Title

Accuracy and Feasibility of Real-time Continuous Glucose Monitoring in Critically Ill Patients After Abdominal Surgery and Solid Organ Transplantation.

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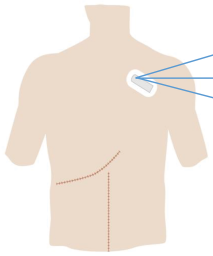
Accuracy and Feasibility of Real-time Continuous Glucose Monitoring in Critically Ill Patients after Abdominal Surgery and Solid Organ Transplantation

61 patients requiring ICU stay after major abdominal surgery
Median APACHE II score 13, on ventilatory and vasopressor support

Real-time continuous glucose monitoring sensor is initiated after surgery on admission to ICU

Sensor accuracy assessment of 1,546 paired glucose values, using blood gas analyzer as reference

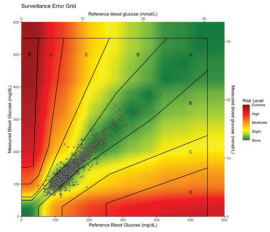


Patients after solid organ transplantation (liver, kidney, pancreas/islet) and total or partial pancreas resection

Alternative placement in the infraclavicular region, not interfering with postoperative care after abdominal surgery

Mean absoute relative difference 9.4%

98.9% paired values in clinically safe zones A and B in the Surveillance error grid



CGM monitoring with rtCGM sensor in the ICU setting was shown to be feasible and clinically accurate.

ARTICLE HIGHLIGHTS

- **Why did we undertake this study?**
  The possibility of implementing real-time continuous glucose monitoring (CGM) in critical care arises with the increasing sensor accuracy, but the clinical evidence in this setting is scarce.
- **What is the specific question(s) we wanted to answer?**
  Our aim was to assess the accuracy and feasibility of real-time CGM in patients requiring intensive care after major abdominal surgery.
- **What did we find?**
  We tested CGM in 65 patients, using alternative CGM placement in the infraclavicular region. Sensor mean absolute relative difference was 9.4%, relative bias was 1.4%, and 98.9% of paired values were within clinically safe zones A and B of the surveillance error grid.
- **What are the implications of our findings?**
  CGM is a promising monitoring tool in the critical care setting. However, it requires careful staff training, optimized calibration, and accuracy-testing protocols.

Accuracy and Feasibility of Real-time Continuous Glucose Monitoring in Critically Ill Patients After Abdominal Surgery and Solid Organ Transplantation

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ORIGINAL ARTICLE

OBJECTIVE

Glycemia management in critical care is posing a challenge in frequent measuring and adequate insulin dose adjustment. In recent years, continuous glucose measurement has gained accuracy and reliability in outpatient and inpatient settings. The aim of this study was to assess the feasibility and accuracy of real-time continuous glucose monitoring (CGM) in ICU patients after major abdominal surgery.

RESEARCH DESIGN AND METHODS

We included patients undergoing pancreatic surgery and solid organ transplantation (liver, pancreas, islets of Langerhans, kidney) requiring an ICU stay after surgery. We used a Dexcom G6 sensor, placed in the infraclavicular region, for real-time CGM. Arterial blood glucose measured by the amperometric principle (ABL 800; Radiometer, Copenhagen, Denmark) served as a reference value and for calibration. Blood glucose was also routinely monitored by a StatStrip bedside glucose meter. Sensor accuracy was assessed by mean absolute relative difference (MARD), bias, modified Bland-Altman plot, and surveillance error grid for paired samples of glucose values from CGM and acid-base analyzer (ABL).

RESULTS

We analyzed data from 61 patients and obtained 1,546 paired glucose values from CGM and ABL. Active sensor use was 95.1%. MARD was 9.4%, relative bias was 1.4%, and 92.8% of values fell in zone A, 6.1% fell in zone B, and 1.2% fell in zone C of the surveillance error grid. Median time in range was 78%, with minimum (<1%) time spent in hypoglycemia. StatStrip glucose meter MARD compared with ABL was 5.8%.

CONCLUSIONS

Our study shows clinically applicable accuracy and reliability of Dexcom G6 CGM in postoperative ICU patients and a feasible alternative sensor placement site.

Over the past decade, real-time continuous glucose monitoring (rtCGM) with subcutaneous sensors has transformed our understanding of glucose metabolism and diabetes treatment in outpatient care (1), and is now being considered in the hospital setting (2–5).

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Prior to the coronavirus disease 2019 (COVID-19) pandemic, measuring glucose in the interstitial compartment was deemed insufficiently accurate for the needs of critical care (6). However, this question was revisited during the COVID-19 pandemic (7). Seeing the necessity to optimize patient care and nurse workload in the demanding conditions, a Food and Drug Administration (FDA) statement (8) allowed rtCGM to be used as an adjunctive method of glucose monitoring even in critically ill patients with hyperglycemia and COVID-19. Reports from these studies (9–14) have contained encouraging results about safety, feasibility, and accuracy of rtCGM—even in patients requiring intensive care including assisted ventilation or vasopressor treatment—and have thus rekindled the interest in CGM in ICU settings (9–14).

In the field of perioperative ICU management, trials testing the newer generations of sensors have reported clinically acceptable accuracy and feasibility in patients undergoing cardiac or abdominal surgery (15–17). The Dexcom G6 sensor (Dexcom, Inc., San Diego, CA) (18) was also recently integrated into a fully closed-loop insulin delivery system in surgical patients, with promising results (19–21).

Hyperglycemia of the critically ill is an established driver of increased ICU morbidity and mortality, while its reduction via intensive insulin therapy is associated with reduced complications and improved prognosis (albeit the target glycemic ranges are still a matter of ongoing debate) (22–25). However, considering the fluctuations in insulin sensitivity, and the need for intravenous fluids, vasopressors, parenteral nutrition, frequent corticosteroid therapy, and other rapidly changing factors in patients in the ICU (6), achieving the desired target range in the ICU setting is often an arduous task. Thus, there is a need for a device that can reliably monitor the trends and excursions of blood glucose as closely as possible, with minimal risk and invasiveness, and can be easily implemented in routine care. Furthermore, alterations in the perfusion and oxygenation of peripheral tissues, frequent blood coagulation disorders, and possible use of interfering medications (i.e., acetaminophen, ascorbic acid) and others factors (26) in critical care pose even higher demands on the performance of the sensors. Nevertheless, patients with such characteristics are commonly excluded from clinical trials. Therefore, the aim of this prospective study was to assess the feasibility and accuracy of rtCGM in the postoperative ICU management of patients after major abdominal surgery (pancreas resection and solid organ transplantation). These procedures are often associated with a strong inflammatory response (27) and substantial glycemic excursions (28). Patients after transplantation receive potent induction immunosuppression (including corticosteroids), fluid and vasopressor support, and blood transfusions. Many of them have severe preoperative metabolic disorders (due to impaired kidney or liver function) and, in the case of liver transplantation, also pronounced coagulopathy (29). We decided to test the feasibility of rtCGM in these challenging situations in order to obtain data as close as possible to a real-world setting.

RESEARCH DESIGN AND METHODS

This study is part of an ongoing prospective trial registered on ClinicalTrials.gov (NCT05585801), approved by the local ethics committee of IKEM and TN, Thomayer Hospital, Videnska, Czech Republic (no. 09558/22; G-22-13).

Patient Recruitment

We prospectively enrolled patients who underwent major abdominal surgery at the Institute for Clinical and Experimental Medicine, Prague, Czech Republic, and required postoperative care in the ICU and intermediate care unit. Inclusion criteria were major abdominal surgery or transplantation, written informed consent prior to surgery, and age $\geq$ 18 years.

We purposely included critically ill patients with severe organ dysfunction, who are often excluded from inpatient studies, to determine the utility of rtCGM at the ICU bedside.

The following clinical and laboratory markers were collected: demographics, comorbid conditions, type of immunosuppression, vital signs (mental status, hemodynamic and respiratory parameters, fluid balance), and laboratory markers: glycated hemoglobin (HbA_{1c}), blood glucose values measured by a blood gas analyzer and a glucose meter, and sepsis biomarkers.

Selected clinical parameters and laboratory markers were recorded to estimate organ dysfunction and its severity, using the Acute Physiology and Chronic Health Evaluation II (APACHE II) and Child-Pugh scores to assess the severity of chronic liver disease. The APACHE II score was calculated from the worst parameters within 24 h after ICU admission, and the Child-Pugh score was calculated from the most recent parameters before transplantation.

CGM System and Reference Glucose Measurement

As this study is the pilot feasibility and accuracy part of a larger trial aimed at assessing the effect of rtCGM added to standard glucose monitoring on glycemic control, patients were randomized into either open or blinded rtCGM monitoring. In the open rtCGM group, the sensor readings were used in addition to standard protocol to manage insulin therapy, while, in the control group, the data from blinded rtCGM served as ex post controls, and insulin therapy was guided by a standard in-house protocol. For rtCGM, we used Dexcom G6 Continuous Glucose Monitoring System (Dexcom, Inc., San Diego, CA) (18). As a receiver, we used either the Dexcom receiver (in a blinded mode for the control group) or the Dexcom G6 app running on an iPhone SE (Apple Inc., Cupertino, CA). To compare rtCGM values with blood glucose values, we used a Radiometer ABL 800 blood gas analyzer (Radiometer, Copenhagen, Denmark). This system was intentionally used for the optional calibration of the rtCGM system. A StatStrip glucose meter (Nova Biomedical Corporation, Waltham, MA), FDA cleared for use in critical care (30), was used as a bedside tool for routine blood glucose monitoring.

Blood samples from the arterial line were taken for immediate bedside glucose measurement with the StatStrip and simultaneously sent to the laboratory for analysis on the acid-base analyzer (ABL)—glucose and acid-base parameters. The testing frequency was every 6 h during the first 3 days of ICU stay and at least once daily thereafter. Other blood glucose measurements by StatStrip or ABL were performed according to each patient's needs based on the clinician's considerations (e.g., monitoring of acid-base disturbances, hemoglobin levels, setup of mechanical ventilation, and renal replacement therapy).

CGM Placement and Calibration

Immediately after surgery, a trained nurse placed a G6 sensor and transmitter in the patient's infraclavicular region and paired it with a CGM receiver (iPhone or Dexcom receiver). The sensor was worn for up to

10 days, but we only used data from the intensive and intermediate care units for statistical analysis.

All calibrations of the rtCGM sensors were done using glucose values measured with the ABL analyzer from arterial blood. In the first 24 h after surgery, we calibrated the rtCGM system every 6 h or if the difference between the rtCGM values and the ABL-measured values was greater than 27 mg/dL (1.5 mmol/L) in the nonblinded group. For the next two postoperative days, we calibrated the CGM once a day. On subsequent days, rtCGM in the nonblinded group was recalibrated only if the difference between the rtCGM and the ABL-measured values was greater than 27 mg/dL (1.5 mmol/L). CGM alarm triggers were set at 70 and 288 mg/dL (3.9–16 mmol/L).

Intensive Insulin Therapy Management

A standard sliding scale intensive insulin therapy protocol aimed at the target glucose range of 108–180 mg/dL (6–10 mmol/L) was used to guide insulin therapy. Human rapid-acting insulin was administered intravenously in a continuous fashion via a syringe pump. After the warm-up period, rtCGM was used as a supportive tool to standard treatment in the nonblinded group. In this pilot phase, the nurses were encouraged to use the values and trends from rtCGM in accordance with their expertise and clinical judgement. Specific instructions were given to stop insulin infusion if blood glucose dropped below 180 mg/dL (10 mmol/L) and the prediction arrow was stable. When the arrow indicated a rising prediction and blood glucose was above 108 mg/dL (6 mmol/L), the infusion was started again. The alarms were used to notify the nurse of impending hypoglycemia or severe hyperglycemia. The alarm notifications were performed by the bedside rtCGM device, as the nurses were almost continuously at the patients' bedsides. In the case of a confirmed hypoglycemia, insulin infusion was stopped, and intravenous glucose was administered according to protocol.

Statistical Analysis

Descriptive data are presented as median and interquartile range or mean and SD for continuous variables (age, HbA_{1c}, length of stay, critical care score metrics, medications, clinical parameters) and counts (%) for categorical variables (sex, diabetes type, comorbidities, type of surgery, CGM data).

To assess the clinical accuracy of CGM, we compared *1*) paired glucose values from rtCGM and blood gas analyzer and *2*) paired glucose values measured with StatStrip glucose meter and blood gas analyzer. For the purpose of this pilot accuracy testing, we included both blinded and nonblinded sensor measurements, but, with regard to the possible additional calibrations of the nonblinded sensors, we also present the results separately.

To assess the rtCGM analytical accuracy, we calculated mean absolute relative difference (MARD), bias, SD of the relative difference (SDRD), and lower and upper 95% limits of agreement. We constructed the Bland-Altman plots, and clinical accuracy was assessed by surveillance error grid (SEG) analysis (31) using the SEG with Parkes (32) and Clarke (33) error grid overlay (SEG-PCO) software (34) and according to International Organization for Standardization (ISO) standards (35). We also report the mean glucose values, SD, coefficient of variation, time spent in levels 1 and 2 hypoglycemia and hyperglycemia, and time spent in the 70 to 180 mg/dL (3.9–10.0 mmol/L) range.

GraphPad Prism version 9.0 for Mac (GraphPad Software, San Diego, CA) was used for basic statistics, and SEG-PCO software (34) was used for specific clinical accuracy parameters.

RESULTS

Baseline and Perioperative Data

We included 65 patients admitted to ICU after major abdominal surgery, including solid organ transplantation; 29 received a blinded Dexcom receiver, and 36 were monitored with an iPhone using the sensor data for glucose management. Demographic data, preoperative organ dysfunction, and perioperative data are shown in Table 1. The median age was 60 years. Twenty-three patients had preexisting type 2 diabetes, and 10 patients (undergoing pancreas or islet and kidney transplantation) had type 1 diabetes. Median HbA_{1c} was 5.6 (4.8–7.6)%/38 (29.5–60) mmol/mol. Median HbA_{1c} of patients with diabetes was 7.5 (5.9–8.3)%/59 (40.5–67) mmol/mol. Detailed HbA_{1c} values in each patient group are presented in Supplementary Table 5.

The spectrum of surgical procedures and data related to the perioperative period, ICU, and immunosuppression are summarized in Table 1.

Postoperative Course and ICU Stay

The median length of stay in the ICU was 7 (5.5–10) days. Induction immunosuppressive therapy administered to the organ transplant recipients included corticosteroids in all patients, combined with antithymocyte globulin in eight cases and basiliximab in four cases. All patients required vasopressor support with norepinephrine, with a median duration of support of 28 (12–64) h and a median maximum dose of 0.2 (0.12–0.5) μg/kg/min. Four patients required additional treatment with argipressin. The median duration of assisted ventilation was 10 (7–34) h. Nine patients required continuous renal replacement therapy, with a median duration of 72 (27–90) h (Table 1). All patients required continuous intravenous insulin treatment during the first two postoperative days, with gradual decrease of the doses, transition to subcutaneous insulin, or complete cessation of insulin therapy in the following days (for exact insulin dosage in each patient group, see Supplementary Table 5). Administration of acetaminophen and ascorbic acid that might interfere with the rtCGM accuracy was also recorded (Table 1).

rtCGM Feasibility and Accuracy Assessment

Sixty-five patients participated in the study, and CGM data from 61 patients were included in the analysis of rtCGM accuracy. Two patients were excluded from data analysis because of transmitter failure during the first hours of monitoring, and another two were excluded because of a subcutaneous hematoma at the sensor insertion site disabling correct sensor function (one in the blinded group and three from the nonblinded group). Because of very scarce or no data obtained from these sensors, these were not included in the analysis. The median length of rtCGM in the remaining 61 subjects was 7 days, with 95.1% time of active sensor use.

For accuracy assessment, we obtained a total of 1,546 paired values from rtCGM and ABL and 1,123 paired values from StatStrip and ABL measurement. We used the glucose values from ABL as reference values.

When comparing the glucose values from rtCGM and the ABL analyzer, the

Table 1—Demographics, comorbidities and type of surgery, perioperative and intensive care course, immunosuppression, and CGM data (presented as proportion [percent] or median and interquartile range)

Characteristic	Value
Patients (*N*)	65
Age (years)	60 (47.5–69.5)
Male sex, *N* (%)	40 (61.5)
BMI (kg/m^2)	26.9 (24.15–30.1)
HbA_{1c} (%) (mmol/mol)	5.6 (4.8–7.6)/38 (29.5–60)
Hemoglobin (g/L)	119 (108–134)
APACHE II	13 (10–15)
SOFA score	8 (7–10)
Child-Pugh score 0/A/B/C, *N* (%)	24 (37)/14 (21.5)/18 (27.7)/9 (13.8)
Diabetes mellitus type 1/2, *N* (%)	10 (15.4)/23 (35.4)
Chronic pulmonary disease, *N* (%)	10 (15.4)
Cancer, *N* (%)	29 (44.6)
Ischemic heart disease, *N* (%)	16 (24.6)
Arterial hypertension, *N* (%)	51 (78.5)
Heart failure, *N* (%)	2 (3.1)
Stroke or transient ischemic attack, *N* (%)	3 (4.6)
No. receiving surgery	65
Liver transplantation, *N* (%)	38 (58.5)
Liver and kidney transplantation, *N* (%)	3 (4.6)
Kidney and pancreas transplantation, *N* (%)	9 (13.8)
Kidney and pancreatic islets transplantation, *N* (%)	1 (1.6)
Partial pancreatectomy, *N* (%)	9 (13.8)
Total pancreatectomy, *N* (%)	3 (4.6)
Total pancreatectomy and autologous pancreatic islets transplantation, *N* (%)	2 (3.1)
Length of stay in ICU/total (days)	7 (5.5–10)/17 (13.5–26)
Length of surgery (min)	345 (248.5–397.5)
Blood loss (mL)	1,000 (500–4,250)
Norepinephrine, *N* (%)/duration (h)	65 (100)/28 (12–64)
Norepinephrine, maximal dose (μg/kg/min)	0.2 (0.12–0.5)
Norepinephrine, average dose (μg/kg/min)	0.05 (0.05–0.1)
Argipressin, *N* (%)/duration (h)	4 (7.8)/56 (30–68.5)
Mechanical ventilation, *N* (%)/duration (h)	65 (100)/10 (7–34)
Continuous renal replacement therapy *N* (%)/duration (h)	9 (13.9)/72 (27–90)
Fluid balance (mL)	+4,630 (3,150–7,820)
Acidum ascorbicum, *N* (%)/average dose (g/day)	33 (51)/2.7
Acetaminophen, *N* (%)/average dose (g/day)	46 (71)/1.6
Induction immunosuppression therapy, *N* (%)	51 (78.5)
Methylprednisolone, *N* (%)/dose (mg)	51 (100)/500
Antithymocyte globulin, *N* (%)	8 (15.7)
Basiliximab, *N* (%)	4 (7.8)

SOFA, Sequential Organ Failure Assessment.

calculated MARD was 9.4%, 95% CI [9.0%, 10.0%], and SDRD was 12.8%, with lower and upper 95% limits of agreement of −23.7% and 26.5%, respectively. The relative bias was 1.4% (Table 3).

We computed the SEG (using SEG-PCO software); 92.8% of the values fell in zone A, 6.1% fell in zone B, and 1.2% fell in zone C (Table 2). SEG and the Bland-Altmann plot are shown in Fig. 1*A* and *B*, respectively.

For comparison, we also assessed the accuracy of the StatStrip glucose meter, where we measured a MARD of 5.8%, 95% CI [5.4%, 6.4%], an SDRD of 8.9%, and bias of −2.4%. The lower and upper 95% limits of agreement were −19.9% and 15.1%, respectively (Supplementary Table 2). SEG analysis and a Bland-Altmann plot for glucose values measured with a StatStrip glucose meter and an ABL analyzer are shown in Supplementary Figs. 1 and 2, respectively. We found that 96.6% of the values fell in zone A, 2.2% fell in zone B, 1.1% fell in zone C, and 0.1% fell in zone D (Supplementary Table 1).

In a separate accuracy analysis of the blinded versus nonblinded sensors, we obtained a MARD of 9.2% (95% CI [8.4%, 9.9%]) in the nonblinded group and a MARD of 10% (95% CI [9.3%, 10.6%]) in the blinded group ($P = 0.0321$). The average number of additional calibrations per sensor in the nonblinded group was 0.8 ± 1 during the first 24 h, 0.50 ± 1 on days 2 and 3, and 0.5 ± 1 thereafter, resulting in 1.8 ± 1 additional calibrations in total for the whole study period (Supplementary Table 8). The percentage of sensors requiring from zero to six additional calibrations (no sensor required more than six) is shown in Supplementary Table 9.

We also performed a detailed MARD analysis according to each surgery type and the presence of diabetes (Supplementary Table 5). We found no significant effect of acetaminophen on MARD, while the use of ascorbic acid was, surprisingly, associated with significantly lower MARD (Supplementary Table 10).

CGM Metrics

Although not the primary aim of this study, we also analyzed basic CGM metrics of these patients (Table 3). The median mean glucose was 153 (135–174.6) mg/dL (8.5 [7.5–9.7] mmol/L) with a median standard deviation of 43.2 (25.2–55.8) mg/dL (2.4 [1.4–3.1] mmol/L) and coefficient of

Table 2—Surveillance, Clarke and Parkes error grid analysis, and ISO criteria assessment of paired rtCGM and reference ABL glucose values

	Count			Frequency, %						
Risk zone	SEG	Clarke	Parkes	SEG	Clarke	Parkes	ISO range	Count	Frequency, %	Cumulative frequency, %
A	1,434	1,384	1,409	92.8	89.5	91.1	≤5% or mg/dL	580	37.5	37.5
B	94	156	136	6.1	10.1	8.8	>5–10% or mg/dL	453	29.3	66.8
C	18	0	1	1.2	0	0.1	>10–15% or mg/dL	236	15.3	82.1
D	0	5	0	0	0.3	0	>15–20% or mg/dL	132	8.5	90.6
E	0	0	0	0	0	0	>20% or mg/dL	145	9.4	100.0
Not included	0	1	0	0	0.1	0				

variation of 27% (19.7–33.3%). The median time in range was 77.5% (63.3–91.8%), and the mean time in range was 76.7 ± 16.8%. Median time in the high and very high ranges was 17.5% (5.5–24%) and 3% (0–9.8%), respectively. Our patients spent minimal time in the low and very low ranges (Table 3). Two short hypoglycemic episodes were recorded, one each in two patients.

A comparison between nonblinded versus blinded sensors showed a slightly higher average glycemia in the blinded group and no clinically significant difference in times in designated time ranges (Supplementary Table 6).

As for the alarms for hypoglycemia (<70 mg/dL [3.9 mmol/L]), the nurses were notified 13 times in 11 patients (twice in 2 patients, once in the remaining 9), and 3 were confirmed as low by the StatStrip and ABL. Similarly, in the blinded group, 15 episodes of hypoglycemia were recorded by rtCGM, out of which 5 were ex post confirmed by reference measurements (Supplementary Table 7).

CONCLUSIONS

We present 61 patients after major abdominal surgery, including solid organ transplantation. All patients required admission to the ICU because of the severity of their surgical procedures.

Most of the enrolled patients suffered from severe organ dysfunction preoperatively, which, combined with a systemic inflammatory response after the surgery, led to various potential obstacles for the use of rtCGM as a reliable glucose measuring tool. Positive cumulative fluid balance, coagulopathy, impaired blood supply to peripheral tissues, hypoxemia, and rapid dynamics of glycemic changes might affect the accuracy of glucose measurement in the interstitial compartment.

Nevertheless, our data show that rtCGM with the Dexcom G6 system might be useful even in these rather unstable conditions. With a MARD of 9.4% and 98.9% of values in the A and B zones of the SEG, we reached accuracy levels comparable with those reported by the manufacturer (overall MARD 9.0%) (18) in more stable physiological conditions in the outpatient setting and in studies performed perioperatively (16,17) and slightly more favorable than some of the reports of the use of CGM during the COVID-19 pandemic (9,10,13,14). We hypothesize that this degree of accuracy might be attributed to our approach to sensor calibration. Even though Dexcom G6 is factory calibrated, we decided to perform a protocol calibration on the first

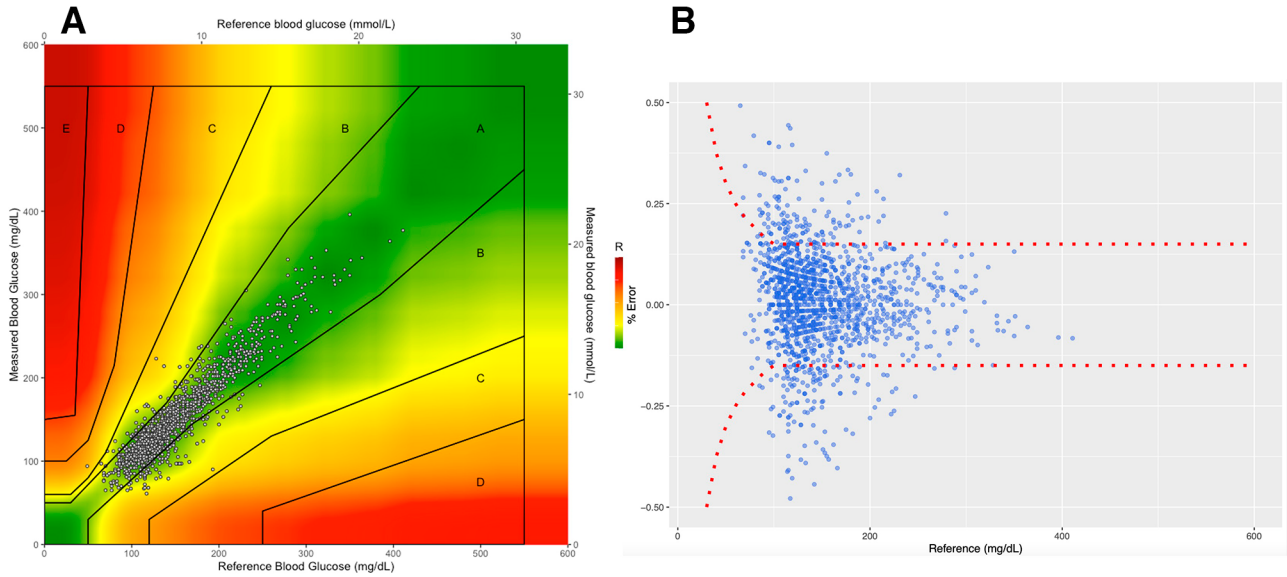

Figure 1—*A*: SEG with Parkes error grid overlay of paired rtCGM and reference ABL glucose values. *B*: Modified Bland-Altmann plot of paired glucose values from rtCGM and reference ABL measurement. The different intensity of blue color reflects repeated values of the same bias. The red dotted lines represent the range of CGM measurements within 15% of reference for reference values >100 mg/dL and within 15 mg/dL of reference for reference value <100 mg/dL.

Table 3—rtCGM accuracy and monitoring data

Characteristic	Value
Length of CGM monitoring in the ICU (days)	7 (5.5–10)
Sensor usage (% of time)	95.1
MARD (%)	9.4
SDRD (%)	12.8
Bias (%)	1.4
Lower 95% limit of agreement (%)	−23.7
Upper 95% limit of agreement (%)	26.5
Average glucose ($mg \cdot dL^{-1}$/$mmol \cdot L^{-1}$)	153 (135–174.6)/8.5 (7.5–9.7)
SD ($mg \cdot dL^{-1}$/$mmol \cdot L^{-1}$)	43.2 (25.2–55.8)/2.4 (1.4–3.1)
Time in range (%)/average ± SD	77.5 (63.3–91.8)/76.7 ± 16.8
Time in high range (%)/average ± SD	17.5 (5.5–24)/16.5 ± 11.5
Time in very high range (%)/average ± SD	3 (0–9.8)/6.2 ± 8
Time in low range (%)/average ± SD (number of episodes)	0 (0–1)/0.6 ± 1 (six episodes)
Time in very low range (%)/average ± SD (number of episodes)	0 (0)/0.1 ± 0.2 (two episodes)

Glycemia monitoring data are expressed as median (interquartile range) and average ± SD, time in range (3.9–10.0 mmol/L [70–180 mg/dL]), time in high range (10.1–13.9 mmol/L [181–250 mg/dL]), time in very high range (>13.9 mmol/L [>250 mg/dL]), time in low range (3.0–3.8 mmol/L [54–69 mg/dL]), time in very low range (<3.0 mmol/L [<54 mg/dL]).

3 days, using glucose values obtained from a regularly validated ABL analyzer. In a separate analysis of blinded versus nonblinded sensors, which were additionally calibrated, we obtained significantly better MARD (9.2% vs. 10%, $P = 0.0321$) in the nonblinded group. This might further support the benefit of additional recalibrations in increasing the accuracy of CGM in ICU patients.

Even though glycemic control itself was not the main goal of this analysis, the time in range reached 77.5%, and, more importantly, the time spent in hypoglycemia in this cohort was very low, with only two episodes of very low glycemia (<54 mg/dL [3.0 mmol/L]). The incidence of low-glucose events was not different between the blinded and nonblinded groups. However, both groups of patients were closely monitored, and the target glucose range was set between 6 and 10 mmol/L, which most probably ensured that the glucose fluctuations were kept within safe levels most of the time despite all patients receiving intensive insulin therapy, often with insulin doses close to or above 1 IU/kg/day (Supplementary Table 5). Interestingly, the presence of diabetes did not seem to significantly affect CGM metrics, except for a slightly higher average glycemia and time spent in hyperglycemia in patients with type 2 diabetes mellitus undergoing liver transplantation (Supplementary Table 6).

We decided to use an alternative sensor placement—in the infraclavicular region—that had not been reported so far. This was based on previous experience from our small pilot study (36). The abdominal region would have been very inconvenient because of the type of surgery performed and the possible need for subsequent revisions. When using the upper-arm placement, we experienced frequent dislodging (during transport or positioning) or sensor disturbances due to compression in sedated patients. The infraclavicular placement proved to be convenient and easily accessible for the nursing staff and yet did not interfere with patient positioning, transport, or any diagnostic or therapeutic procedures. We acknowledge that we do not have any control group to compare the effect of this placement with the standard ones. More data from a direct comparison with standard sites is needed to assess the performance of CGMs in the infraclavicular region in hospitalized patients.

However, we still experienced technical difficulties. Two patients had measurement failures due to a technical fault in the transmitter, and two patients with severe coagulopathy had minor bleeding and hematoma at the insertion site, leading to sensor malfunction. These sensors were not included in the analysis because of very little or no data present. This might have introduced some bias into the final accuracy results.

Another limitation of this study is that we did not perform the monitoring before and during surgery. In our pilot project, we faced very frequent loss of signal due to several factors in the operating room—most notably, interference with other Bluetooth devices, bipolar coagulation technique, and the patient warming system. We therefore decided to focus on reaching maximal accuracy in the postoperative period. As for computed tomography scans, we decided to leave the sensor in place and evaluate its functioning and accuracy after the procedure, during which we used no lead shielding. We did not observe any discrepancies in blood glucose values or signal loss. We did not see any significant differences in MARD 48 h before and after computed tomography scan (Supplementary Table 11). No MRI studies were performed. We also compared the accuracy in patients treated with paracetamol and ascorbic acid, and these did not seem to negatively affect sensor accuracy in our patients (Supplementary Table 10).

We acknowledge that our choice of the blood gas analyzer as the reference method might have affected our measured analytical accuracy. The analytical

accuracy and variability might have been even better if we had used a laboratory glucose analyzer, or a benchtop glucose analyzer with documented accuracy in a range considered adequately accurate by the United States FDA for reference testing (37). Blood gas analyzers are not typically used as reference methods in pivotal studies of CGM accuracy. However, in our study, the Radiometer ABL accuracy was frequently internally validated by the Laboratory Methods division. To compare it with previous reports, Liang et al. (38) evaluated the accuracy of blood gas analyzers, in comparison with central laboratory analyzers (Beckman DxC and Abbott Architect). They found a bias of −2.9 mg/dL for Abbott Architect analyzers with a 95% limit of agreement (LOA) of −34.1 to 28.3 mg/dL, that is, a width of LOA of 62.4 mg/dL. During our experiment, the bias (Radiometer ABL versus Abbott Architect) was between 1.8 and 4.9 mg/dL (0.1 to 0.27 mmol/L) for five ABL analyzers. However, we found better precision of blood glucose measurements—widths of LOAs of 29.0, 35.9, 39.6, 45.0, and 48.6 mg/dL, respectively, for five ABL analyzers. Therefore, we believe that the accuracy and precision of blood gas analyzers was under sufficient control during the whole study period. This reference method was also perceived by the nursing staff as feasible and practical on a long-term basis.

As the StatStrip glucose meter is the current ICU standard of care, widely used in critical care settings, we also analyzed its performance and compared it with the rtCGM. Unsurprisingly, StatStrip showed a significantly better accuracy, with a MARD of 5.8% and a superior performance in the SEG as well as Bland-Altmann analysis compared to rtCGM (Supplementary Tables 1–4 and Supplementary Figs. 1–4).

Despite favorable MARD and SEG results, the sensor accuracy parameters would still not meet the ISO criteria (35) for blood glucose meters for inpatient use. These require that *1*) at least 95% of compared glucose value pairs are within ±15 mg/dL at glucose concentrations of <100 mg/dL and within ±15% at >100 mg/dL and *2*) at least 99% of results are within zones A and B of the consensus (Parkes) error grid. In our analysis, 82.1% of pairs were compliant with the first requirement, therefore not meeting the 95% threshold. But, in the Parkes consensus error grid, 99.9% of values were within zones A and B and showed high clinical accuracy of rtCGM measurements. Furthermore, the strength of rtCGM lies in showing the trends of glucose excursions and the possibility of remote monitoring and alarms.

Therefore, we believe that, when used along with standard blood glucose measurement and an optimized adequate calibration method, rtCGM might reduce the need for frequent blood glucose testing and provide reliable insight into the glycemic trends in these specific groups of patients.

Summary

Our data from a single-center prospective study suggest that rtCGM is, in conjunction with an additional calibration protocol, a feasible and reliable method of blood glucose surveillance in postoperative intensive care after major abdominal surgery, including solid organ transplantation.

Safe and reliable CGM use in the ICU setting requires careful staff training, optimized calibration, and accuracy-testing protocols.

Further evidence is needed to support rtCGM use as a full-fledged monitoring modality and allow CGM-based insulin dosage and adjustments. Nevertheless, rtCGM shows promising potential to contribute to and improve the still challenging glycemic management in the intensive care units.

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