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【 ORIGINAL ARTICLE 】

# Impact of the COVID-19 Pandemic on Glycemic Control and Blood Pressure Control in Patients with Diabetes in Japan

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**Abstract:**
**Objective** In this study, we investigated whether and how the COVID-19 pandemic affected glycemic control and blood pressure (BP) control in patients with diabetes mellitus (DM).
**Methods** DM patients whose HbA1c level was measured regularly before and after the declaration of a state of emergency were included in this study. Some patients were given questionnaires about changes in their lifestyle to determine the factors affecting glycemic control and BP control.
**Results** The median HbA1c level of the 804 patients increased significantly from 6.8% before the state of emergency to 7.1% and 7.0% during and after the state of emergency, respectively. This was in contrast to the decrease one year earlier due to seasonal variations. In the 176 patients who responded to the questionnaire, the HbA1c level also increased significantly during and after the state of emergency. The worsening of glycemic control was more pronounced in the group that had achieved HbA1c of <7% before the state of emergency than in those with higher values. Unlike the rise in HbA1c, the BP did not rise during the state of emergency but did rise significantly afterwards. There was no marked decrease in HbA1c or BP after the state of emergency, even in patients who responded that they were much more careful with their diet, ate less, or exercised more.
**Conclusions** The COVID-19 pandemic worsened glycemic control and BP control, even in patients who perceived no marked change in their diet or exercise, suggesting that more active lifestyle guidance is necessary for good treatment of DM patients.

**Key words:** COVID-19 pandemic, glycemic control, blood pressure, diabetes mellitus

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## Introduction

The coronavirus disease 2019 (COVID-19) pandemic has posed a global threat to public health. Lockdown has been implemented in many countries, and individuals' social lives have been altered due to restrictions on activities. Restricting the movement of individuals is likely to have an undesirable impact on diet and exercise. Since diet and exercise are very important for the treatment of diabetes mellitus (DM), these lifestyle changes may have had a significant impact on glycemic control in DM patients. Indeed, there have been a number of studies in which glycemic control before and after lockdown in patients with type 1 DM and patients with type 2 DM was investigated, but the results were different (1-13). Differences in the glycemic control status of the patients studied and the amount of food eaten and amount of exercise may have affected the results. In addition to gly-

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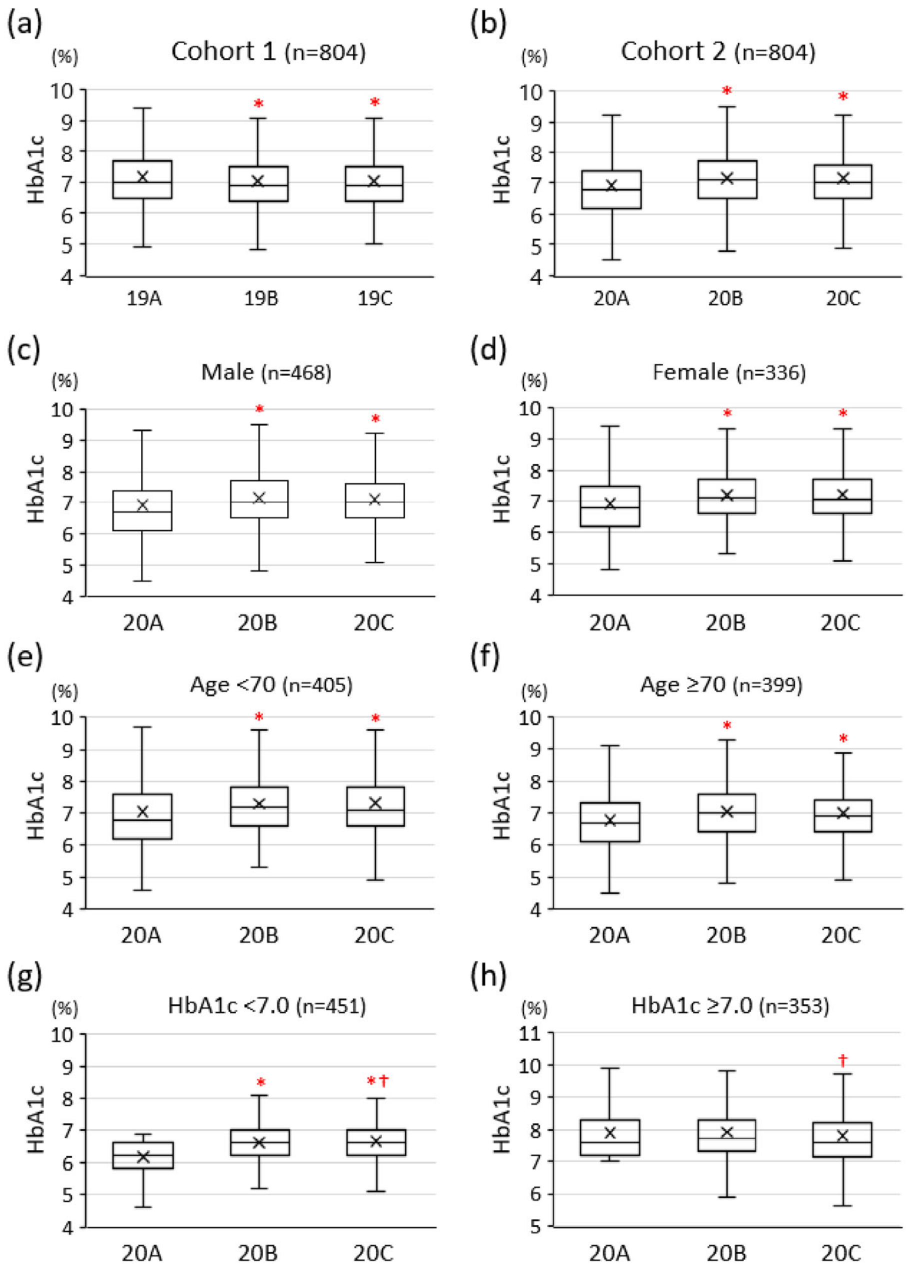


**Figure 1.** **The horizontal line in each box is the median, and the boxes show the 25th to 75th percentiles of the distribution of values in each group. The x mark indicates the mean value. (a) Changes in the HbA1c in all patients in the three periods: from December 2018 to February 2019 (19A), from March to May 2019 (19B), and from June to September 2019 (19C), one year before the declaration of a state of emergency (cohort 1). (b) Changes in HbA1c in all patients in the three periods: from December 2019 to February 2020 (20A), before the declaration of a state of emergency, from March to May 2020 (20B), during the state of emergency, and from June to September 2020 (20C), after the state of emergency (cohort 2). Effects of (c, d) gender, (e, f) age and (g, h) glycemic control at baseline on changes in HbA1c in cohort 2. *p<0.05 vs. 19A or 20A, †p<0.05 vs. 20B.**

cemic control, blood pressure (BP) control is also important in DM patients. It is well known that BP increases with stress, such as stress from a disaster, but there have been only a few reports on how BP was affected by a lockdown due to the COVID-19 pandemic, and there have been no reports on changes in BP in DM patients during such times (14-17).

In Japan, the government issued the first declaration of a national state of emergency on April 16, 2020, and the state of emergency lasted until May 25, 2020. During that period, schools were closed, large-scale events were cancelled, and restaurants and bars closed early in the evening. Unlike lockdowns in other countries, however, there were no enforcements in the state of emergency in Japan, and people were simply requested to refrain from going out. However, at that time, there was no vaccine to prevent the disease, and

**Table 1. Clinical Characteristics of Patients Who Completed the Questionnaire.**

| | |
|---|---|
| Number | 176 |
| Male, n (%) | 96 (54.5) |
| Age, years | 67 (56, 73) |
| Type 1 DM, n (%) | 5 (2.8) |
| HbA1c, % | 7.0 (6.4, 7.6) |
| ALT, IU/L | 22 (17, 34) |
| eGFR, mL/min/1.73m$^2$ | 67.5±22.4 |
| Hb, g/dL | 14.5±1.8 |
| Systolic BP, mmHg | 130 (120, 138) |
| Diastolic BP, mmHg | 70 (64, 76) |
| Body weight *, kg | 66.3 (55.5, 76.1) |
| Anti-DM medication | |
| DPP-4 inhibitor, n (%) | 119 (67.6) |
| SGLT2 inhibitor, n (%) | 99 (56.3) |
| Metformin, n (%) | 97 (55.1) |
| Sulfonylurea, n (%) | 43 (24.4) |
| Glinide, n (%) | 5 (2.8) |
| Pioglitazone, n (%) | 27 (15.3) |
| $\alpha$-glucosidase inhibitor, n (%) | 22 (12.5) |
| Insulin, n (%) | 43 (24.4) |
| GLP-1 RA, n (%) | 19 (10.8) |
| Anti-HT medication | |
| ACE inhibitor/ARB, n (%) | 118 (67.0) |
| Ca blocker, n (%) | 84 (47.7) |
| $\beta$ blocker, n (%) | 54 (30.7) |
| Diuretics, n (%) | 30 (17.0) |
| Others, n (%) | 4 (2.3) |

Data are presented as number of events with percentage, mean with SD or median with interquartile range (25th, 75th percentiles). Values before the declaration of a state of emergency (20A) are shown except for body weight *, which was measured after the state of emergency (20C). DM: diabetes mellitus, ALT: alanine transaminase, eGFR: estimated glomerular filtration rate, Hb: hemoglobin, BP: blood pressure, DPP-4: dipeptidyl peptidase-4, SGLT2: sodium-glucose cotransporter 2, GLP-1 RA: glucagon-like peptide-1 receptor agonist, HT: hypertension, ACE: angiotensin-converting enzyme, ARB: angiotensin II receptor blocker

no treatment had been established. As a result, there was a strong fear of the disease, and with the first declaration of a state of emergency, restrictions on daily life, such as going out were followed quite strictly in Japan. Furthermore, Hokkaido, the northernmost island of Japan, declared its own state of emergency from February 28 to March 19 prior to the national declaration. As a result, people in Hokkaido had to refrain from going about their normal lives for about three months.

In the present study, we investigated whether and how the COVID-19 pandemic and the declaration of a state of emergency affected glycemic control and BP control in DM patients living in Hokkaido.

## Materials and Methods

This study was conducted in strict adherence with the principles of the Declaration of Helsinki and was approved by the Clinical Investigation Ethics Committee of Oji General Hospital (OGH2020-12 and OGH2020-25). Informed consent for this retrospective study was obtained via study information publicized on the Internet, and written consent was obtained from patients who responded to a questionnaire.

Hokkaido's own state of emergency was declared from February 28 to March 19, 2020, and a further national state of emergency was declared from April 16 to May 25, 2020. Therefore, we included DM patients regularly attending our hospital who had blood tests for HbA1c performed in three periods: from December 2019 to February 2020 (20A), before the declaration of a state of emergency, from March to May 2020 (20B), during the state of emergency, and from June to September 2020 (20C), after the state of emergency (cohort 2). Data were also collected for the same period one year earlier (19A-C, cohort 1). If there was more than one data set within a period, the one taken at the latest time was used. In addition, patients who visited the outpatient clinic in our department in 20C were asked to complete a brief questionnaire about changes in their diet and exercise habits.

One hundred and seventy-six patients consented to the study and completed the questionnaire, and none of those patients were hospitalized or used steroids during the study periods of 20A or 20C. Blood tests and BP measurements were done in our outpatient clinic as part of our regular practice, and the results were extracted retrospectively from electronic medical records. The results were analyzed to determine factors affecting glycemic control and BP control.

Variables are shown as means with SD or medians with interquartile range (25th, 75th percentiles). The Friedman test was used to examine differences in HbA1c levels and BP levels among the three periods, and Bonferroni correction was used to test all detected differences for significance. Differences were considered to be significant if the p value was less than 0.05.

## Results

A total of 804 patients, including 16 with type 1 DM and 788 with type 2 DM, who had undergone blood tests for HbA1c at all time points were included in this study. The median age of the patients was 69 (61-76) years old, and 58.2% were men. In cohort 1, the HbA1c level decreased significantly from 7.0% (6.5-7.7%) in 19A to 6.9% (6.4-7.5%) in 19B and 6.9% (6.4-7.5%) in 19C, indicating seasonal variation (Fig. 1a). In contrast, the HbA1c level was significantly increased during and after the state of emergency, being 6.8% (6.2-7.4%) in 20A, 7.1% (6.5-7.7%) in 20B and 7.0% (6.5-7.6%) in 20C (Fig. 1b). The worsening of glycemic control in cohort 2 was independent of gender and age (Fig. 1c-f). In the group that achieved an HbA1c value of <7% at 20A (451 patients), the HbA1c level increased from 6.2% to 6.6% (20B) and 6.6% (20C), while in the group with an HbA1c value of ≥7%, the HbA1c level

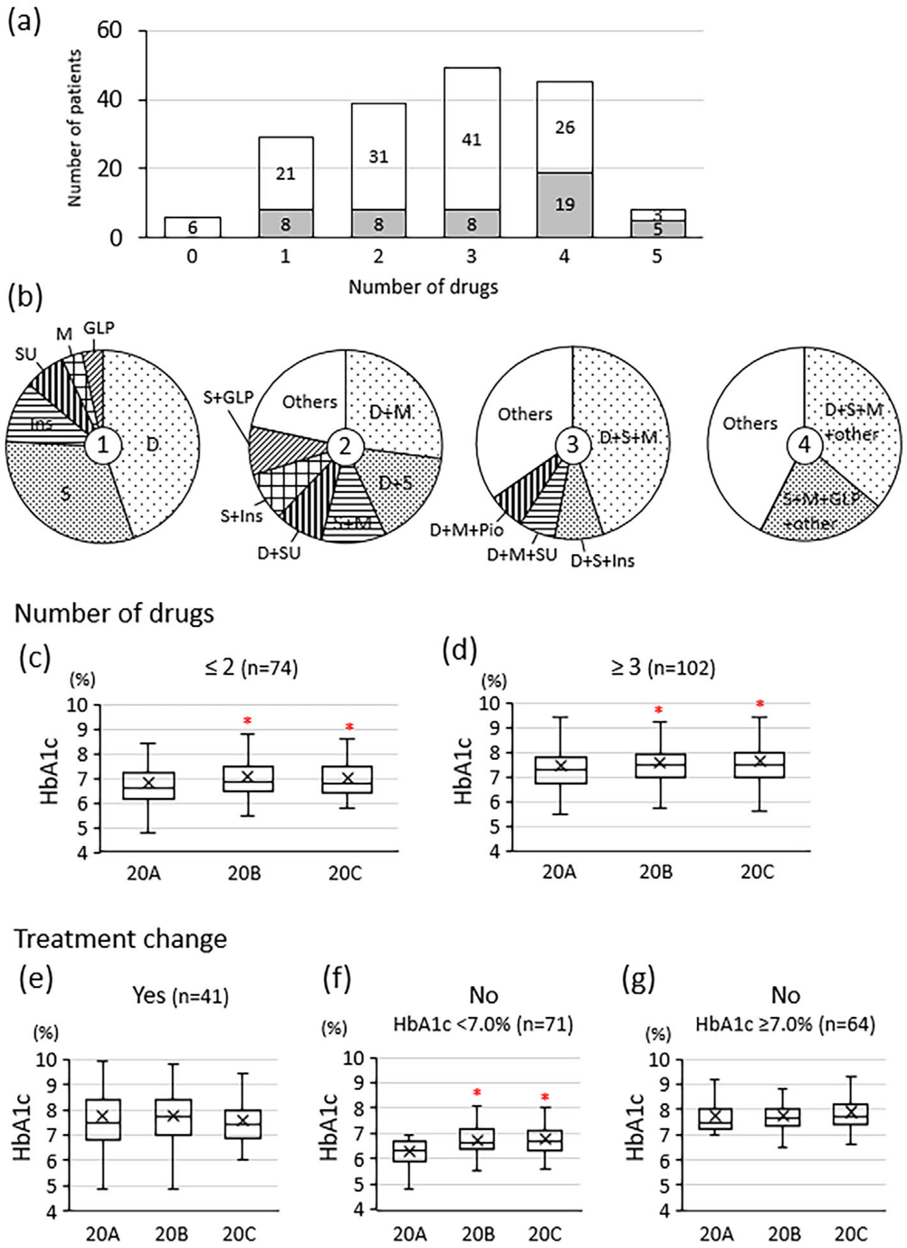


**Figure 2.** **(a) Distribution of the number of anti-DM drugs. Gray bars show the individual number of patients treated with insulin. (b) Distribution of individual drug types if one, two, three, or four drugs were used. Effects of (c, d) number of drugs used and (e-g) treatment change on changes in HbA1c in cohort 2. D: DPP-4 inhibitors, S: SGLT2 inhibitors, Ins: insulin, SU: sulfonylureas, M: metformin, GLP: GLP-1 receptor agonists, Pio: pioglitazone. *p<0.05 vs. 20A.**

remained unchanged in the group with values of 7.6%, 7.7% and 7.6%, respectively (Fig. 1g, h).

The clinical characteristics of the 176 patients who completed the questionnaire before the state of emergency (20A) are shown in the Table 1. The median age of those patients was 67 (56-73) years old, and 54.5% were men, which was comparable to the overall population. The patients were receiving a mean number of 2.7±1.2 anti-DM treatments, including oral medications and insulin (Table 1 and Fig. 2a, b). In cohort 1, the HbA1c level decreased from 7.2% (6.7-7.8%) in 19A to 7.1% (6.6-7.7%) in 19B and 7.1% (6.6-7.7%) in 19C (Fig. 3a). In contrast, the HbA1c level significantly increased from 7.0% (6.4-7.6%) in 20A to 7.3% (6.7-7.8%) in 20B and 7.3% (6.7-7.8%) in 20C (Fig. 3b). The worsening of glycemic control seen in cohort 2 was independent of gender and age and more pronounced in the group that had achieved an HbA1c of <7% at 20A than in those with a value ≥7%, similar to the overall results (Fig. 3c-h). Worsening of glycemic control was observed regardless of the number of treatments, and no specific treatment had an effect on glycemic control (Fig. 2c, d).

During the study periods of 20A-20C, treatment for DM was changed in 41 patients, including 29 with relatively poor glycemic control (HbA1c ≥7.0% at 20A), so the

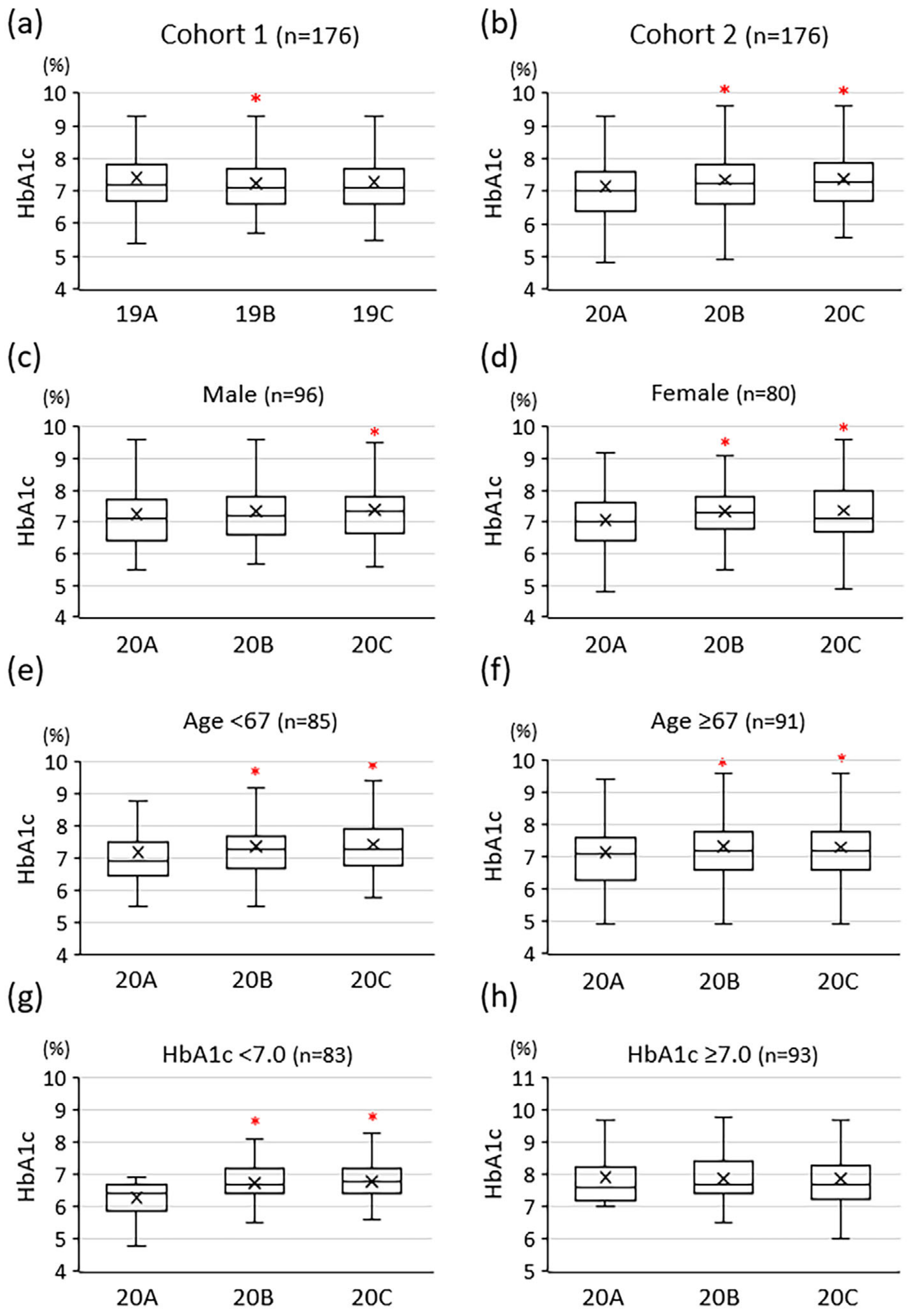


**Figure 3.** **(a) Changes in HbA1c in patients who answered the questionnaire in three periods: from December 2018 to February 2019 (19A), from March to May 2019 (19B), and from June to September 2019 (19C), one year before the declaration of a state of emergency (cohort 1). (b) Changes in HbA1c in patients who answered the questionnaire in three periods: from December 2019 to February 2020 (20A), before the declaration of a state of emergency, from March to May 2020 (20B), during the state of emergency, and from June to September 2020 (20C), after the state of emergency (cohort 2). Effects of (c, d) gender, (e, f) age and (g, h) glycemic control at baseline on changes in HbA1c in cohort 2. *p<0.05 vs. 19A or 20A.**

HbA1c level in those patients tended to decrease (Fig. 2e). Fourteen patients had their insulin doses adjusted, and this adjustment was made several times during the study periods. Anti-DM medications were added or changed in 24 patients, including 22 in whom medications were changed only once during the study periods. In three patients, treatment with a GLP-1 receptor agonist was newly initiated, or its dose was increased. To exclude the effects of treatment changes, the 135 patients in whom treatment was not changed during the study periods were divided into 2 groups according to whether or not they had achieved an HbA1c of <7% at 20A. Worsening of glycemic control was still observed in the group that had achieved an HbA1c level of <7% at 20A, while the HbA1c level remained unchanged in the group with a value of ≥7% (Fig. 2f, g).

Table 2 shows the relationships between changes in

**Table 2. Questionnaire Results and HbA1c (%) in Cohort 2.**

| | | | |
|---|---|---|---|
| Q.1. Have you been paying attention to your diet? | | | |
| | Quit (n=39) | A little (n=118) | No (n=19) |
| 20A | 7.1 (6.4, 7.5) | 7.1 (6.4, 7.6) | 6.8 (6.7, 8.0) |
| 20B | 7.0 (6.5, 7.7) | 7.3 (6.7, 7.8)* | 7.3 (6.8, 8.0) |
| 20C | 7.0 (6.5, 7.9) | 7.3 (6.8, 7.8)* | 7.5 (6.9, 8.0) |
| Q.2. Has the amount of food you eat changed due to the change in lifestyle caused by the COVID-19 pandemic? | | | |
| | Increase (n=27) (Much: n=6, Slightly: n=21) | No change (n=133) | Decrease (n=16) (Much: n=1, Slightly: n=15) |
| 20A | 6.9 (6.3, 7.2) | 7.0 (6.4, 7.6) | 7.6 (7.0, 8.8) |
| 20B | 7.2 (6.7, 7.5)* | 7.2 (6.6, 7.8)* | 7.8 (7.2, 8.3) |
| 20C | 7.3 (7.0, 7.7)* | 7.2 (6.6, 7.8)* | 7.9 (7.0, 8.4) |
| Q.3. Do you drink alcohol? | | | |
| | No (n=116) | Yes (n=60) (Almost every day: n=20, 2-3 times/w: n=18, 2-3 times/m: n=22) | |
| 20A | 7.1 (6.3, 7.6) | 6.9 (6.6, 7.5) | |
| 20B | 7.3 (6.6, 7.8)* | 7.3 (6.8, 7.7) | |
| 20C | 7.2 (6.7, 7.9)* | 7.4 (6.7, 7.7)* | |
| Q.4. Did you have a habit of exercising? | | | |
| | No (n=74) | Yes (n=93) (Almost every day, 3-4 times/w, 1-2 times/w) | Yes (n=54) (Almost every day, 3-4 times/w) |
| 20A | 7.0 (6.4, 7.8) | 7.1 (6.4, 7.5) | 7.1 (6.4, 7.4) |
| 20B | 7.2 (6.7, 7.8)* | 7.4 (6.6, 7.7)* | 7.3 (6.6, 7.7) |
| 20C | 7.4 (6.9, 7.9)* | 7.2 (6.6, 7.8)* | 7.2 (6.6, 7.7) |
| Q.5. Has your physical activity changed due to the change in lifestyle caused by the COVID-19 pandemic? | | | |
| | Increase (n=12) (Much: n=2, Slightly: n=10) | No change (n=104) | Decrease (n=47) (Much: n=22, Slightly: n=25) |
| 20A | 7.1 (6.5, 7.6) | 6.9 (6.4, 7.6) | 7.2 (6.5, 7.5) |
| 20B | 7.8 (6.9, 8.0) | 7.2 (6.6, 7.8)* | 7.2 (6.8, 7.6) |
| 20C | 7.3 (6.5, 7.9) | 7.3 (6.6, 7.8)* | 7.2 (6.8, 7.8) |
| No change in meal amount (Q.2) and momentum (Q.5), n=89 | | | |
| 20A | 6.9 (6.4, 7.6) | | |
| 20B | 7.2 (6.6, 7.8)* | | |
| 20C | 7.2 (6.6, 7.7)* | | |

Data are presented as median with interquartile range (25th, 75th percentiles). 20A: period before the declaration of a state of emergency, 20B: period during the state of emergency, 20C: period after the state of emergency. * $p<0.05$ vs. 20A

HbA1c and the results of a questionnaire on diet and exercise. There was little change in the HbA1c value among the 39 patients who said they had always been careful about their diet during and after the declaration of a state of emergency. The exacerbation of glycemic control was not related to the presence or absence of drinking habits. The HbA1c increased significantly in those with no exercise habit, but there was no seasonal decline in HbA1c, even in patients who reported an exercise habit of three or more times a week or increased exercise during the period of self-restraint. Notably, the HbA1c values in patients who perceived no change in either diet or exercise significantly increased from 6.9% (6.4-7.6%) in 20A to 7.2% (6.6-7.8%) in 20B and 7.2% (6.6-7.7%) in 20C.

Fig. 4 shows the changes in BP levels in cohorts 1 and 2. The BP values in 19A, 19B and 19C were unchanged at 126/68 (120/64-134/72), 128/68 (120/62-138/74) and 126/68 (120/62-136/76) mmHg, respectively. In contrast, the BP values in 20A, 20B and 20C were 130/70 (120/64-138/76), 130/70 (122/65-138/76) and 137/74 (124/67-148/85) mmHg, respectively, indicating that the BP increased significantly after the state of emergency but not during the state of emergency. The increase in systolic BP seen in cohort 2 was independent of gender and age (Fig. 5a-d). In patients who had achieved a systolic BP of <130 mmHg at 20A, there were significant increases in the systolic BP in 20B and 20 C, with no marked increase in systolic BP observed in the patients whose systolic BP was ≥130 mmHg at 20A (Fig. 5e, f). Changes in diastolic BP were similar to those in systolic BP (data not shown). Only eight patients had their anti-hypertensive medication changed; medication was reduced in 1 one patient due to a low BP and increased in seven patients due to a high BP from 20A to 20C. After excluding those eight patients from the analysis, the results were the same (data not shown). Patients were receiving a total of 1.6±1.2 BP-lowering drugs, and no specific treatment had an effect on BP control (Table 1 and Suppelementary material). The increase in systolic BP seen in 20C was

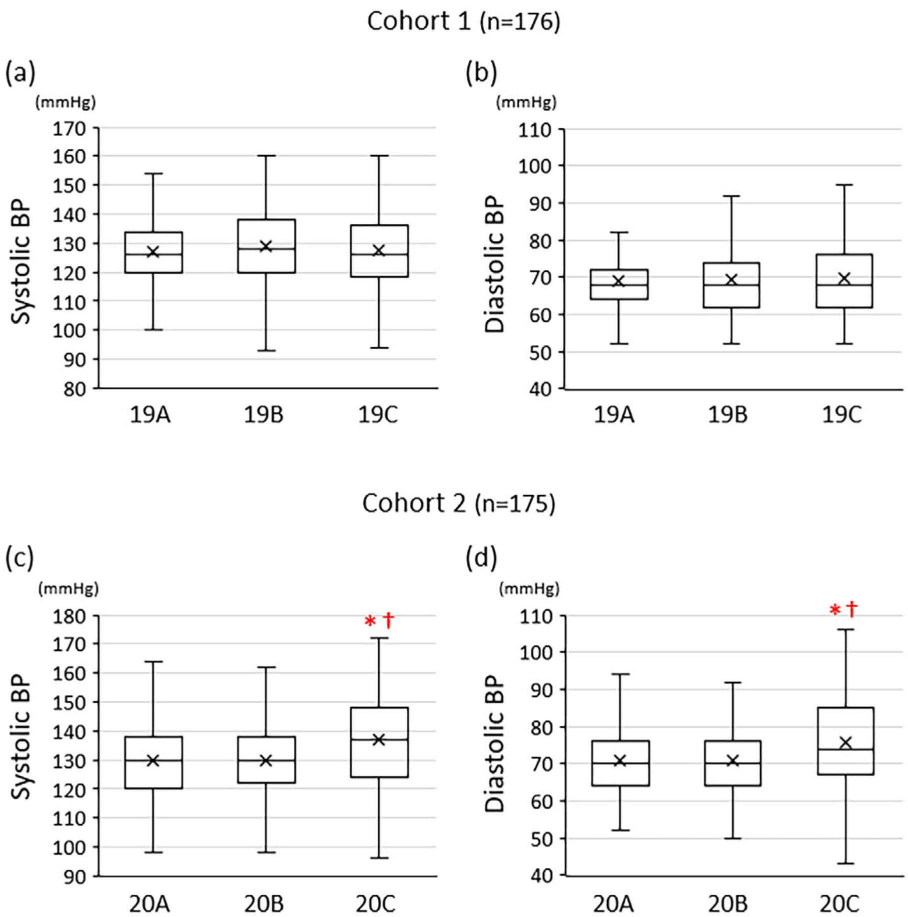


**Figure 4.** **Changes in (a) systolic BP and (b) diastolic BP in patients who answered the questionnaire in three periods: from December 2018 to February 2019 (19A), from March to May 2019 (19B), and from June to September 2019 (19C), one year before the declaration of a state of emergency (cohort 1). Changes in (c) systolic BP and (d) diastolic BP in patients who answered the questionnaire in three periods: from December 2019 to February 2020 (20A), before the declaration of a state of emergency, from March to May 2020 (20B), during the state of emergency, and from June to September 2020 (20C), after the state of emergency (cohort 2). *p<0.05 vs. 20A, †p<0.05 vs. 20B.**

found to have relatively little relation to diet, drinking habits or exercise habits (Table 3). Even among the patients who reported no marked change in their diet or exercise, the BP in 20C was 138/74 (126/67-149/85) mmHg, which was significantly higher than that in 20A and 20B (Table 3). Interestingly, the BP increased in not only patients whose HbA1c worsened with the declaration of emergency but also those whose HbA1c decreased or remained unchanged (Fig. 6a, b). Furthermore, there was also no relationship between changes in the HbA1c level and changes in systolic BP (Fig. 6c).

## Discussion

It is well known that DM patients are not only more susceptible to COVID-19 infection but also have a worse prognosis after infection than the non-DM population (18-21). Among DM patients, those with poor glycemic control have a higher rate of mortality and longer hospitalization than those with good glycemic control (18, 22). Hypertension is also associated with an increased prevalence and severity of COVID-19 (20, 21). A pooled analysis showed that hypertension was associated with an up to 2.5-fold higher risk for both severity and mortality in COVID-19 patients (23). Since hypertension is common in DM patients, this combination may lead to a worse prognosis for COVID-19. Therefore, proper control of blood glucose and BP values is very important for DM patients during the ongoing COVID-19 pandemic. However, the present study revealed for the first time that not only glycemic control but also BP control worsened in DM patients after the declaration of a state of emergency in Japan.

One year before the COVID-19 pandemic, the HbA1c values in 19B and 19C were significantly lower than those in 19A. This better glycemic control in summer and autumn than in winter may have been due to the seasonal decline reported in many DM patients. Possible factors for seasonal variation include increased an caloric intake and decreased physical activity in winter and endogenous biological rhythms (24-26). However, there was no seasonal decline in

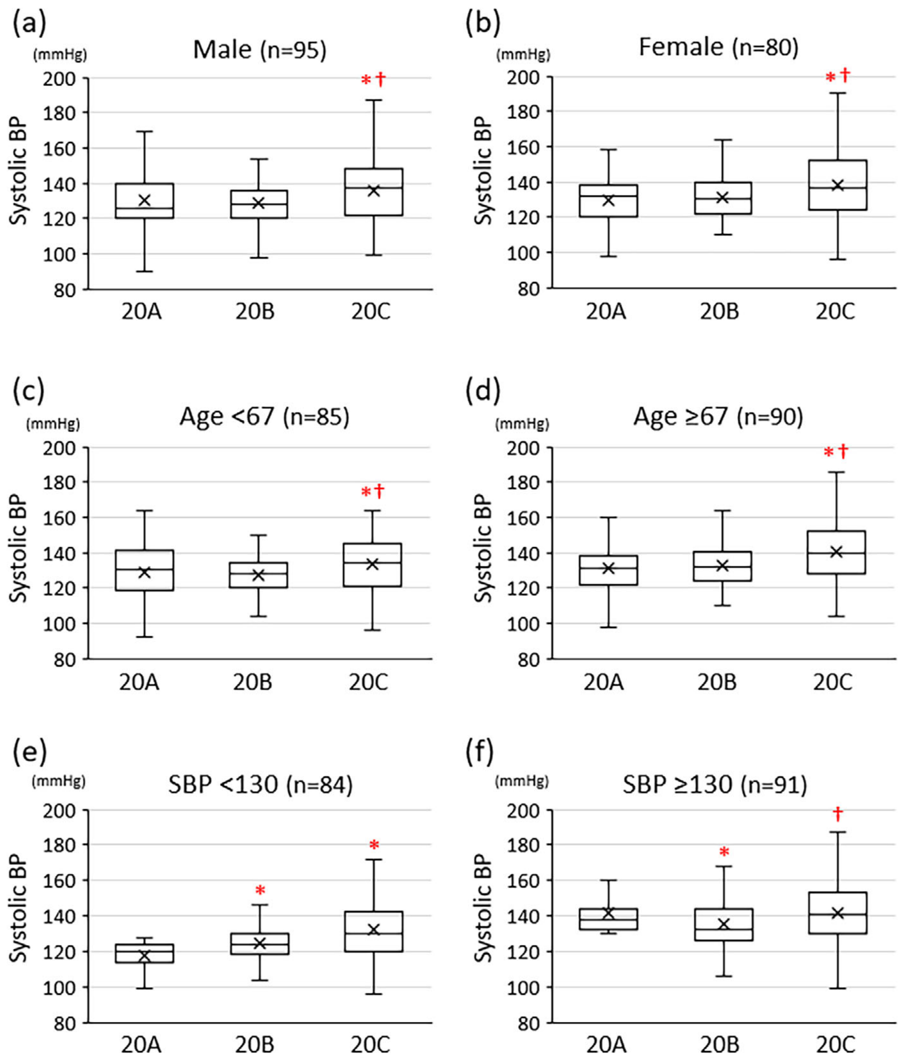


**Figure 5. Effects of (a, b) gender, (c, d) age and (e, f) BP control at baseline on changes in systolic BP in patients who answered the questionnaire in cohort 2. *p<0.05 vs. 20A, †p<0.05 vs. 20B.**

HbA1c in 2020, and in fact, the HbA1c value increased during and after the state of emergency (Fig. 1b). This result is different from the results of a study by Aso et al. showing that glycemic control was not affected by the declaration of a state of emergency in Japan (27). In the study by Aso et al., the average HbA1c level in patients was 7.63%, whereas the median HbA1c level in our patients was 6.8% (average 6.92%); this difference in the glycemic control status might be one of the reasons for the difference in results. Ruissen et al. reported that the HbA1c level was not markedly different after the declaration of a lockdown in patients with type 2 DM, but when the patients were divided into three subgroups based on baseline HbA1c, the HbA1c value in the low-HbA1c subgroup worsened, while that in the high-HbA1c subgroup improved (8). Similar results were obtained in a study conducted in Korea (13). Therefore, we divided our patients into 2 subgroups based on whether or not they had achieved an HbA1c target of <7%, and we found that the subgroup of well-controlled patients who had achieved the target was more strongly affected by the declaration of a state of emergency than those with weaker control. Indeed, of the 451 patients who achieved the HbA1c target, 365 (80.9%) had worsening glycemic control, while of the 353 patients who did not achieve the HbA1c target, 150 (42.5%) had worsening glycemic control. When we analyzed data for the 176 patients who responded to the questionnaire, we found that a larger percentage of patients in the well-controlled HbA1c group ate more food during the observation period than did those in the poorly controlled HbA1c group (18.3% vs. 12.9%), and a smaller percentage of patients ate less food (3.7% vs. 12.9%). Thus, it is possible that the COVID-19 pandemic made it easier for patients to loosen their dietary habits, especially those in the well-controlled HbA1c group who usually managed their diet well, although the details of the diet were unable to be gleaned from the questionnaire. Whatever the reason, the results indicate the importance of more carefully monitoring patients with good glycemic control in situations where social distancing is necessary.

There have been a number of studies in which changes in glycemic control during lockdown in DM patients were investigated, but the results have differed (1-13). These differ-

**Table 3. Questionnaire Results and Systolic Blood Pressure (mmHg) in Cohort 2.**

| | | | |
|---|---|---|---|
| Q.1. Have you been paying attention to your diet? | | | |
| | Quit (n=39) | A little (n=117) | No (n=19) |
| 20A | 126 (120, 132) | 132 (120, 140) | 128 (124, 139) |
| 20B | 126 (120, 136) | 130 (122, 138) | 132 (123, 136) |
| 20C | 133 (121, 143)* | 139 (124, 149)*† | 136 (128, 142) |
| Q.2. Has the amount of food you eat changed due to the change in lifestyle caused by the COVID-19 pandemic? | | | |
| | Increase (n=27) (Much: n=6, Slightly: n=21) | No change (n=132) | Decrease (n=16) (Much: n=1, Slightly: n=15) |
| 20A | 124 (112, 135) | 130 (122, 140) | 128 (116, 145) |
| 20B | 128 (118, 139) | 130 (122, 138) | 130 (125, 135) |
| 20C | 136 (126, 145)*† | 138 (124, 149)*† | 133 (121, 147) |
| Q.3. Do you drink alcohol? | | | |
| | No (n=115) | Yes (n=60) (Almost every day: n=20, 2-3 times/w: n=18, 2-3 times/m: n=22) | |
| 20A | 130 (120, 136) | 130 (122, 142) | |
| 20B | 128 (120, 134) | 132 (123, 143) | |
| 20C | 135 (124, 147)*† | 138 (126, 150)* | |
| Q.4. Did you have a habit of exercising? | | | |
| | No (n=74) | Yes (n=92) (Almost every day, 3-4 times/w, 1-2 times/w) | Yes (n=53) (Almost every day, 3-4 times/w) |
| 20A | 130 (120, 142) | 130 (122, 138) | 130 (122, 138) |
| 20B | 127 (121, 134) | 130 (124, 140) | 130 (124, 138) |
| 20C | 140 (122, 150)*† | 136 (124, 148)*† | 138 (124, 148)* |
| Q.5. Has your physical activity changed due to the change in lifestyle caused by the COVID-19 pandemic? | | | |
| | Increase (n=12) (Much: n=2, Slightly: n=10) | No change (n=103) | Decrease (n=47) (Much: n=22, Slightly: n=25) |
| 20A | 133 (120, 138) | 130 (122, 142) | 129 (117, 138) |
| 20B | 128 (123, 140) | 132 (124, 139) | 128 (119, 136) |
| 20C | 131 (122, 152) | 138 (124, 149)*† | 136 (121, 150)*† |
| No change in meal amount (Q.2) and momentum (Q.5), n=88 | | | |
| 20A | 130 (122, 142) | | |
| 20B | 132 (124, 139) | | |
| 20C | 138 (126, 149)*† | | |

Data are presented as median with interquartile range (25th, 75th percentiles). 20A: period before the declaration of a state of emergency, 20B: period during the state of emergency, 20C: period after the state of emergency. * p<0.05 vs. 20A, † p<0.05 vs. 20B

ences in results may be due in part to the fact that the amount of food eaten and the amount of exercise during the lockdown varied among the target patients. As expected, an increased overall dietary intake and increased consumption of snacks were associated with worse HbA1c values, although the results varied slightly between studies (28, 29). It was also found that, as expected, the amount of physical activity was associated with glycemic control during the COVID-19 pandemic (7, 29). Indeed, in our study, there was no notable worsening of the HbA1c value in patients who responded in the questionnaire that they had eaten less or exercised more during the state of emergency (Table 2). In our study, most patients perceived no marked change in either their diet or exercise, with 76% of patients citing no change in their diet, 64% citing no change in their exercise habits and 51% citing no change in either. These results are similar to those reported by Takahara et al. (29). The problem is that even in patients who reported no notable change in these lifestyle habits, the blood glucose control worsened. We have no clear explanation as to why the HbA1c value worsened even in patients who perceived no change in their diet or exercise regimen. Even if the patients felt that there had been no change, there may have been subtle changes in their habits, although we were unable to determine possible subtle changes from the questionnaire in this study. In addition, factors other than diet and exercise, such as the sleep quality and mental stress, may have contributed to the deterioration of HbA1c. What is important, however, is that the glycemic control deteriorated in patients who considered that there had been no changes in their lifestyle. Therefore, it is necessary to proactively provide interventions, such as lifestyle guidance, during a declared state of emergency.

Since lifestyle changes also affect BP control, it is possible that the BP control worsened during the COVID-19 pandemic. Indeed, the systolic and diastolic BP significantly increased by 7 and 4 mmHg, respectively, after the declaration of a state of emergency in our study. Interestingly, worsening of glycemic control was seen during the state of emer-

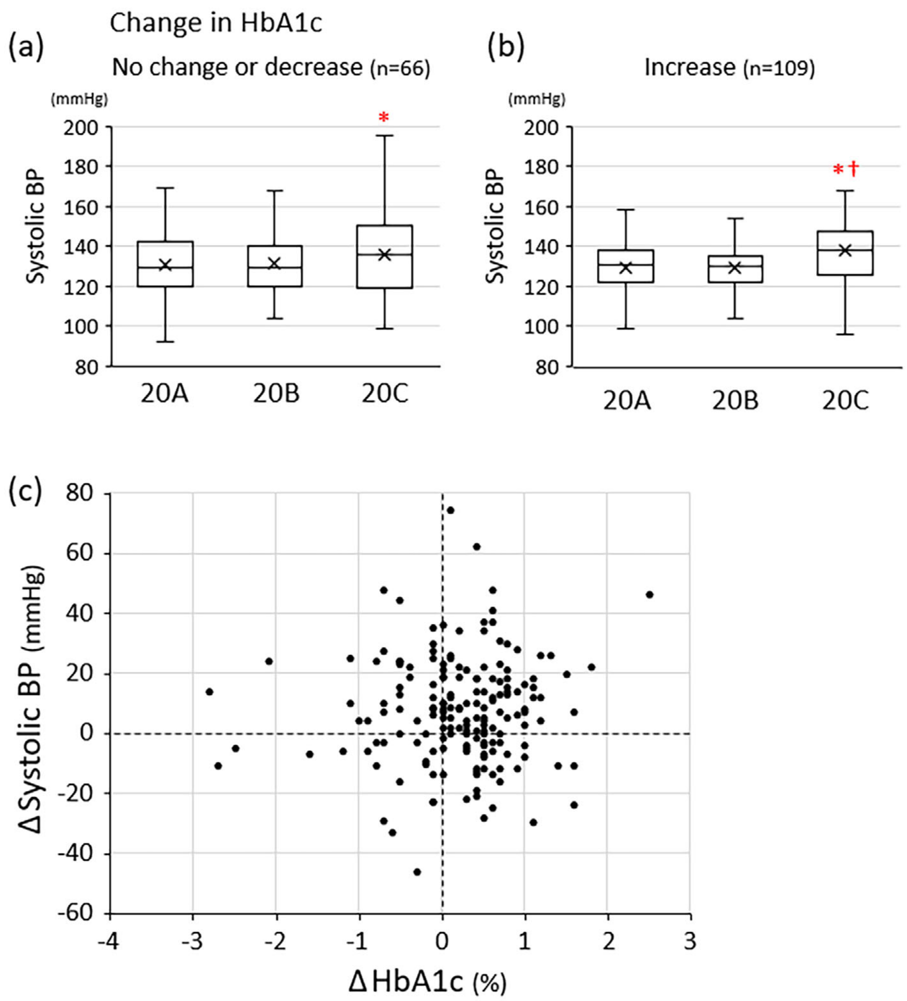


**Figure 6. Effects of (a, b) glycemic control during the state of emergency on changes in systolic BP in patients who answered the questionnaire in cohort 2. (c) Relationships between changes in HbA1c and changes in systolic BP in the periods of 20A and 20C. *p<0.05 vs. 20A, †p<0.05 vs. 20B.**

gency, whereas an increase in BP became apparent after the end of the state of emergency, at a later point than the worsening of glycemic control (Fig. 3, 4). There have been two studies thus far concerning the effect of the COVID-19 pandemic on BP in hypertensive patients. Pengo et al. showed that home BP decreased after two weeks of a COVID-19 lockdown (16). In contrast, Celik et al. found that daytime, nighttime and 24-hour BP levels all increased during the COVID-19 pandemic and that anxiety intensity was associated with increased BP (17). Although there have been no reports on the effect of the COVID-19 pandemic on BP control in DM patients, the results of the present study are consistent with those of the above two studies, as the BP increased in the delayed phase rather than the acute phase. In our study, the BP increased without a strong relationship to changes in the diet or physical activity. In addition, there was no marked association between increases in the BP and the deterioration of glycemic control (Fig. 6). The factors that cause different responses to worsening glycemic control and BP control are unclear, but a variety of chronic factors, including the influence of mental stress, may be involved (14, 15, 17, 30). It is known that mental stress also affects blood glucose levels, but changes in the diet, activity, and medical treatment may have a greater impact on glycemic control. In fact, the BP rises significantly after major stresses, such as surviving an earthquake, but the impact of such stresses on glycemic control has varied among studies (31-35). It is unclear to what extent mental stress caused by anxiety about an infectious disease pandemic and prolonged restrictions on daily life due to the COVID-19 pandemic affect the blood glucose and BP values, but the effects may differ with regard to timing and degree (36).

Several limitations associated with the present study warrant mention. First, because the questionnaire was designed with very simple questions, detailed dietary information was not available. For example, there was no information on changes in the estimated salt intake, snack food intake, or frequency of eating out. In addition, there were no questions about how stressed the patients were. Second, we were unable to investigate changes in the body weight. Although an association between poor glycemic control and weight gain during lockdown has been reported (11), the association between changes in the diet and physical activity and changes in the body weight and the association between changes in the body weight and changes in the blood glucose and BP could not be investigated in this study. Third, we do not know how many patients did not respond to the questionnaire or were hesitant to come to the hospital due to fear of the COVID-19 pandemic. The possibility of bias in the results therefore cannot be denied, as the study was conducted among patients who regularly visited the hospital. Finally, the present study was a single-center retrospective study, and the results may not be applicable to other regions.

In conclusion, glycemic control and BP control in DM patients deteriorated following the declaration of a state of emergency due to the COVID-19 pandemic. These deteriorations were more pronounced in patients with better control than others and were also observed in patients who perceived no marked lifestyle changes during the state of emergency. How long this worsening of glycemic control and BP control will continue is a subject that should be explored in future research, but correction through appropriate therapeutic intervention seems to be important.

**Author's disclosure of potential Conflicts of Interest (COI).**
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