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

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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. 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.

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. 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. In contrast, the state of emergency (SoE) in Japan entailed less strict
restrictions; people were requested to stay at home, and the use of public transportation and facilities was restricted. 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. In fact, an approximately 50% reduction in the flow of people in several commercial districts 2 weeks after the DSE was reported. Some reports showed altered lifestyles and metabolic influences in patients with diabetes, mainly during the initial 1–2 months after the DSE. 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. 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. 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 in patients with diabetes, mainly during the initial 2 months after the DSE. We excluded early effects of the SoE, which were previously reported. In the present study, the patients whose HbA1c levels increased ≥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.

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 χ²-test was applied appropriately. Correlations were evaluated with...
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/m². 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/m²; 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/m²; 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/m². 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/m² (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 percentage (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)| 6.8 ± 1.3     | 9 (3, 15)     |               | −1.6 ± 0.79               | <0.001*                | −0.38 ± 0.38                 | 0.556                         |
| eGFR (mL/min/1.73 m²)    | 68.2 ± 18.3   | 665 ± 18.1    | 66.2 ± 18.9   | −1.6 ± 0.79               | <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   | 700 ± 16.5    | 70.3 ± 17.0   | −0.22 ± 2.75              | 0.127                  | 0.32 ± 0.15                  | 0.034*                        |
| BMI (kg/m²)              | 26.2 ± 5.0    | 261 ± 4.9     | 26.2 ± 5.2    | −0.09 ± 1.02              | 0.089                  | 0.13 ± 0.05                  | 0.018*                        |
| Skeletal muscle mass (kg)| 25.3 ± 6.0    | 262 ± 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  | 377 ± 4.9     | 37.4 ± 4.9    | 0.04 ± 1.56               | 0.635                  | −0.32 ± 0.08                 | <0.001*                       |
| SMI (kg/m²)              | 9.7 ± 1.4     | 97 ± 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   | 221 ± 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    | 308 ± 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   | 479 ± 9.9     | 478 ± 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%)
- Sulfonylurea: 82 (19.8%)
- Glinide: 23 (5.5%)
- Metformin: 156 (37.6%)
- Thiazolidine: 9 (2.2%)
- SGLT2 inhibitor: 78 (18.8%)
- α-Glucosidase inhibitor: 25 (6.0%)
- GLP-1 receptor agonist: 25 (6.0%)
- Insulin: 84 (20.2%)

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.
The data are presented as mean ± standard deviation. Each parameter is shown as the mean (95% confidence interval) with *value). 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 = 0.59, 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).

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/m²)            | 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/m²)            | –0.04 ± 0.03              | –0.05 ± 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% 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 and 23 (10.2%) in the non-worsening group. Increased frequency and duration of physical activity were reported by 77 patients: 24 (19.6%) in the worsening group and 23 (10.2%) in the non-worsening group.

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**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 \( \geq 65 \) years (the elderly group) and 57 patients aged <65 years (the younger group) according to the previous report\(^6\). 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 bodyfat mass and bodyfat 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\(^3\)–\(^8\),\(^16\)–\(^21\). 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 |
| \( \Delta \text{HbA1c} \) (%) | 0.76 ± 0.06 | 0.91 ± 0.09 | 0.172 |
| \( \Delta \text{Bodyweight} \) (kg) | 1.44 ± 0.28 | 2.16 ± 0.55 | 0.220 |
| \( \Delta \text{BMI} \) (kg/m\(^2\)) | 0.56 ± 0.10 | 0.78 ± 0.20 | 0.297 |
| \( \Delta \text{Skeletal muscle mass} \) (kg) | −0.13 ± 0.10 | −0.10 ± 0.16 | 0.876 |
| \( \Delta \text{Skeletal muscle percentage} \) (%) | −0.99 ± 0.19 | −0.98 ± 0.15 | 0.976 |
| \( \Delta \text{SMI} \) (kg/m\(^2\)) | −0.04 ± 0.04 | −0.03 ± 0.06 | 0.831 |
| \( \Delta \text{Body fat mass} \) (kg) | 1.56 ± 0.27 | 2.37 ± 0.39 | 0.082 |
| \( \Delta \text{Body fat percentage} \) (%) | 1.64 ± 0.30 | 1.81 ± 0.28 | 0.690 |
| \( \Delta \text{Lean body mass} \) (kg) | −0.12 ± 0.16 | −0.21 ± 0.26 | 0.755 |
| \( \Delta \text{Hospital visits (times/year)} \) | −0.35 ± 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 (21.34%) | 0.676 |

The elderly group and younger group are defined as the patients whose ages were \( \geq 65 \) years, and those who were aged \( \leq 65 \) 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 <0.05. 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 reported25, 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 lockdowns25–27. 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 available28–29. 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, and body fat mass and body fat percentage 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**

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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.