Clinical feasibility of remote intermittently scanned continuous glucose monitoring in coronavirus disease 2019 patients with and without diabetes during dexamethasone therapy

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Abstract. The clinical utility of intermittently scanned continuous glucose monitoring (isCGM) in patients with coronavirus disease 2019 (COVID-19) is unclear. Hence, we investigated the accuracy of isCGM in COVID-19 patients during dexamethasone therapy. We evaluated the accuracy of the FreeStyle Libre via smartphone isCGM device compared to point-of-care (POC) fingerstick glucose level monitoring in 16 patients with COVID-19 (10 with and 6 without diabetes, 13 men; HbA1c 6.9 ± 1.0%). Overall, isCGM correlated well with POC measurements (46.2% and 53.8% within areas A and B of the Parkes error grid, respectively). The overall mean absolute relative difference (MARD) for isCGM compared to POC measurements was 19.4%. The MARDs were 19.8% and 19.7% for POC blood glucose measurements ranging from 70 to 180 mg/dL and >180 mg/dL, respectively. When divided according to the presence and absence of diabetes, both groups of paired glucose measurements showed a good correlation (56.3% and 43.7%, and 27.1% and 72.9% within the A and B areas in patients with and without diabetes, respectively), but the MARD was not significant but higher in patients without diabetes (16.5% and 24.2% in patients with and without diabetes). In conclusion, although isCGM may not be as accurate as traditional blood glucose monitoring, it has good reliability in COVID-19 patients with and without diabetes during dexamethasone therapy.

Key words: Coronavirus disease 2019, Device accuracy, Intermittently scanned continuous glucose monitoring, Remote continuous glucose monitoring, Dexamethasone
particular, the LibreLink (Abbott Diabetes Care, Alameda, CA, USA) smartphone application can be used to remotely access glycemic profiles by scanning the FreeStyle Libre sensor. Libre system has the advantage of being cheaper than previously reported remote real-time CGMs [5-11]. Furthermore, the FreeStyle Libre 14-day system is recommended for use in hospital settings during the COVID-19 pandemic by the U.S. Food and Drug Administration [5, 12]. To date, few studies have evaluated remote glucose monitoring during the COVID-19 pandemic. Further investigation is needed to understand the efficacy, safety, barriers to implementation, and costs associated with the use of remote glucose monitoring technology in hospitals.

In this pilot study, we evaluated the clinical feasibility of glucose monitoring by remote isCGM using the LibreLink application and LibreView web-based platform in COVID-19 patients with and without diabetes, undergoing dexamethasone therapy at a hospital.

Material and Methods

Subjects

We enrolled 10 COVID-19 patients with diabetes and 6 COVID-19 patients without diabetes who, were hospitalized and were undergoing dexamethasone therapy at Kitasato University Hospital. COVID-19 was confirmed by polymerase chain reaction (PCR) testing or antigen testing, and patients were grouped on the basis of diabetes status. Diabetes patients were defined by a diabetic history, previous or current diabetes treatment, and/or glycated hemoglobin (HbA1c) level ≥6.5% at admission. Study protocol was approved by the Research Ethics Committee of the Kitasato University School of Medicine (B20-390) and registered with the UMIN Clinical Trial Registry (registration no. UMIN000044456). All study protocols were in accordance with the relevant guidelines and regulations of Kitasato University Hospital, the Ethical Guidelines for Medical and Health Research Involving Human Subjects in Japan, and the Code of Ethics of the Helsinki Declaration. All diabetic and non-diabetic patients treated with dexamethasone, who had access to their smartphone, were recruited without bias. All patients provided written informed consent prior to participation in this study.

Study design

A FreeStyle Libre (Abbott Diabetes Care, Alameda, CA, USA) sensor was attached to the upper arm before dexamethasone therapy was initiated for COVID-19 treatment. All patients downloaded the LibreLink application to their smartphones and used it as a scanner for the Libre sensor and uploaded their glucose data to the LibreView platform. After attaching the Libre sensor, participants performed point-of-care (POC) fingerstick blood glucose monitoring using a Medisafe® Fit (Terumo Corporation, Tokyo, Japan) at least four times per day, before each meal and before bedtime, and simultaneously scanned the Libre sensor with a smartphone. We investigated the relationships between the scanned sensor glucose level (SGL) and the glucose level reported by the POC test during the Libre sensor wear period. If the sensor was mishandled (e.g., it fell off the arm), data from the prior session were used. We calculated the absolute difference and absolute relative difference between isCGM and POC measurements of glucose levels.

Biochemical measurement

The patients were given blood tests, including white blood cell (WBC) count, lymphocyte count, high-sensitivity C-reactive protein (hsCRP), D-dimer, fibrinogen degradation products (FDP), ferritin, and lactate dehydrogenase (LDH), as COVID-19 activity markers [13] and estimated glomerular filtration rate (eGFR), within 7 days prior to Libre sensor placement to establish a baseline. HbA1c level was measured by high performance liquid chromatography using an automated analyzer (HLC-723®G11; Tosoh Corp., Japan; reference range 4.6%–6.2%).

Statistical analysis

Statistical analyses were performed using Prism 5.02 software (GraphPad Software Inc. San Diego, CA, USA) and JMP version 14 (SAS, Cary, NC, USA). Concordance between Libre and POC measurements was analyzed using the Parkes Error Grid [14], which divides the linear correlation plot into clinically meaningful areas (from A to E). The mean absolute difference (MAD) and mean absolute relative difference (MARD) for isCGM versus POC measurements were computed for each patient as well as pooled data from all patients [15-18]. We used the Bland–Altman method to evaluate the difference between the POC and isCGM methods. Statistical analyses were performed using Student’s t-test. Correlation was measured using Pearson’s correlation coefficient. Data are presented as mean ± standard deviation unless otherwise indicated. Statistical significance was defined as $p < 0.05$.

Results

Demographic and baseline characteristics

Sixteen admitted COVID-19 patients were recruited for this study. Clinical characteristics at admission are presented in Table 1, and their SGL profiles are shown in Fig. 1. All patients had COVID-19 pneumonia, and all
required dexamethasone treatment. The dose of dexamethasone therapy was determined based on pneumonia severity, oxygen demand, and days since onset. The median maximum dexamethasone dose during the treatment period was 13.2 (6.6–100) mg and the median duration of treatment was 9.5 (6–25) days. Dexamethasone was administered once daily (at 10 am) or twice daily (at 10 am and 10 pm). The mean length of hospitalization was 14.8 ± 7.4 days, and patients were discharged 3 (1–18) days after the completion of dexamethasone therapy. Six participants did not have diabetes (HbA1c 5.6–6.3%) and ten had diabetes (HbA1c 6.7–9.7%). Four patients with diabetes were newly diagnosed with diabetes, and six patients were diagnosed with diabetes prior to admission. Of the patients with diabetes, four patients were treated with sodium-glucose cotransporter 2 inhibitor (SGLT2i) (one with canagliflozin, one with dapagliflozin, one with ipragliflozin, and one with

**Table 1** Characteristics of the enrolled participants with COVID-19 at admission

|                   | All          | Diabetic     | Non-diabetic | p value |
|-------------------|--------------|--------------|--------------|---------|
| n                 | 16           | 10           | 6            |         |
| Sex, male         | 13           | 9            | 4            | 0.5179  |
| Age (years)       | 52.5 ± 7.6   | 55.6 ± 7.1   | 47.3 ± 5.5   | 0.0569  |
| BMI               | 28.9 ± 5.9   | 31.6 ± 5.9   | 24.4 ± 2.0   | 0.0312  |
| Casual blood glucose (mg/dL) | 124 (92–282) | 137 (115–282) | 111 (92–132) | 0.0067  |
| CPR (ng/mL)       | 3.37 (2.03–9.66) | 4.19 (2.95–9.66) | 3.10 (2.03–5.86) | 0.1179  |
| HbA1c (%)         | 6.9 ± 1.0    | 7.3 ± 0.9    | 6.0 ± 0.3    | 0.0013  |
| Oxygen requirement (L/min) | 2.5 (0–5.0)   | 2.5 (0–5.0)  | 2.5 (0–4.0)  | 0.9559  |
| WBC (μL)          | 5,750 (3,600–9,300) | 5,550 (3,600–9,300) | 5,950 (3,800–7,400) | 0.4278  |
| Lymphocyte counts (/μL) | 951 (223–1,527) | 1,245 (223–1,527) | 823 (626–1,110) | 0.1179  |
| hsCRP (mg/dL)     | 5.05 (0.85–22.84) | 5.24 (0.85–22.84) | 4.83 (3.41–11.25) | 0.6354  |
| D-dimer (μg/mL)   | 1.08 (0.65–6.68) | 1.00 (0.65–6.68) | 1.16 (0.66–1.90) | 0.6642  |
| FDP (μg/mL)       | 3.8 (2.5–18.7) | 3.7 (2.5–18.7) | 4.2 (2.5–6.2) | 0.5502  |
| Ferritin (ng/mL)  | 525 (21–3,390) | 442 (21–3,390) | 1,084 (147–2,304) | 0.4923  |
| LDH (U/L)         | 364 (203–735) | 364 (203–735) | 385 (303–579) | 0.8707  |
| eGFR (mL/min/1.73 m²) | 62.0 (44.0–93.0) | 59.0 (49.0–72.0) | 63.5 (44.0–93.0) | 0.6237  |
| Maximum steroid dose (mg/day)* | 13.2 (6.6–100) | 13.2 (6.6–100) | 9.9 (6.6–13.2) | 0.6264  |

Data are presented as n (%), mean ± SD, or median (minimum to maximum)

BMI, body mass index; CPR, C-peptide immunoreactivity; HbA1c, glycated hemoglobin; WBC, white blood cell; hsCRP, high sensitivity C-reactive protein; FDP, fibrinogen degradation products; LDH, lactate dehydrogenase; eGFR, estimated glomerular filtration rate

* dexamethasone equivalent

**Fig. 1** Differences in mean ± SD sensor glucose profiles 3–6 days after starting dexamethasone therapy between diabetic (red) and non-diabetic (blue) patients.
tofogliflozin), four with dipeptidyl peptidase-4 inhibitor (DPP4i) (two with sitagliptin, one with teneligliptin and one with vildagliptin), one with biguanide (metformin), and two with sulfonylurea (glimepiride) before admission. Of the five patients who were treated for diabetes before admission, one was treated with only SGLT2i; one with DPP4i and SGLT2i; one with a sulfonylurea and DPP4i; one with a sulfonylurea, DPP4i, and SGLT2i; and one with DPP4i, SGLT2i, and biguanide. One patient with diabetes was managed by diet control alone. Following dexamethasone administration in patients with diabetes, oral hypoglycemic agents were continued in four and newly started oral hypoglycemic agents in one patients, and five started insulin lispro and one was administered basal insulin in combination with the sliding-scale insulin regimen. The sliding scale was established as follows: 2 units of regular insulin were administered for every 50 mg/dL increase above 200 mg/dL in blood glucose level as measured by POC testing, with a maximum dose of 10 units administered when POC measurement was 401 mg/dL or higher. After dexamethasone administration, sliding scale insulin administration was indicated for all patients without diabetes, but only one of six patients required treatment with insulin. Only two patients wore the FreeStyle Libre sensor for all 14 days. The remaining 14 participants discontinued using the sensor before 14 days due to hospital discharge in 13 patients and worsening of COVID-19 condition in 1 patient. In addition to dexamethasone therapy, five patients were treated with anticoagulants, one with favipiravir, ten with remdesivir, and one with baricitinib for the treatment of COVID-19.

**Accuracy analyses**

Our analysis of the relationship between isCGM and POC measurements based on 604 glucose reading pairs revealed an overall $r^2$ value of 0.8792. According to the Parkes Error Grid, 279 (46.2%) and 325 (53.8%) of the glucose pairs were within areas A and B of the linear correlation plot, respectively, whereas none were in areas C, D, and E (Fig. 2A). The mean and range of isCGM values were 137.8 mg/dL and 55–346 mg/dL, respectively, and the mean SGL determined by isCGM was significantly lower (31.7 mg/dL) than that determined by POC testing ($p < 0.001$) (Fig. 2B). The overall MAD and MARD for isCGM measurements were $32.3 \pm 11.3$ mg/dL and $19.4 \pm 6.8\%$, respectively (Table 2). The ranges of daily POC measurements were 75–408 mg/dL, including 420 points (69.5%) indicating euglycemia (70–180 mg/dL), 184 points (30.5%) indicating hyperglycemia (>180 mg/dL), and no points in the hypoglycemic range (<70 mg/dL). The MAD and MARD were 27.8 ± 9.0 mg/dL and 19.8 ± 6.6% in euglycemia (70–180 mg/dL of POC), and 42.9 ± 14.3 mg/dL and 19.7 ± 7.4% in hyperglycemia (>180 mg/dL). In the euglycemic range of POC measurements, 184 (43.8%) and 236 (56.2%) of glucose measurement pairs were within zones A and B, respectively, with no points in the C, D, and E zones of the Parkes Error Grid (Table 2). Additionally, in the hyperglycemic range of POC measurements (>180 mg/dL), 95 (51.6%) and 89 (48.4%) of glucose measurement pairs were within zones A and B, respectively, with no points in zones C, D, and E (Table 2). The MARD was not significant but higher in patients without diabetes than in those with diabetes ($p = 0.0559$). Furthermore,

![Fig. 2](image-url) Parkes error grid analysis for the clinical validation of isCGM using POC measurements as a comparator (A). Differences in glucose levels of isCGM relative to POC measured values (B). Straight and dashed lines represent the mean and standard deviation of the differences in glucose levels, respectively. isCGM, intermittently scanned continuous glucose monitoring; POC, point-of-care.
the MAD and MARD were not correlated with age, WBC count, lymphocyte count, or hsCRP, D-dimer, FDP, ferritin, LDH, or eGFR levels. In patients with diabetes, 222 (56.3%) and 172 (43.7%) of the glucose measurement pairs were within the A and B areas of the Parkes Error Grid, respectively, whereas none were in the C, D, and E areas. The MAD and MARD of SGL values measured by isCGM in COVID-19 patients with diabetes were 31.2 ± 12.6 mg/dL and 16.5 ± 5.6%, respectively. In the COVID-19 patients without diabetes, 57 (27.1%) and 153 (72.9%) of the glucose measurement pairs were within the A and B areas of Parkes Error Grid, respectively, whereas none were in the C, D and E areas. The MAD and MARD of isCGM measurements were 34.0 ± 9.4 mg/dL and 24.2 ± 6.3%, respectively, in the COVID-19 patients without diabetes.

The daily MARD in all patients from day 1 to day 10 ranged from 17.7 to 22.0%, with no difference among days (p = 0.7189) (Table 3), and the daily MARD in patients without diabetes ranged 22.0–26.3%, which were higher than the MARD of patients with diabetes (15.1–19.2%) at all days (Table 3).

### Adverse events

No adverse events were observed during the study period, including skin redness and itchiness at the isCGM placement site; there were no occurrences of displacement of the isCGM device.

Additionally, none of the patients who did not have diabetes before dexamethasone treatment were diagnosed with steroid-induced diabetes or required continued treatment for diabetes after this study.

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**Table 2** Summary of the accuracy of isCGM

|                     | All        | Diabetic   | Non-diabetic | p value |
|---------------------|------------|------------|--------------|---------|
| Overall             | 604        | 394 (65.2) | 210 (34.8)   |         |
| p value             | <0.0001    | <0.0001    | <0.0001      |         |
| $r^2$               | 0.8792     | 0.8923     | 0.6046       |         |
| MAD (mg/dL)         | 32.3 ± 11.2 [2.8] | 31.2 ± 12.6 [4.0] | 34.0 ± 9.4 [3.8] | 0.4278 |
| MARD (%)            | 19.4 ± 6.8 [1.7] | 16.5 ± 5.6 [1.8] | 24.2 ± 6.3 [2.6] | 0.0559 |
| Parkes Error Grid   |            |            |              |         |
| Zone A              | 279 (46.2) | 222 (56.3) | 57 (27.1)    |         |
| Zone B              | 325 (53.8) | 172 (43.7) | 153 (72.9)   |         |
| Zone C + D + E      | 0          | 0          | 0            |         |
| Glucose level 70–180 mg/dL | 420        | 230 (54.8) | 190 (45.2)    |         |
| p value             | <0.0001    | <0.0001    | <0.0001      |         |
| $r^2$               | 0.5829     | 0.6442     | 0.5061       |         |
| MAD (mg/dL)         | 27.8 ± 9.0 [2.2] | 25.0 ± 8.2 [2.6] | 32.5 ± 8.8 [3.6] | 0.1179 |
| MARD (%)            | 19.8 ± 6.6 [1.7] | 17.3 ± 5.6 [1.8] | 24.0 ± 6.4 [2.6] | 0.0934 |
| Parkes Error Grid   |            |            |              |         |
| Zone A              | 184 (43.8) | 128 (55.7) | 56 (29.5)    |         |
| Zone B              | 236 (56.2) | 102 (44.3) | 134 (70.5)   |         |
| Zone C + D + E      | 0          | 0          | 0            |         |
| Glucose level >180 mg/dL | 184        | 164 (89.1) | 20 (10.9)     |         |
| p value             | <0.0001    | <0.0001    | 0.0573       |         |
| $r^2$               | 0.7732     | 0.7555     | 0.1865       |         |
| MAD (mg/dL)         | 42.9 ± 14.3 [3.8] | 38.7 ± 13.9 [4.6] | 50.7 ± 12.7 [5.7] | 0.2398 |
| MARD (%)            | 19.7 ± 7.4 [2.0] | 16.1 ± 5.4 [1.8] | 26.1 ± 6.3 [2.8] | 0.0120 |
| Parkes Error Grid   |            |            |              |         |
| Zone A              | 95 (51.6)  | 94 (57.3)  | 1 (5)        |         |
| Zone B              | 89 (48.4)  | 70 (42.7)  | 19 (95)      |         |
| Zone C + D + E      | 0          | 0          | 0            |         |

Data are presented as n (%) or mean ± SD [SEM].

MAD, mean absolute difference; MARD, mean absolute relative difference.

Mann Whitney test are used to compare patients between with and without diabetes.
Table 3  Change in MARD by day

| Day | 1   | 2   | 3   | 4   | 5   | 6   | 7   | 8   | 9   | 10  |
|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|
| All, n | 16  | 16  | 16  | 16  | 16  | 16  | 15  | 14  | 13  | 9   |
| Mean  | 17.7| 19.1| 20.6| 21.4| 20.0| 19.8| 22.0| 20.2| 18.3| 18.2|
| SD    | 7.4 | 6.8 | 8.3 | 8.7 | 8.1 | 8.3 | 9.3 | 8.9 | 7.3 | 7.5 |
| Diabetic, n | 10  | 10  | 10  | 10  | 10  | 10  | 9   | 9   | 8   | 7   |
| Mean  | 15.1| 16.5| 17.3| 18.7| 17.5| 16.1| 19.2| 18.6| 15.5| 16.9|
| SD    | 6.4 | 5.9 | 7.2 | 7.9 | 6.8 | 6.2 | 8.5 | 10.2| 4.9 | 5.3 |
| Non-diabetic, n | 6   | 6   | 6   | 6   | 6   | 6   | 5   | 5   | 5   | 2   |
| Mean  | 22.0| 23.5| 26.1| 25.9| 24.0| 26.0| 26.3| 23.0| 22.7| 22.8|
| SD    | 7.4 | 6.6 | 7.3 | 8.6 | 8.9 | 8.0 | 9.5 | 5.9 | 8.9 | 15.1|

*p value 0.0438 0.0192 0.0010 0.0029 0.0031 0.0006 0.0152 0.1255 0.0270 0.0483*  
Mann-Whitney test are used to compare patients between with and without diabetes.

**Discussion**

In this study, we investigated the feasibility of remote isCGM via smartphone during dexamethasone therapy in COVID-19 patients with and without diabetes. We evaluated the relationships between glucose levels measured by isCGM and those measured by POC fingerstick glucose monitoring and found that the accuracy of isCGM was acceptable in clinical settings. This study is the first to evaluate the accuracy of isCGM in COVID-19 patients with and without diabetes who were treated with dexamethasone therapy. Several studies have reported a good correlation between glucose measured using isCGM compared with that measured using POC monitoring, and recent studies have revealed the overall MARD of isCGM to be 8.1–16.6% with respect to POC measurements [16, 18-23]. Furthermore, a previous study investigated the accuracy of other real-time CGM in COVID-19 patients on dexamethasone treatment, which could be calibrated, showed a MARD of 10.9–14.0% [24]. However, the accuracy of isCGM measurements we report in patients with COVID-19 treated with dexamethasone is lower than that reported in previous reports. Thus, our results suggest that the MARD for isCGM compared to POC assessment is higher in COVID-19 patients treated with dexamethasone than in patients with diabetes not complicated with COVID-19 [16, 18-23]. The reason for the lower accuracy of isCGM in COVID-19 patients than previously reported may be due to the inflammatory condition caused by COVID-19 and/or changes in interstitial fluid caused by steroid use [25]. Furthermore, a previous study of the accuracy of isCGM in COVID-19 patients treated in an intensive care unit showed a relatively higher MARD of 22.4% similar to our results, suggesting that inflammation, mean corpuscular hemoglobin concentration, and electrolyte changes caused by COVID-19 may have an effect [26]. However, the accuracy of isCGM did not correlate with COVID-19 activity markers, such as WBC count, lymphocyte count, hsCRP, D-dimer, FDP, ferritin, and LDH levels, in this study and there are no studies that have evaluated the accuracy of isCGM in such specific population. Additionally, there was no significant difference in MAD or MARD between the group using 6.6 mg of dexamethasone per day and the group using more than 6.6 mg of dexamethasone per day and isCGM cannot be calibrated, which may be one of the reasons for the higher MARD in our study. In Addition, isCGM via smartphone have improved accuracy compared to isCGM via first-generation FreeStyle Libre Reader [27]. Therefore, we should keep in mind that the accuracy of isCGM via Libre Reader may be even worse in COVID-19 patients. Furthermore, our results highlight the precautions needed when using isCGM in COVID-19 patients treated with dexamethasone. First, the SGL measured by isCGM was 31.7 (~33 to 101) mg/dL lower than that measured by POC testing. Additionally, the accuracy of isCGM was lower in patients without diabetes than in those with diabetes. MAD and MARD were higher in patients without diabetes than in those with diabetes. Actually in patients without diabetes, isCGM was 34.4 (~13 to 85) mg/dL lower than POC measurement and higher in only 3 of 210 pairs (isCGM vs. POC; 168 mg/dL vs. 155 mg/dL, 134 mg/dL vs. 124 mg/dL and 105 mg/dL vs. 104 mg/dL). In other words, the isCGM of non-diabetic patients is rarely over-estimated, and almost all of the data underestimates it. This may be because the FreeStyle Libre sensors are factory-calibrated, but this correction formula is based on data from diabetic population, not non-diabetic, and the accuracy of isCGM in the low-glucose areas is even lower [18, 28]. Therefore, if isCGM is to be used in patients without diabetes, we must be more cautious about its accuracy, and although COVID-19 non-diabetic
patients treated with dexamethasone show the lowest glucose levels during early morning fast, we believe that isCGM should be used in conjunction with regular glucose monitoring by POC at least once a day. Although several previous studies have shown the benefits of using CGMs in COVID-19 patients with diabetes [5-11], we have demonstrated that certain CGMs may have poor accuracy in such patients.

Despite this limitation, isCGM has several advantages over other glucose monitoring methods in the clinical management of COVID-19 patients. Most importantly, isCGM, especially when combined with remote monitoring via smartphone, could reduce the frequency of bedside blood glucose testing and decrease the exposure risk of healthcare staff to SARS-CoV-2. Additionally, isCGM devices do not require calibration and can be used for up to 14 days. Glucose measurement by POC methods provides intermittent glucose measurements but may not be able to detect glycemic excursion induced by dexamethasone therapy and/or hypoglycemia in COVID-19 patients.

The limitations of the present study are the small number of patients and the lack of a gold standard reference for plasma glucose level measurements. Glucose monitoring in clinical settings is performed using a variety of sampling methods; however, it is most practical to use a single standard method as a reference. Thus, we chose POC fingerstick testing, a common clinical method, as our reference. Although the number of patients was low, the number of paired measurements taken from each patient was high, which may alleviate some concerns regarding the small sample size. Although we abstracted a greater number of paired glucose measurements, the numbers remained small in the hypoglycemic categories. Additionally, at least in Japan, determination of insulin dose based on scanned glucose level by isCGM is not allowed. Considering less accuracy of isCGM in COVID-19 patients in this study, it is clinically important to determine when to perform more accurate glucose measurement by POC and reduce the frequency of contacts with those patients, rather than making insulin treatment and/or dose decisions based on isCGM. Finally, the feasibility and accuracy of isCGM in patients with severe COVID-19 could not be determined in our study.

In summary, our results suggest that remote isCGM can be used reliably and safely in COVID-19 patients with and without diabetes undergoing dexamethasone therapy, although isCGM may not be as accurate as POC blood glucose monitoring.

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Disclosure

No potential conflicts of interest relevant to this article were reported.

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Contribution Statement

All authors have contributed significantly, N.S., A.H., and K.M. were responsible for the conception and design of the study. N.S., A.H., A.S., K.M., K.T., M.K. and M.S. had full access to all the data in the study and take responsibility for the integrity of the data and the accuracy of the data analysis. N.S., S.I., A.S., R.F., K.M. and T.W. collected and analyzed the data. N.S. and A.H. evaluated the data and were the primary authors of the manuscript. All authors reviewed the data and took responsibility for the final assembly and editing of the manuscript. A. H. is the guarantor of this work and, as such, had full access to all the data in the study and takes responsibility for the integrity of the data and the accuracy of the data analysis. All authors reviewed the data and take responsibility for the final assembly and editing of the manuscript.

References

1. Gandhi RT, Lynch JB, Del Rio C (2020) Mild or moderate Covid-19. N Engl J Med 383: 1757–1766.
2. Xu XW, Wu XX, Jiang XG, Xu KJ, Ying LJ, et al. (2020) Clinical findings in a group of patients infected with the 2019 novel coronavirus (SARS-Cov-2) outside of Wuhan, China: retrospective case series. BMJ 368: m606.
3. Aguas R, Mahdi A, Shretta R, Horby P, Landray M, et al. (2021) Potential health and economic impacts of dexamethasone treatment for patients with COVID-19. Nat Commun 12: 915.
4. Rayman G, Lumb AN, Kennon B, Cottrell C, Nagi D, et al. (2021) Dexamethasone therapy in COVID-19 patients: implications and guidance for the management of blood glucose in people with and without diabetes. Diabet Med 38: e14378.

5. Galindo RJ, Alepp G, Klonoff DC, Spanakis EK, Agarwal S, et al. (2020) Implementation of continuous glucose monitoring in the hospital: emergent considerations for remote glucose monitoring during the COVID-19 pandemic. J Diabetes Sci Technol 14: 822–832.

6. Reuterakul S, Genco M, Salinas H, Sargas RM, Paul C, et al. (2020) Feasibility of inpatient continuous glucose monitoring during the COVID-19 pandemic: early experience. Diabetes Care 43: e137–e138.

7. Sadhu AR, Serrano IA, Xu J, Nisar T, Lucier J, et al. (2020) Continuous glucose monitoring in critically ill patients with COVID-19: results of an emergent pilot study. J Diabetes Sci Technol 14: 1065–1073.

8. Shehav-Zaltzman G, Segal G, Konvalina N, Tirosh A (2020) Remote glucose monitoring of hospitalized, quarantined patients with diabetes and COVID-19. Diabetes Care 43: e75–e76.

9. Agarwal S, Mathew J, Davis GM, Shephardson A, Levine A, et al. (2021) Continuous glucose monitoring in the intensive care unit during the COVID-19 pandemic. Diabetes Care 44: 847–849.

10. Shen Y, Zhang L, Fan X, Zhou J (2021) Effectiveness of remote continuous glucose monitoring on adverse outcomes among patients with diabetes complicated with COVID-19. J Diabetes Investig 12: 1923–1924.

11. Ushigome E, Yamazaki M, Hamaguchi M, Ito T, Matsubara S, et al. (2021) Usefulness and safety of remote continuous glucose monitoring for a severe COVID-19 patient with diabetes. Diabetes Technol Ther 23: 78–80.

12. Pasquel FJ, Umpierrez GE (2020) Individualizing inpatient diabetes management during the coronavirus disease 2019 pandemic. J Diabetes Sci Technol 14: 705–707.

13. Mammen JJ, Kumar S, Thomas L, Kumar G, Zachariah A, et al. (2021) Factors associated with mortality among moderate and severe patients with COVID-19 in India: a secondary analysis of a randomised controlled trial. BMJ Open 11: e050571.

14. Parkes JL, Slatin SL, Pardo S, Ginsberg BH (2000) A new consensus error grid to evaluate the clinical significance of inaccuracies in the measurement of blood glucose. Diabete Care 23: 1143–1148.

15. Javherani RS, Purandare VB, Bhatt AA, Kumaran SS, Sayyad MG, et al. (2018) Flash glucose monitoring in subjects with diabetes on hemodialysis: a pilot study. Indian J Endocrinol Metab 22: 848–851.

16. Kumagai R, Muramatsu A, Fujii M, Katakura Y, Ito K, et al. (2019) Comparison of glucose monitoring between Freestyle Libre Pro and iPro2 in patients with diabetes mellitus. J Diabetes Investig 10: 851–856.

17. Matoba K, Hayashi A, Shimizu N, Moriguchi I, Kobayashi N, et al. (2020) Comparison of accuracy between flash glucose monitoring and continuous glucose monitoring in patients with type 2 diabetes mellitus undergoing hemodialysis. J Diabetes Complications 34: 107680.

18. Olafsdottir AF, Attvall S, Sandgren U, Dahlqvist S, Pivodic A, et al. (2017) A clinical trial of the accuracy and treatment experience of the Flash Glucose Monitor FreeStyle Libre in adults with type 1 diabetes. Diabetes Technol Ther 19: 164–172.

19. Bailey T, Bode BW, Christiansen MP, Klaff LJ, Alva S (2015) The performance and usability of a factory-calibrated Flash Glucose Monitoring System. Diabetes Technol Ther 17: 787–794.

20. Bonora B, Maran A, Ciciliot S, Avogaro A, Fadini GP (2016) Head-to-head comparison between flash and continuous glucose monitoring systems in outpatients with type 1 diabetes. J Endocrinol Invest 39: 1391–1399.

21. Sato T, Oshima H, Nakata K, Kimura Y, Yano T, et al. (2019) Accuracy of flash glucose monitoring in insulin-treated patients with type 2 diabetes. J Diabetes Investig 10: 846–850.

22. Scott EM, Bilous RW, Kautzky-Willer A (2018) Accuracy, user acceptability, and safety evaluation for the Freestyle Libre Flash Glucose Monitoring System when used by pregnant women with diabetes. Diabetes Technol Ther 20: 180–188.

23. Ancona P, Eastwood GM, Lucchetta L, Ekinci EI, Bellomo R, et al. (2017) The performance of flash glucose monitoring in critically ill patients with diabetes. Crit Care Resusc 19: 167–174.

24. Longo RR, Elias H, Khan M, Sley JI (2021) Use and accuracy of inpatient CGM during the COVID-19 pandemic: an observational study of general medicine and ICU patients. J Diabetes Sci Technol : 19322968211008446.

25. Burt MG, Roberts GW, Aguilar-Loza NR, Frith P, Stranks SN (2011) Continuous monitoring of circadian glycemic patterns in patients receiving prednisolone for COPD. J Clin Endocrinol Metab 96: 1789–1796.

26. Zhang Y, Liu X, Zhang J, Fu J, Li S, et al. (2021) Evaluation for the feasibility and accuracy of Freestyle Libre Flash Glucose Monitoring System used by COVID-19 patients in intensive care unit. J Diabetes 13: 603–605.

27. Alva S, Bailey T, Brazg R, Budiman ES, Castorino K, et al. (2020) Accuracy of a 14-day factory-calibrated continuous Glucose Monitoring System with advanced algorithm in pediatric and adult population with diabetes. J Diabetes Sci Technol : 1932296820958754.

28. Toyoda M, Murata T, Saito N, Kimura M, Takahashi H, et al. (2021) Assessment of the accuracy of an intermittent-scanning continuous glucose monitoring device in patients with type 2 diabetes mellitus undergoing hemodialysis (AIDT2H) study. Ther Apher Dial 25: 586–594.