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Original Research Article

Continuous glucose monitoring in critically ill adult patients: results of a pilot study in Greece

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ABSTRACT

Background: Continuous glucose monitoring has emerged as a promising tool in managing glycemic control for patients with type 2 diabetes admitted to the intensive care unit. This paper provides a comprehensive review of the potential benefits, challenges, and implications associated with continuous glucose monitoring utilization in intensive care unit settings for type 2 diabetic patients.
Methods: In a prospective observational study continuous glucose monitoring systems were applied in adult intensive care unit patients in two centers. Eighty patients were randomly assigned into 2 groups: one with continuous glucose monitoring system one with standard glucose monitoring, previous medical history, reason for intensive care unit admission, demographic characteristics and laboratory parameters were recorded.
Results: Recordings from six patients were excluded from analysis. Patients on home insulin and tablet combination therapy had worse glycemic control than subjects on insulin monotherapy or oral tablets alone. There was no difference in the glycemic profile of patients before and within the unit between those who were Covid-19 positive and those who had different reasons for admission to the unit. However, obese subjects had significantly worse glycemic control. Glucose measurements with continuous glucose monitoring and standard method were in almost total agreement.
Conclusions: While continuous glucose monitoring benefits may allow a more personalized therapeutic strategy, further research is necessary to evaluate the cost-effectiveness and long-term implications of continuous glucose monitoring implementation in the intensive care unit setting.

Keywords: Continuous glucose monitoring, Intensive care unit, Type 2 diabetes

INTRODUCTION

Diabetes mellitus affects people worldwide (451 million people in 2017 and expected to increase to 693 million by 2045) and management of its acute complications or treatment-related adverse events is particularly important in critically ill patients.[1]

Glycemic control in the critically ill has three distinct domains: i) Though hypoglycemia is often an adaptive response to critical illness and can be found in, up to 52% of all intensive care unit (ICU) admission, excessive hyperglycemia should be avoided. ii) Moderate to severe hypoglycemia is too detrimental for the patients.[2] Even a single episode of hypoglycemia has been related to increased mortality.[1,2] iii) Large glucose variability is also an independent predictor of mortality, especially in patients with sepsis.[2] Currently, no optimal blood glucose target for ICU patients is known, and according to the latest standards of care in diabetes of the American Diabetes Association, a target of 140 to 180 mg/dl is the most acceptable.[3,4]

Continuous glucose monitoring systems (CGMS) appeared like a solution for the ICU environment. In general, they are including three components: the biosensor, transmitter, and the monitor. The biosensor is obtaining interstitial fluid glucose levels via a tiny skin penetrating cannula and can stay *in situ* for 7-14 days.[1] Transmitter is a small coin-like reusable device that sends recording data wirelessly and the monitor (either a dedicated device or smart phone application) can display real-time data and trends in time for several parameters. Thus, it provides valuable data that can be used for daily adjustment of therapeutic plan.[1] The first report from CGMS application in ICU was in 2003, and since then multiple reports exist both from adult and children or neonatal populations.[2,5-9] The Covid-19 pandemic boosted the interest about CGMSs' use can decrease the caregiver's time of contact with the patient and thus reduce the risk of infection.[10-11]

In Greece, there are recent data only from CGMS use in pediatric ICU; yet data from adult ICUs are still (Jul 2024) lacking.[11] This study aimed to evaluate and assess the use of subcutaneous continuous glucose level monitoring systems in patients with diabetes mellitus in Greek intensive care units. The present research article represents the initial effort to determine the "worth" of the CGM in patients with T2DM who are receiving treatment in Covid-19 intensive care units.

METHODS

During the Covid-19 pandemic, 80 subjects with admission glucose values of 200 mg/dl who were hospitalized during the Covid-19 pandemic at the ICU of AHEPA General Hospital and "Agios Pavlos" General Hospital (positive for Covid-19 infection or not) were randomized after their relatives' consent. The 40 patients were fitted with a continuous glucose monitoring system (CGMS- Abbott FreeStyleLibre 1), and their values were compared with those of the other 40 control patients concerning the study endpoints.

The study protocol was approved by the Scientific Board of AHEPA University General Hospital and "Agios Pavlos" General Hospital (Number 546 and Diaygeia.gov Online publication document no: ΩΜΥ446906Ι-ΚΔ2).

Inclusion criteria

The selection criteria were as follows: i) glucose values on admission of 200 mg/dl, ii) hospitalization in the ICU during the Covid-19 pandemic at the AHEPA and "Agios Pavlos" General Hospital, and iii) the possibility of sensor placement. The fact that they were positive for Covid-19 virus infection or not, was not relevant to inclusion in the study.

Exclusion criteria

Exclusion criteria were as follows: i) age less than 18 years, ii) pregnancy, and iii) expected duration of ICU hospitalization (due to severity or other conditions) of less than 24 hours. Patient selection was based on the CGM placement requirements of the ICU medical staff.

The research questions posed at the beginning of the study were as follows: 1) To what extent is glycemic control achieved in the ICU?; 2) Is glycemic control improved in patients using CGM compared with blood gas measurement alone?; 3) Is the detection of undiagnosed hypoglycemia facilitated by sedation?; 4) To what extent is glycemic control easier for patients and physicians, and thus, the regulation of critically ill patients?.

The main aim of this study was to assess the applicability of CGM in the ICU, evaluate its potential role in the ICU, and compare blood gas measurements to CGM in these patients.

Statistical analysis

Statistical analyses were performed using IBM Corp. Released 2023. IBM SPSS Statistics for Windows, Version 29.0.2.0 Armonk (NY: IBM Corp). Kolmogorov Smirnov normality test and independent samples t-test were used, and correlations were performed with Pearson and Spearman correlation coefficients. Descriptive statistics of the sample are presented as means and standard deviations, and the graphs are pie charts to illustrate categories, and a scatter plot to test the correlation of glucose values with the two methods. The significance level was set at $p<0.05$.

RESULTS

Of the 80 enrolled patients, 74 eventually entered the study because they met the eligibility criteria and provided informed consent. Six patients were excluded for various reasons, such as failure to meet the inclusion criteria or death or refusal to participate. Despite these exclusions, the study was adequately powered to achieve its primary objective. Patients were randomly divided into 2 groups: one (n=37) with CGMS monitoring and the other (n=37), where standard Glu monitoring was used.

Descriptive statistics are presented in Tables 1 and 2, and Figures 1 and 2. The age of subjects differed between insulin and tablet-treated subjects (73.7±7.2 vs 66.7±10.8, p=0.010). Patients on home insulin and tablet combination therapy had worse glycemic control [glycated hemoglobin (HbA1c) 8.1±1.8] than subjects on insulin monotherapy (6.9±0.9) or oral tablets alone (6.9±0.9) (p=0.011) (p=0.011). No other indicators of the glycemic profile differed. Fifty-four (54) patients had hematocrit (Hct) values below 35 (76.1%), whereas fifteen (15) patients had Hct values below 30 (21.1%). Biochemical profiles of the patients are presented in Table 3. The glycemic profiles of the patients (HbA1c, estimated HbA1c, mean sensor glucose (SG), time 70-180, time <70, time >180, and mean blood gas glucose) did not differ significantly between patients with low Hct (<30 or <35) and normal Hct (>30 or >35).

Table 1: Descriptive sample statistics (n=74).

Descriptive statistics	(Mean±SD)	Range (min-max)
Age (years)	68.2±11	(19-94)
Body mass index (kg/m^2)	30.8±5.9	(18-49)
HbA1c (%)	7.029±1.1	(5.5-12)
Blood sugar (blood gas measurement)	159.9±43.9	(102.6-307.8)
Average sensor glucose	161.2±46.7	(88-289)
Estimated HbA1c (%)	7.130±1.4	(5.3-11.7)
TIR (70-180) (%)	58.3±28.7	(0-100)
TBR (<70) (%)	0.74±2.2	(0-13)
TAR (>180) (%)	36.8±27.2	(0-100)
Glucose variability %	24.9±13	(0.2-50)
Active sensor time	48.3±37.8	(0.7-90)

* HbA1c= glycated hemoglobin, TIR= time in range, TBR=time below range, TAR=time above range

Table 2: Comorbidities and causes of ICU admission.

Comorbidities and causes of ICU admission	Number (%)
T2DM	66 (89.2)
IGT	8 (10.8)
Reason for ICU admission	
Covid-19	42 (56.8)
Acute respiratory failure	17 (23)
Car accident	5 (6.8)
Cerebral hemorrhage	4 (5.4)
Ischemic stroke	1 (1.4)
Pancreatitis	2 (2.7)
Pulmonary embolism	1 (1.4)
Sepsis	1 (1.4)

Correlation between glucose sensor values and blood glucose levels

The mean glucose level from the sensor did not differ from the mean glucose level of the subjects measured using blood gas alone. The same was true for glycemic control measured by laboratory HbA1c compared to the estimated HbA1c from the sensor (p=0.510). Mean blood gas glucose levels did not differ between subjects with the recording system and those measured using blood gas alone (p=0.566) (Table 4).

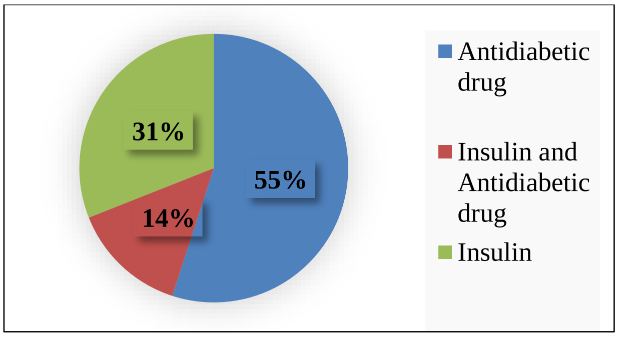

Figure 1: Home-based treatment.

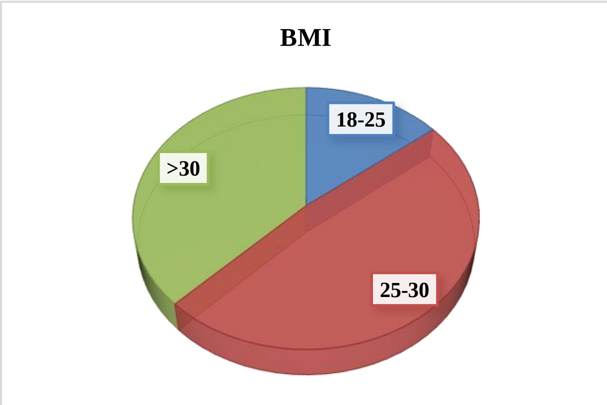

Figure 2: Distribution of body weight categories.

Table 3: Biochemical sample data (n=74).

Biochemical sample data	Mean±SD
SGOT (IU/dl)	28.8±10.7
SGPT (IU/dl)	29.1±17.4
BUN (mg/dl)	72.1±43.6
Creatinine (mg/dl)	1.08±0.6
Total cholesterol	134.1±42.2
HDL (mg/dl)	22.9±10.1
LDL (mg/dl)	64.3±47.9
Triglycerides (mg/dl)	217.7±176.8
WBC (k/μl)	14292.9±12092.6
PLT (k/μl)	241481.5±131113.4
Hct (%)	32.8±3.5
Hb (gr/dl)	10.5±1.3

*SGOT= aspartate aminotransferase, SGPT=Alanine Aminotransferase, BUN=blood urea nitrogen, HDL= high-density lipoprotein, LDL=low-density lipoprotein, WBC=white blood count, PLT=platelet count, Hct=hematocrit, Hb= hemoglobin

The average glucose from the sensor and that from the blood gases were not normally distributed. Mean glucose from the sensor and mean glucose from blood gas showed a strong positive correlation (r= 0.928, p<0.001) in the Spearman and Pearson correlation tests, even after bootstrap simulation in 1000 subjects (Figure 3).

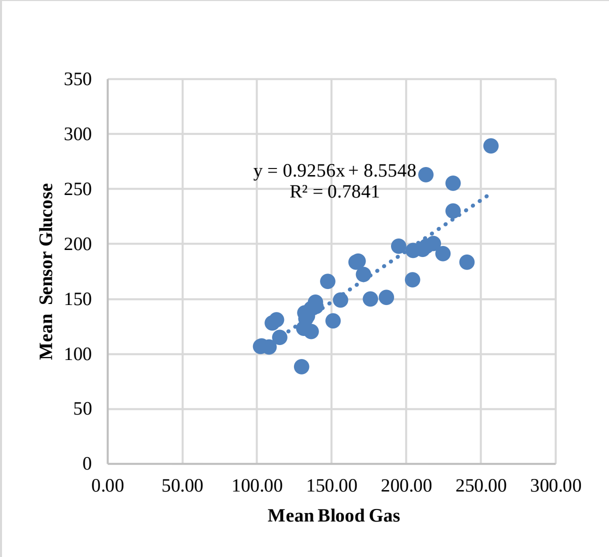

Figure 3: Scatter plot of sensor glucose and blood gas values.

Investigation of the factors involved in glycemic regulation

There was no difference in the glycemic profile of patients (HbA1c, estimated HbA1c, mean SG, time 70-180, time <70, time >180, and mean blood gas glucose) before and within the unit between those who were Covid-19 positive and those who had different reasons for admission to the unit (acute respiratory failure, car accident, bleeding, and sepsis).

There was a significant difference in glycosylated hemoglobin and mean blood glucose levels between normal-weight and obese individuals. Obese subjects had significantly worse glycemic control (Table 5). The other indicators of the glycemic profile did not differ significantly.

Table 4: Differences in glycemic control depend on the glucose measurement system.

	HbA1c	Estimated HbA1c	P value
	7.1±1.4	7.1±1.4	0.510
	CGM (sensor glucose)	Blood gas (glucose)	
Average blood gas glucose level	165.1±45.6	154.7±42.1	0.317

Table 5: Glycemic control and body mass index categories.

	BMI<30	BMI>30	P value
HbA1c (%)	6.6±0.9	7.3±1.3	0.014
Average blood gas glucose	142.1±37.5	172.1±48.3	0.013

DISCUSSION

CGM in the ICU is an important new tool for doctors and nurses in the management of patients with type 2 diabetes. The benefits of CGM have been extensively studied in various settings, such as the OR and ICU.[8] In this discussion, we consider the potential advantages, challenges, and implications of implementing CGM in the ICU setting for individuals with type 2 diabetes.[1,7] The benefit of CGM in T2DM patients in the ICU is the advantage of real-time glycemic monitoring, offering a comprehensive knowledge of glycemic patterns in type 2 diabetic patients admitted to the ICU. This real-time data allows us to identify and manage a potential hyperglycemic or hypoglycemic event, contributing to improved glycemic control.[1,5] Moreover, we can individualize treatment strategies because of the dynamic nature of glucose levels in critically ill patients with T2DM in the ICU, necessitating individualized treatment plans. CGM can help with the customization of insulin therapy based on real-time glucose levels, enabling healthcare providers to plan the treatment according to the specific needs of each patient. This ultimately leads to euglycemia in patients in the ICU. This proactive approach minimizes the risk of severe complications associated with extreme blood glucose levels, including cardiovascular events, infections, and delayed wound healing, which are common complications in T2DM patients.[3,6] These are all very important because they contribute to enhance patient safety. Timely interventions based on CGM data can contribute to patient safety by preventing prolonged periods of hypoglycemia or hyperglycemia. This is particularly crucial in patients with T2DM in the ICU, where glycemic control plays a pivotal role in mitigating the risk of complications and influencing overall patient outcomes.[2,5,7]

Some challenges that need to be considered are that the seamless integration of CGM technology into the ICU environment may pose challenges, including compatibility with existing monitoring systems and electronic health records. Ensuring good workflow and effective communication of CGM data to healthcare providers is essential for successful implementation. This means that healthcare professionals in the ICU must receive comprehensive training in CGM technology, interpretation of glucose trends, and adjustment of insulin therapy. Adequate education is crucial to maximize the benefits of CGM and avoid potential failures related to the misinterpretation of data we also need to consider the cost implications.[5] The initial investment and ongoing maintenance costs associated with CGM technology may present financial challenges for healthcare institutions, especially in frugal healthcare systems. However, considering the potential reduction in complications and improved patient outcomes, the cost-effectiveness of CGM implementation in T2DM patients in the ICU should be carefully evaluated and decided individually regarding cost efficiency. As technology continues to advance and more studies are being conducted, CGM is likely to become an integral component of personalized care in the ICU for patients with type 2 diabetes.

Like all other studies, this study had both limitations and strengths. The merits of this study were the comparison between the sensor system and the blood gas method, which is widely regarded as the gold standard, and the fact that the study was conducted across two ICU centers, namely, AHEPA University General Hospital and "Agios Pavlos" General Hospital. In addition, participants were generally in good health upon admission. However, the drawbacks of the study were the relatively small sample size (compared with previous studies that included 11 patients, it was nevertheless larger) and the diverse grounds for ICU admission contributed to the heterogeneity of the outcome.

This study aimed to assess the usefulness of CGMS in T2DM patients being treated in Covid-19 ICUs, which marks the initial attempt to evaluate its effectiveness in such a specific context.

CONCLUSION

The incorporation of CGM into the ICU has proven to be both convenient and dependable, with a robust relationship with blood gas values, making it an asset for the ICU medical team. The glucose monitoring system effectively exposed undiagnosed hypoglycemia in the ICU, a phenomenon that is not entirely captured by blood gas glucose measurements. A substantial positive correlation exists between the sensor values and blood gas glucose values, making the glucose-recording sensor system a valuable tool for the ICU medical team in the management of critically ill patients. Although blood gas measurements are reliable (considered the gold standard), they only provide a momentary glimpse and do not provide a complete picture.

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Conflict of interest: None declared
Ethical approval: The study was approved by the Institutional Ethics Committee

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