Clinical application of real-time continuous glucose monitoring system during perioperative enteral nutrition therapy in esophageal cancer patients

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Abstract

BACKGROUND/OBJECTIVES:

The degree of blood glucose fluctuation between hyperglycemia and hypoglycemia during the perioperative period affects the recovery and prognosis of patients. Enteral nutrition (EN) support therapy can cause dramatic fluctuation of blood glucose, especially, the risk of hyperglycemia and death is higher in non-diabetic patients treated with EN. The aim of this study is to explore the clinical value of real-time continuous glucose monitoring (rt-CGM) system in blood glucose monitoring during perioperative enteral nutrition support therapy in patients with esophageal cancer.

SUBJECTS/METHODS: Non-diabetic esophageal cancer patients who planned to receive postoperative enteral nutrition were enrolled. With self-monitoring of blood glucose (SMBG) value as the reference blood glucose, the accuracy of rt-CGM was evaluated by MARD value, correlation analysis, consistency analysis and Parkes and Clark error grid plot. Finally, paired t-tests were used to compare the differences in glycemic fluctuations between EN and non-EN days and slow and fast days.

RESULTS: The total MARD value of rt-CGM system was 13.53%. There was a high correlation between interstitial glucose (IG) and fingertip capillary blood glucose (BG) \( r = 0.925, P<0.001 \). The proportion of consistency analysis of 15/15%, 20/20% and 30/30% was 58.45%, 84.71% and 99.65%, respectively. Parkes and Clark error grid showed that the proportion of A + B region was 100% and 99.94%, respectively. The fluctuation of blood glucose on EN days than non-EN days and on fast days than slow days was large, and the difference was statistically significant \( P<0.001 \).

CONCLUSIONS: rt-CGM achieved clinical accuracy and can be used as a new option for glucose monitoring during perioperative EN therapy. The magnitude of glucose fluctuation during EN therapy remains large even in the perioperative population without a history of diabetes mellitus.

INTRODUCTION

Perioperative patients are often in a state of negative nitrogen balance due to factors such as postoperative oral feeding incapably and stress, and their nutritional status will seriously affect the development and prognosis of the disease. Therefore, nutritional support for these patients has become an important therapeutic measure. Enteral nutrition (EN) is more in line with the physiological characteristics of the human body than parenteral nutrition, and plays an important role in maintaining the structure and function of the intestinal mucosa and preventing bacterial translocation [1, 2]. However, hyperglycemia is the most common metabolic complication of EN, which is closely related to the incidence of mortality and adverse clinical outcomes in patients. The prevalence of hyperglycemia has been shown to reach 30% to 47% in patients during EN treatment, half of whom have no previous diagnosis of diabetes mellitus [3, 4]. Meanwhile, hypoglycemia is prone to occur during the intermittent period of EN. Persistent hyperglycemia is associated with oxidative stress, inflammatory responses, systemic tissue damage, and insulin resistance [5]. However, the degree of glycemic fluctuation between
high and low blood glucose has been shown to result in higher levels of oxidative stress and endothelial dysfunction [6]. Due to the lack of adaptation to acute hyperglycemia, non-diabetic patients have worse prognosis and higher mortality when their blood glucose levels are the same as those of diabetic patients before and after surgery [7-10].

Reducing the incidence of hyperglycemia in perioperative patients, decreasing blood glucose fluctuations, and detecting symptoms of hypoglycemia in a timely manner is critical to improving patient prognosis. An important prerequisite for avoiding abnormal glycemic events is adequate glucose monitoring [11]. Glycated hemoglobin (HbA1c) does not reflect the short-term fluctuation of blood glucose because it only reflects the average level of the last 2 to 3 months. Self-monitoring of blood glucose (SMBG) has poor compliance due to the pain of fingertip blood collection, and is limited by the environment and time. In recent years, real-time continuous glucose monitoring (rt-CGM) systems have been increasingly used for clinical blood glucose management because they provide continuous measurement of blood glucose levels and trends in blood glucose changes, and reduce the pain of frequent fingertip blood collection, which is more advantageous than SMBG in terms of blood glucose monitoring and adherence [12]. However, the application of rt-CGM in patients treated with perioperative EN has not been reported. Therefore, the present study was designed to monitor the blood glucose fluctuation of perioperative EN patients with esophageal cancer by rt-CGM to provide theoretical basis and technical support for the occurrence of blood glucose fluctuation and hypoglycemia in these patients.

**MATERIALS AND METHODS**

The study complied with the requirements of the Declaration of Helsinki and was approved by the Ethics Committee of the First Affiliated Hospital of Bengbu Medical College (approval number: 2020042). All enrolled patients were fully informed of the trial, associated benefits and risks and signed an informed consent form.

**Subjects**

Forty-two patients who attended the Department of Thoracic Surgery of the First Affiliated Hospital of Bengbu Medical College from May 2022 to July 2023 and required nasogastric enteral nutrition during the perioperative period after the physician’s assessment of their condition. Exclusion criteria: (1) age <18 years; (2) diabetes of any type (meeting the 2023 ADA diagnostic criteria for diabetes)[13]; (3) pregnant or breastfeeding women; (4) known allergy to the sensor adhesive; (5) extensive skin lesions or scars that make it difficult for the sensors to adhere; (6) infections or edemas at the application site of the sensors; (7) use of medications that may affect the sensor’s blood glucose measurement (e.g. thiazide diuretics, drugs of the glucocorticoid type, etc.); and (8) severe hepatic or renal insufficiency.

**Study design**
**Data collect:** Collect baseline information (such as age, sex, height, weight, blood pressure, etc.) and fasting blood indicators (such as fasting blood glucose, fasting serum insulin, HbA1c, hemoglobin, leukocytes, platelets, coagulation function, triglycerides, total cholesterol, etc.).

**Glucose monitoring:** All enrolled patients wore the MicroTech AiDEX CGMS ® (MicroTech Medical Devices (Hangzhou) Co. Ltd., Zhejiang, China, product model G7, registration certificate No. 20213070872) for glucose monitoring for 7-14d. After routine alcohol disinfection of the skin on the dorsal side of the upper arm, the sensor was placed and activated under sterile conditions. The sensor was preheated for 1 hour and turned on. The Interstitial glucose (IG) concentration was automatically measured and recorded every 5 minutes. Fingertip capillary blood glucose (BG) was measured on the second day of wear, and was monitored at least 7 times a day (7:00, 9:30, 11:30, 13:30, 15:30, 17:30, 21:00, respectively with a time window of ± 5 min.)[14]. All fingertip capillary blood glucose measurements were performed using the same batch of blood glucose test strips and the same blood glucose meter (MicroTech Insight type Wireless Blood Glucose Meter (Hangzhou) Co. Ltd., Zhejiang, China, product model A-2, registration certificate No. 20172220981).

**Nutritional support therapy:** (1) Nasointestinal tube placement: all patients were placed in a spiral nasoenteric tube, about 20cm from the flexor ligament, properly fixed to prevent pulling dislocation. (2) Selection of nutritional preparation: enteral nutritional preparation was Peptisorb ® [produced by Newdia Pharmaceutical (Wuxi) Co. Ltd., specification 500 ml/bottle; formula: protein 20 g, fat 8.5 g, carbohydrate 88 g, dietary fiber 0 g, minerals 2.8 g, vitamin 304.8 mg]. (3) Infusion method: intermittent gravity drip. Follow the principle from slow to fast, from less to more. The initial rate was generally 25 to 50mL/h, followed by an increase of 25 mL/h every 12 to 24 h, with a maximum rate of 125 to 150 mL/h [15]. When the requirement (1000-1500 Kcal) was reached on the 4th postoperative day, the infusion rate was adjusted to the recommended infusion rate of 125-150 ml/h and maintained for 4 days. Among them, the slow adjustment of the drip rate and total volume in the first three days of the postoperative period was called a slow day, and the maintenance of the drip rate of 125-150 ml/h after the fourth day of the postoperative period was called a fast day. Keep the head of the bed elevated at 30° 45° and the appropriate temperature of the nutrient solution around 37°C during infusion.

**Data analysis:** numerical accuracy (also known as analytical accuracy) refers to the consistency analysis between interstitial fluid glucose values and the fingertip glucose values, which can be evaluated by Pearson correlation analysis, mean absolute difference (MAD), mean absolute relative difference (MARD), and concordance rate of %15/15, %20/20, %30/30 with reference values, etc. Clinical accuracy refers to the assessment of the impact of the monitoring results on clinical decision-making, and is generally evaluated using Parkes error grid or Clark error grid diagrams, with values in zones A and B considered clinically acceptable, and values in zones C, D, and E considered unsafe. SMBG measurements were analyzed against CGMS measurements to assess numerical and clinical accuracy using the International Organization for Standardization [ISO 15197:2013] criteria. The following two minimum criteria for acceptable system accuracy need to be met: (1) when BG ≥ 5.56 mmol/L (100 mg/dL), >95% of the absolute relative differences (MARD) between IG and BG measurements should be within 15%; when BG
<5.56 mmol/L (100 mg/dL), >95% of the absolute differences (MAD) between IG and BG measurements should be <0.83 mmol/L (15 mg/dL). (2) ≥99% of IG measurements results should fall within zones A and B of the Parkes error grid analysis for type 1 diabetes [16].

Statistical analysis

Statistical analyses were carried out using R version 4.2.3 software (R Foundation for Statistical Computing, Vienna, Austria) and SPSS 25.0 software (IBM Corporation, Armonk, NY, USA). (Approximate) quantitative data obeying normal distribution was expressed as $\bar{x} \pm s$ and non-normally distributed as $M (P_{25}, P_{75})$. Comparisons of pre- and postglycemia between EN and non-EN days and between slow and fast days were performed using paired t-test or Wilcoxon sign-rank test. Statistical differences were expressed as $P<0.05$.

RESULTS

Patient’s characteristics

Of the 42 perioperative enteral nutrition patients, 4 were withdrawn with previous denial of diabetes mellitus but with HbA1c $\geq 6.5\%$, 2 were withdrawn due to pressure damage and unwillingness to reimplant the sensor, 3 were withdrawn due to unwillingness to repeatedly monitor their blood glucose, and 2 were withdrawn due to hemorrhage on the night of the operation and transfer to the intensive care unit after a second operation, resulting in the final inclusion of 31 patients (Supplementary Fig. 1).

The basic characteristics of the patients are shown in Supplementary Table 1. Of the 31 patients analyzed, 21 were male and 10 were female, with a mean age of 67.2 years, 28 underwent thoracoscopic esophagectomy and 3 underwent open esophagectomy. There were no obvious abnormalities in fasting blood glucose, fasting insulin, glycosylated hemoglobin, liver and kidney function, coagulation function nutritional status and etc. of the enrolled patients.

Accuracy analysis of rt-CGM measurements and SMBG measurements

Correlation and precision analysis

A total of 1733 pairs of glucose results were obtained, of which 17.20% (298/1733) were in the hyperglycemic group (>10 mmol/L or >180 mg/dL), 82.40% (1428/1733) were in the normoglycemic group (3.9-10.0 mmol/L or 70-180 mg/dL), and 0.40% (7/1733) were in the hypoglycemic group (<3.9 mmol/L or <70 mg/dL). IG was strongly positively correlated with BG overall [$r=0.925, P<0.001$], as well as in the hyperglycemic group [$r=0.852, P<0.001$], normoglycemic group [$r=0.815, P<0.001$], and
hypoglycemic group \[ r = 0.882, \ P = 0.009 \]. The overall MARD was 13.51% and MAD was 1.08 mmol/L. MARD was lowest in the normoglycemic group and highest in the hypoglycemic group (Table 1).

**Analysis of the agreement rate**

The results of the %15/15, %20/20, and %30/30 deviation agreement rate analyses are shown in Fig.1 and Table 2. Of the 1733 capillary glucose results obtained, 248 had a BG < 5.56 mmol/L (100 mg/dL) and 1485 had a BG ≥ 5.56 mmol/L (100 mg/dL). When BG < 5.56 mmol/L (100 mg/dL), 99.60% of sensor readings were within the ±1.67 mmol/L (±30 mg/dL) BG reference range, 88.71% of sensor readings were within the ±1.11 mmol/L (±20 mg/dL) BG reference range, and 74.19% of sensor readings were within the ±0.83 mmol/L (±15 mg/ dL) BG reference range; when BG was ≥ 5.56 mmol/L (100 mg/dL), 99.66% of sensor readings were within the ±30% BG reference range, 84.04% of sensor readings were within the ±20% BG reference range, and 55.82% of sensor readings were within the ±15% BG reference range. Overall 99.65%, 84.71%, and 58.45% of sensor readings were within the ±1.67 mmol/L (±30 mg/dL) or ±30%, ±1.11 mmol/L (±20 mg/dL) or ±20%, and ±0.83 mmol/L (±15 mg/ dL) or ±15% capillary glucose reference ranges, respectively.

**Impact of enteral nutrition on perioperative blood glucose fluctuations**

**Comparison of glucose fluctuations on EN days and non-EN days**

A total of 76,771 blood glucose counts were recorded in 31 patients. All 31 patients had hyperglycemia, and 18 patients had hypoglycemia. Mean blood glucose (MBG) was higher in patients on EN days than on non-EN days and time in target range (TIR) was lower than on non-EN days, and the differences were statistically significant \( (P<0.001, \text{Table 3}) \). Indicators of glucose fluctuation in patients on EN days, such as the coefficient of variation (CV), standard deviation (SD), mean glucose fluctuation amplitude (MAGE) and maximum glucose fluctuation amplitude (LAGE), were higher than those on non-EN days, and the differences were statistically significant \( (P<0.001, \text{Table 3}) \).

**Comparison of glucose fluctuations at different drip rates during enteral nutrition**

Patients' maximal blood glucose (MAX), mean blood glucose (MBG), blood glucose fluctuation indexes, such as coefficient of variation (CV), standard deviation (SD), mean blood glucose fluctuation amplitude (MAGE), and maximal blood glucose fluctuation amplitude (LAGE) on the fast day were higher than that on the slow day, and time in the target range (TIR) was lower than that on the slow day, and the differences were statistically significant \( (P<0.001, \text{Table 4}) \).

**DISCUSSION**
EN therapy is the preferred form of nutritional support for perioperative fasting patients. Perioperative glycemic control in diabetic patients has been widely emphasized by clinicians, but perioperative glycemic status in nondiabetic patients is often overlooked. However, nondiabetic patients have a higher risk of hyperglycemia with EN therapy and a greater risk of death from postoperative hyperglycemia compared with diabetic patients [17, 18]. Reasonable glycemic control before, during, and after surgery to avoid acute hyperglycemia and hypoglycemia requires the development of standardized glycemic monitoring measures. We evaluated the accuracy of the CGM during perioperative EN therapy and monitored multiple abnormal glucose events and their durations. The results of this study showed that the rt-CGM has high accuracy and can be used as a tool for glucose monitoring during perioperative EN therapy in esophageal cancer patients. EN supportive therapy increases the risk of glucose fluctuation in patients. The rt-CGM can provide a visual indicator of glucose fluctuations for clinicians and patients, which can help them to take timely and effective interventions and improve the long-term prognosis of patients.

Since CGM measures interstitial fluid glucose concentration, it takes time for the glucose concentration of blood and interstitial fluids to reach equilibrium, i.e., the results are "delayed". Moreover, the body’s natural inflammatory response to the inserted sensor affects the glucose concentration in the interstitial fluid as prolonged sensor application[19]. However, a number of studies have shown that CGM has a high clinical accuracy in T1DM [20], T2DM[21], gestational diabetes mellitus [22], for patients in the early post-liver transplantation period [23], diabetic ketoacidosis [24], patients with diabetes mellitus combined with hemodialysis [25] and patients with rapid changes in blood glucose during standardized meal experiments [26]. EN treatment during perioperative period can cause dramatic glucose fluctuations, and whether the enhancement of the "delayed effect" affects the accuracy of CGM monitoring has rarely been reported. In this study, the accuracy of this RT-CGMS was evaluated from multiple perspectives.

Table 1 shows that although the correlation was different in different glycemic ranges, the overall IG and BG were strongly correlated (r=0.925, P<0.001, Table 1). Currently, a MARD value of <15% is used as a listing criterion for CGM instruments [12]. Table 1 shows that the overall MARD value of CGM was 13.53%. The MRAD values varied across different glycemic ranges, with the largest MARD value in the hypoglycemic group and the smallest in the normoglycemic group, which is in agreement with the study by Cao et al., where a rapid decrease in blood glucose concentration affects the accuracy of the sensor glucose [20]. Although CGM systems with MRAD values <10% are considered to have good analytical performance [27], and smaller MARD values are also being pursued in clinical studies. However, the 2017 edition of the International on Use of Continuous Glucose Monitoring had clearly stated that : the cut-off value for accuracy remains controversial, and a further reduction of ≤10% in MARD relative to the reference value provides little additional benefit for insulin dose adjustment. Thus smaller MARD values may not be indicative of higher performance of the CGM system [28]. In addition, the agreement rate analysis of 20/20% deviation showed that 84.71% of the sensor readings were within the margin of error, which is in line with the requirement of >65% of the Guiding Principles for Technical Review of CGMS Registrations (Table 2, Fig. 1).
According to ISO 15197:2013, although only 58.45% of the CGM values obtained in our study fell within the analytical accuracy range (Table 2, Fig. 1), Parkes error grid analysis showed a total percentage of 100% for zones A and B (Fig. 2A), which provides good numerical accuracy. The ISO 15197:2013 standard requires that blood glucose meter measurements be compared with the results from standard reference methods that are designed for comparing results from a single chamber (usually blood), whereas comparisons between two different chambers (blood and interstitial fluid) may not be appropriate because of the physiologic differences between these chambers. In the absence of a recognized standard for evaluating the accuracy of IG measurements, the ISO standard for evaluating blood glucose meters provides a relevant alternative to identify devices that are as close as possible to the accuracy standard and that are not dangerous to human health. This approach is currently used in research in both human and veterinarian medicine. With this caveat, the good numerical accuracy of the rt-CGM, despite not meeting the analytical accuracy requirements, is considered clinically usable, i.e., this rt-CGM system could be a glucose-monitoring tool for perioperative EN-treated patients.

In the healthy nondiabetic population, postprandial glucose rarely exceeds 7.8 mmol/L (140 mg/dL), and there is no standard for what level of postoperative glycemic elevation in nondiabetic patients is considered harmful to the organism. Researchers have shown that postoperative hyperglycemia is an independent predictor of short-term infectious complications and have recommended that target blood glucose levels be kept below 11.1 mmol/L (200 mg/dL) to reduce the risk of infection [29]. For every 2.2 mmol/L (40mg/dL) increase in postoperative glucose, the risk of postoperative infection increases by 30% [30]. When postoperative blood glucose is around 11.1 mmol/L (200 mg/dL), the 30-day risk of death is 10 times higher in nondiabetic patients than in diabetic patients [8]. In critically ill patients in the intensive care unit (ICU), blood glucose levels >180 mg/L (>10.0 mmol/L) were associated with impaired neutrophil function, increased risk of infection, prolonged hospitalization and increased mortality [31].

The aim of this trial was to observe the status of perioperative blood glucose levels in nondiabetic patients, defining hyperglycemia as blood glucose exceeding 7.8 mmol/L (140 mg/dL) at any level in the hospital. We observed that the maximum value (MAX) on EN days could reach 10.77 mmol/L, the TIR could be reduced to 78.22%, and the glycemic fluctuation indexes (MAGE, CV, SD, and LAGE), were statistically different from those on non-EN days (P < 0.001). This suggests that the prevalence of hyperglycemia and glycemic fluctuations during perioperative EN therapy is very common, which is in line with Pancorbo-Hildago et al. who concluded that initiation of EN therapy resulted in hyperglycemia in 34.5% of adult patients and that nutritional support in the form of EN increased the risk of hyperglycemia in critically or noncritically hospitalized patients [32].

Further, we categorized EN days into fast days (Peptisorb recommended drip rate of 100-125 mmol/L) and slow days with the aim of observing glucose fluctuations in the presence of different drip rates. The results showed that even when the EN titration rate was slow (i.e., slow days), the TIR value was just 84.52% and the LAGE value was 4.53 mmol/L. When the recommended rate of intravenous infusion was reached (i.e., fast days), the TIR value was lower and the index of glycemic fluctuation was greater, and both of them were statistically different (P < 0.001). This reinforces the fact that glycemic fluctuations
during EN therapy are not appreciated and that management of hyperglycemia in hospitalized patients is challenging. Increasing in EN dose and drip rate prolonged the time to glycemic abnormality while meeting the patient's daily caloric needs, whereas the relatively slow drip rate had less effect on glycemic fluctuations. It appears that the recommended titration rate for the EN formulation is in need of updating, and that the optimal titration rate suitable for this population can be explored in the future using a CGM system.

The main cause of perioperative hyperglycemia is the activation of the body's systemic inflammatory response and the increased release of various counter-regulatory hormones during surgical stress, which ultimately causes insulin resistance [33]. Among them, Ljungqvist et al. observed a 7-fold increase in insulin resistance in surgical patients [34]. The addition of glucose or gluconeogenic components to nutritional support further challenges the already compromised state of glucose regulation and exacerbates the hyperglycemic state. Acute hyperglycemia affects key components of innate immunity, and short-term fluctuations in blood glucose levels have a greater impact on inflammatory cytokine levels than persistent hyperglycemia, weakening the host's ability to fight infection [35]. Studies have shown an even higher risk of hyperglycemia with the addition of EN in nondiabetic patients and a higher risk of death compared to patients with diabetes [17, 18]. Therefore, there is a greater need for timely documentation of various glycemic events in patients receiving nutritional support therapy to prevent overfeeding and worsening hyperglycemia.

However, this does not mean that postoperative glycemic control within a strict range is optimal. Several studies have shown that hypoglycemia is an adverse risk factor for increased morbidity and mortality in critically ill patients, and that tight glycemic control increased the risk of postoperative hypoglycemia, even to the extent that mortality is increase[36]. Even when mean glycemic control is 3.9-5.5 mmol/L, the difference in mortality between patients with the highest and lowest glycemic fluctuations can be up to fivefold [37]. In this trial, EN was performed by intermittent gravity drip and patients were free to move around during the EN interval. Although Table 3 shows that MBG on the EN day was not high (6.82±1.22 mmol/L), the LAGE value of blood glucose fluctuation during the day was as high as 6.16±2.00 mmol/L. Similarly, although the percentage of TBR was not high on the EN day, 19 of 31 patients had hypoglycemic events, including one patient who had sudden panic attacks with sweating during the EN interval. At this time, the patient's blood glucose was 4.2 mmol/L on SMBG and 3.3 mmol/L on CGM, with multiple hypoglycemic alarms of sensor. Hypoglycemic symptoms resolved within a few minutes of high-glucose intravenous injection immediately, suggesting that the rt-CGM not only indicates the blood glucose status in real time, but also send alarm signals to abnormal blood glucose indicators in time. Although studies conducted in animals and healthy humans suggest that intermittent enteral nutrition improves protein synthesis, preserves autophagy and maintains enterokinetic response to luminal nutrients compared to continuous administration of nutrition [38], and also attenuates the progressive elevation of plasma leptin and insulinemia that occurs with continuous feeding, attenuating the degree of impairment of hepatic insulin sensitivity [39]. But because the optimal glycemic range is unclear, the type of hospitalization (critical, noncritical, surgical, medical), nutritional status, and cause of
hyper/hypoglycemic state of the patient vary, it is necessary to establish a protocol for glycemic monitoring and hyper/hypoglycemic response, with particular vigilance for hypoglycemic episodes.

CONCLUSIONS

Perioperative enteral nutrition causes abnormal blood glucose fluctuations while providing nutritional support, and routine blood glucose monitoring should be performed even in normal populations. A real-time continuous glucose monitoring system could be a new option to provide accurate continuous glucose monitoring for EN patients without diabetes in the perioperative period and be used to guide clinical practice. However, the sample size of this trial was small, with a limited number of data points in the hypoglycemic range, and the study used a single formulation of Peptisorb, applied to a single population of esophageal cancer, with other types of enteral nutrition formulations and other populations to be further explored. More rigorous, larger, and more sophisticated studies should also be conducted in the future to assess the clinical value of this system, including reducing the risk of infection, decreasing length of hospitalization, and improving survival.

Declarations

ACKNOWLEDGEMENTS

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AUTHOR CONTRIBUTIONS

RRZ and XLH designed the research. YW, RX and ML extracted and analysed data. WW, LZ, ASW and WJ screened potentially eligible subjects. RRZ interpreted the data and wrote the first draft of the paper. GXJ, and XLH critically edited the manuscript and approved the final version.

COMPETING INTERESTS

The authors declare no competing interests.

DATA AVAILABILITY

All materials described in the manuscript, including all relevant raw data, will be freely available to any researcher wishing to use them for non-commercial purposes.

FUNDING

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References


Tables

Table 1. Correlation and precision between CGM and SMBG in different blood glucose ranges
<table>
<thead>
<tr>
<th>SMBG (mmol/L)</th>
<th>Number of pairs of IG and BG</th>
<th>r</th>
<th>MARD(%)</th>
<th>MAD(mmol/L)</th>
</tr>
</thead>
<tbody>
<tr>
<td>10</td>
<td>298</td>
<td>0.852</td>
<td>14.53</td>
<td>1.82</td>
</tr>
<tr>
<td>3.9 - 10.0</td>
<td>1428</td>
<td>0.815</td>
<td>13.30</td>
<td>0.93</td>
</tr>
<tr>
<td>3.9</td>
<td>7</td>
<td>0.882</td>
<td>18.11</td>
<td>0.60</td>
</tr>
<tr>
<td>All</td>
<td>1733</td>
<td>0.925</td>
<td>13.53</td>
<td>1.08</td>
</tr>
</tbody>
</table>

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

**Table 2. Agreement rate between CGM and SMBG values in different deviation ranges**

<table>
<thead>
<tr>
<th>BG 100mg/dL</th>
<th>BG ≥ 100mg/dL</th>
<th>All</th>
</tr>
</thead>
<tbody>
<tr>
<td>n=248</td>
<td>n=1485</td>
<td>N=1733</td>
</tr>
<tr>
<td>≤30 mg/dL</td>
<td>≤30 %</td>
<td>≤30/30</td>
</tr>
<tr>
<td>99.60</td>
<td>99.66</td>
<td>99.65</td>
</tr>
<tr>
<td>≤20 mg/dL</td>
<td>≤20 %</td>
<td>≤20/20</td>
</tr>
<tr>
<td>88.71</td>
<td>84.04</td>
<td>84.71</td>
</tr>
<tr>
<td>≤15 mg/dL</td>
<td>≤15 %</td>
<td>≤15/15</td>
</tr>
<tr>
<td>74.19</td>
<td>55.82</td>
<td>58.45</td>
</tr>
</tbody>
</table>

**Table 3. Comparison of glycemic indexes between EN and non-EN days**

<table>
<thead>
<tr>
<th>Indicators of observation</th>
<th>non-EN days</th>
<th>EN days</th>
<th>t/z</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Number of blood glucose</td>
<td>16395</td>
<td>60376</td>
<td>-3.042</td>
<td>0.005</td>
</tr>
<tr>
<td>MBG (mmol/L)</td>
<td>6.25±0.71</td>
<td>6.82±1.22</td>
<td>-3.042</td>
<td>0.005</td>
</tr>
<tr>
<td>CV(%)</td>
<td>14.58±4.92</td>
<td>21.08±6.04</td>
<td>-5.417</td>
<td>0.001</td>
</tr>
<tr>
<td>SD (mmol/L)</td>
<td>0.91±0.35</td>
<td>1.47±0.60</td>
<td>-5.200</td>
<td>0.001</td>
</tr>
<tr>
<td>MAGE (mmol/L)</td>
<td>1.99±0.85</td>
<td>3.79±1.56</td>
<td>-6.717</td>
<td>0.001</td>
</tr>
<tr>
<td>LAGE (mmol/L)</td>
<td>4.03±1.66</td>
<td>6.16±2.00</td>
<td>-5.636</td>
<td>0.001</td>
</tr>
<tr>
<td>MAX (mmol/L)</td>
<td>8.80(7.40,9.50)</td>
<td>10.77(9.01,12.15)</td>
<td>-4.076</td>
<td>0.001</td>
</tr>
<tr>
<td>MIN (mmol/L)</td>
<td>4.84±0.95</td>
<td>4.72±0.77</td>
<td>0.650</td>
<td>0.521</td>
</tr>
<tr>
<td>≥13.9mmol/L (%)</td>
<td>0</td>
<td>0.04(0,0.79)</td>
<td>-3.517</td>
<td>0.001</td>
</tr>
<tr>
<td>≥7.8mmol/L(TAR,%)</td>
<td>8.96±11.61</td>
<td>20.31±13.85</td>
<td>-5.473</td>
<td>0.001</td>
</tr>
<tr>
<td>3.9–7.8mmol/L(TIR,%)</td>
<td>90.45±11.53</td>
<td>78.22±13.54</td>
<td>5.783</td>
<td>0.001</td>
</tr>
<tr>
<td>≤3.9mmol/L(TBR,%)</td>
<td>0</td>
<td>0.12(0,1.77)</td>
<td>-2.173</td>
<td>0.030</td>
</tr>
</tbody>
</table>
Table 4. Comparison of glycemic indexes at different drip rates

<table>
<thead>
<tr>
<th>Indicators of observation</th>
<th>Slow days</th>
<th>Fast days</th>
<th>t/z</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>MBG (mmol/L)</td>
<td>5.87(5.39,6.94)</td>
<td>6.40(5.61,7.44)</td>
<td>-2.075</td>
<td>0.007</td>
</tr>
<tr>
<td>CV (%)</td>
<td>16.63±6.15</td>
<td>25.52±7.40</td>
<td>-7.096</td>
<td>0.001</td>
</tr>
<tr>
<td>SD (mmol/L)</td>
<td>1.05(0.79,1.39)</td>
<td>1.79(1.37,2.08)</td>
<td>-4.664</td>
<td>0.001</td>
</tr>
<tr>
<td>MAGE (mmol/L)</td>
<td>1.72(1.09,2.48)</td>
<td>3.49(2.85,4.52)</td>
<td>-4.703</td>
<td>0.001</td>
</tr>
<tr>
<td>LAGE (mmol/L)</td>
<td>3.33(2.25,4.53)</td>
<td>5.81(4.84,7.25)</td>
<td>-4.782</td>
<td>0.001</td>
</tr>
<tr>
<td>MAX (mmol/L)</td>
<td>9.45(8.20,10.66)</td>
<td>12.15(10.14,13.20)</td>
<td>-4.703</td>
<td>0.001</td>
</tr>
<tr>
<td>MIN (mmol/L)</td>
<td>4.82±0.93</td>
<td>4.63±0.86</td>
<td>1.143</td>
<td>0.262</td>
</tr>
<tr>
<td>≥13.9mmol/L(%)</td>
<td>0</td>
<td>0.08(0,1.58)</td>
<td>-3.258</td>
<td>0.001</td>
</tr>
<tr>
<td>≥7.8mmol/L(TAR,%)</td>
<td>13.54(3.38,23.57)</td>
<td>24.47(14.40,34.79)</td>
<td>-4.468</td>
<td>0.001</td>
</tr>
<tr>
<td>3.9-7.8mmol/L(TIR,%)</td>
<td>84.52(75.69,95.74)</td>
<td>74.77(60.38,83.75)</td>
<td>-4.586</td>
<td>0.001</td>
</tr>
<tr>
<td>≤3.9mmol/L(TBR,%)</td>
<td>0</td>
<td>0(0,2.54)</td>
<td>-1.448</td>
<td>0.148</td>
</tr>
</tbody>
</table>

Figures
Figure 1

Analysis of 15/15%, 20/20% and 30/30% deviation concordance rates of blood glucose in the real-time glucose monitoring system (rt-CGM) and the self-blood glucose monitoring (SMBG). Vertical coordinates indicate the blood glucose values of the two differences, and horizontal coordinates indicate the SMBG blood glucose values. The three black symmetrical lines are defined as the distribution of CGM measurements in SMBG measurements ±30 mg/dL, ±20 mg/dL, and ±15 mg/dL when SMBG <100 mg/dL, and the distribution of CGM measurements in SMBG measurements ±30%, ±20%, and ±15% when SMBG ≥100 mg/dL.
Figure 2

Parkes (A) and Clark (B) error grid consistency analysis of blood glucose in the real-time glucose monitoring system (rt-CGM) and the self-blood glucose monitoring (SMBG). Vertical coordinates indicate rt-CGM blood glucose values and horizontal coordinates indicate SMBG blood glucose values.

Supplementary Files

This is a list of supplementary files associated with this preprint. Click to download.

- SupplementaryMaterial.docx