports, and we carried out longitudinal analyses of data from periods 2018, 2019 and 2020–2021.

In conclusion, the present study showed that the prolonged SoE, a COVID-19 restriction without lockdown in Japan, caused unfavorable changes in body composition, including weight gain, increased body fat mass and decreased skeletal muscle in patients with GI. The increases in bodyweight, fat mass and snack intake during the SoE were significantly associated with worsening glycemic control. Of note, patients showed distinct patterns of changes in glycemic control. Thus, clinicians should consider changes in body composition and their association with worsening glycemic control in patients with GI during periods of social restrictions. Snack intake should be monitored, and diet intervention might be warranted in such situations.

DISCLOSURE

NI received clinical commissioned/joint research grants from Daiichi Sankyo, Terumo and Drawbridge Inc.; speaker honoraria from Kowa, MSD, Astellas Pharma, Novo Nordisk Pharma, Ono Pharmaceutical, Nippon Boehringer Ingelheim, Takeda, Eli Lilly Japan, Sumitomo Dainippon Pharma and Mitsubishi Tanabe Pharma; and scholarship grants from Kissei Pharmaceutical, Sanofi, Daiichi Sankyo, Mitsubishi Tanabe Pharma, Takeda, Japan Tobacco, Kyowa Kirin, Sumitomo Dainippon Pharma, Astellas Pharma, MSD, Eli Lilly Japan, Ono Pharmaceutical, Sanwa Kagaku Kenkyusho, Nippon Boehringer Ingelheim, Novo Nordisk Pharma, Novartis Pharma, Teijin Pharma and Life Scan Japan. The other authors declare no conflict of interest.

Approval of the research protocol: The Kyoto University Graduate School and Faculty of Medicine, Ethics Committee (No. R2377).

Informed consent: N/A.

Registry and the registration no. of the study/trial: N/A.

Animal studies: N/A.

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SUPPORTING INFORMATION

Additional supporting information may be found online in the Supporting Information section at the end of the article.

Figure S1 | Changes in glycated hemoglobin (HbA1c) and body mass index from 2018 to the period 2020–2021 in only the participants whose data during the period 2018 were available.

Figure S2 | Changes in body composition from period 2018 to period 2020–2021 in the participants whose data during the period 2018 were available.

Table S1 | Clinical characteristics of the patients with and without worsening of glycemic control during the declaration of a state of emergency.

Table S2 | Clinical characteristics of the elderly and younger patients with worsening of glycemic control during the declaration of a state of emergency.