RAPID LITERATURE REVIEW

# Monitoring Devices for glucose in critical patients during the COVID-19 pandemic:

## an update on International Evidence

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# ABSTRACT

**Background:** Hyperglycemia is common in Intensive Care Unit (ICU) and was reported with high mortality and adverse patients' outcomes. The infection of COVID-19 is identified as a main source of increase in the incidence of hyperglycemia and associated elevated mortality. In order to reduce the healthcare providers exposure and the personal protective equipment use during the pandemic, the US Food and Drug Administration (FDA) regulated the usage of continuous glucose monitoring (CGM) devices to address these concerns as well as control the glucose level at a desired range. What are the benefits of using CGM applications? The article updates knowledge on this topic.

**Methods**: We did our search on the following databases: MEDLINE, EMBASE and Cochrane database, articles included were all recent and between January 2020 to July 2022. Our main focus was on articles with evidence concerning the effectiveness and the accuracy of continuous blood glucose monitoring methods in ICU during the COVID-19 pandemic.

**Results:** A few recent articles were identified and scrutinized. These allow the article to present an overview of the most recent international evidence on the topic, ts benefits and a comparison between methods and devices.

**Main Contribution to Evidence-Based Practice:** The article puts together the most recent evidence on the demonstrated benefits of continuous glucose monitoring and identifies the few glucose Monitoring Devices about which there is recent published scientific evidence on its application to critical care.

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**What do we already know about this topic?**

There is available evidence that supports the adoption of monitoring devices for continuous glucose monitoring (CGM) in different settings. In critical care contexts there is a need for an update on recent concrete evidence.

**What is the main contribution to Evidence-Based Practice from this article?**

It is an update on recent evidence related to CGM and glucose management for critical patients during COVID-19 pandemic and the benefits for maintaining CGM and its impacts on patient data accuracy and patient safety. The authors report on the recent evidence available to support clinical decision and evidence-based practice by health professionals around the World.

**What are your research's implications towards theory, practice, or policy?**

The article identified the need for further research on the different devices available in the global markets. In addition, the article identifies evidence demonstrating that CGM management can reduce the workload of nurses, the healthcare providers' exposure and the PPE use during a pandemic. Increased nurses' satisfaction levels are associated with its application. The article also identified one monitoring device commonly used, namely Dexcom G6. The device was approved by FDA in 2021 for use in outpatient but is also being used in critical patient care of COVID-19 patients in ICUs.

**Authors' Contributions Statement:**

Made substantial contributions to conception and design, or acquisition of data Xiujuan Xue, Cuiping Xu

Involved in drafting the manuscript or revising it critically for important intellectual content; Yeqing Wang, Jing Wang, Jinyan Zhao,Yalin Tang. Acquisition of data and analysis and interpretation of data: Xueqing Song. Given final approval of the version to be published. Each author should have participated sufficiently in the work to take public responsibility for appropriate portions of the content; Xiujuan Xue, Yeqing Wang, Jing Wang, Jinyan Zhao,Yalin Tang, Xueqing Song，Cuiping Xu. All authors agreed to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

*Stress*-induced hyperglycemia occurs in over 90% of the patients admitted to Intensive Care Unit (ICU), irrespective of a previous diagnosis of diabetes (van Steen et al., 2017). Hyperglycemia was reported with high mortality and adverse patients' outcomes (Sardu et al., 2020; Yao et al., 2020) and these findings have highlighted the importance of glucose control in critical patients.

However, as for the patients with COVID-19, the glucose control would be more complicated. Numerous factors, including stress imposed by COVID-19 infection, critical illness, and frequent glucocorticoid use, patients with COVID-19 and diabetes can develop severe hyperglycemia or diabetic ketoacidosis. Elevated blood glucose in hospitalized patients with COVID-19 has also been associated with increased mortality (Zhu et al., 2020). Although intravenous (IV) insulin infusion is the standard of care for hyperglycemia management in the intensive care unit (ICU), however, this protocol requires frequent blood glucose measurements point-of-care (POC) every one to two hours which can increase the workload of nurses. Besides, the increased frequencies of glucose measurements will present a significant challenge amid the COVID-19 pandemic because of increased personal protective equipment (PPE) use and increased transmission risk to health care providers (HCP)(Sadhu et al., 2020).

To address these concerns, the US Food and Drug Administration (FDA) issued a policy in March 2020 to allow the use of real-time continuous glucose monitoring (rtCGM) systems reduce HCP exposure and the PPE use during the current pandemic. rtCGM devices sample interstitial glucose levels every 5 minutes and the data are automatically transmitted to a handheld receiver outside of the patient's room that displays the current glucose level, glucose trends, and trend arrows, which indicate the direction and velocity of changing glucose (Chow, Kelly, Gupta, & Miller, 2021).

However, despite the advantages, there are specific concerns that several factors may affect CGM performance in the ICU, including changes in tissue perfusion or edema, hydration, acid-base balance, and medication interference and several CGM trials in critically ill patients in the ICU focused on accuracy, reliability and other aspects.

This article is a topic focused rapid review of articles published in the period January 2020–July 2022 regarding CGM in critical patient glucose management during COVID-19. The review examines two questions. First, does the evidence indicate whether CGM used in critical performed comparable or even better results as the traditional method? Second, what CGM devices are recommend to be used?

## Methods

We did our search on the following databases: MEDLINE, EMBASE and Cochrane database, from January 2020 to July 2022. Our main observations are effectiveness and the accuracy of continuous blood glucose monitoring method in ICU during the COVID-19 pandemic. These were searched for English-language articles with search terms as described below. Search strategies: blood glucose[MeSH Terms]) OR (blood sugar)) OR (glycemic)) OR (glycaemia)) OR (Hyperglycemia)) OR (blood glucose)) AND (((((management) OR (control)) OR (intervention)) OR (monitor)) OR (monitoring))) AND ((((intensive care unit[MeSH Terms]) OR (critical care[MeSH Terms])) OR (ICU)) OR (critical illness[MeSH Terms]))) AND (((((COVID 19[MeSH Terms]) OR (SARS-CoV-2 Infection[MeSH Terms])) OR (COVID-19)) OR (SARS-CoV-2)) OR (novel corona virus)) Filters: from 2020 – 2022.

Additional articles were found by manually screening references of relevant articles and reviews on the same topic. Articles that met any of the following criteria to be included: every study with reference to “glucose management in critical care patients during the COVID-19 pandemic, published after January 2020, reported outcomes data on glucose related indicators, identified the monitoring device used.

## Results

The first relevant article identified is a case report about continuous glucose monitoring to assess parenteral nutrition （PN） induced hyperglycemia in an adult patient with severe COVID-19(Chow, Kelly, Gupta, et al., 2021). PN-induced hyperglycemia, especially within 24 hours of PN initiation, has been shown to be a predictor of hospital mortality and is associated with increased length of stay. This case demonstrates the potential utility of real-time continuous glucose monitoring （rtCGM） in the critical care setting and highlights its potential to help conserve personal protective equipment and minimize unnecessary staff exposure in the setting of COVID-19. Meanwhile, this article demonstrated that rtCGM correlated well to the gold-standard venous glucose measurements. The lesson learned from this case is the need for earlier initiation of rtCGM, which would have allowed for more rapid titration of insulin infusion when glucose levels were rising subsequent to starting PN. The monitoring device is real-time continuous glucose monitoring (rtCGM) in this article.

The second relevant article was performed by Archana et al(Sadhu et al., 2020). The article was a feasibility pilot study using CGM in critically ill patients with COVID-19 in the intensive care unit (ICU). In this study, CGM devices were placed on 11 patients to evaluate the feasibility of using CGM in critically ill patients with COVID-19 for real-time sensor glucose (SG) trends with intermittent point-of-care blood glucose (POC-BG) testing to guide insulin therapy. The findings of this study support that CGM is feasible in critically ill patients and has acceptable accuracy to identify trends and guide intermittent blood glucose monitoring with insulin therapy. This article indicated that continuous glucose monitoring (CGM) has emerged as an alternative for inpatient point-of-care blood glucose (POC-BG) monitoring. The monitoring device is CGM a or Dexcom G6.

The third article was performed by Citlalli et al in 2021(Perez-Guzman et al., 2021). It is a clinical trial looked into the accuracy Continuous Glucose Monitoring (CGM) in the Operating Room and Cardiac Intensive Care Unit by comparing the real-time CGM with periodic point-of-care (POC) in 15 patients. This trial provides strong evidence for GCM use in ICU, that we can use the technology in the sickest patients, except during surgery, aiming at achieving better glycemic control while reducing the burden of diabetes care. The monitoring device is Dexcom G6 Continuous Glucose Monitoring (CGM).

The fourth article is a retrospective observational study conducted in 2020. It provides evidence for the safety of IV insulin management using a combined point-of-care blood glucose (POC) plus CGM regimen by

reviewing clinical data from 19 patients with COVID-19 in ICU. In this study, the hybrid POC plus CGM model can be safely applied to patients with critical COVID-19 disease, including those requiring mechanical ventilation, vasopressors and renal replacement therapy, and the sensor monitoring accuracy of the GCM is less affected by oxygen saturation, mean arterial pressure and vasopressors. Data showed that the protocol significantly reduced POC testing, patient pain, blood loss and sleep disruption, and cost. The study was limited by an observational design that requires a prospective multicenter study in a more diverse group of critically ill patients to look at its safety. The monitoring device is Dexcom G6 Continuous Glucose Monitoring.

The fifth study was from Georgia M(Davis et al., 2021). The study involved nine patients requiring mechanical ventilation and corticosteroids. A computerized algorithm called Glucommander is applied to adjusts the multiplier according to glucose trends, insulin sensitivity and response to therapy. The results show that patients with diabetes and active or suspected COVID-19 started the hybrid CGM/POC Glucommander protocol with improvement in glycemic control within 12h and consistent validation for most sensor values. Thus, a protocol involving stakeholders to implement a hybrid approach with hourly HER documentation guiding computerized CII is feasible and can reduce POC glucose testing without compromising glycemic control. Real-time CGM sensors are not yet a replacement for POC testing due to possible disturbances during critical care, resulting in discrepancies between POC and sensor glucoses values, but the technology has advanced significantly and could provide meaningful improvement in patient care. The monitoring device is Real-time CGM sensors and POC testing.

The sixth article aimed to investigate the accuracy of CGM in hospitalized patients on the general care floor and in the intensive care unit. It was conducted by Rebecca et al in 2021(Longo, Elias, Khan, & Seley, 2021). Experimental results demonstrate that, with appropriate protocols and safety measures in place, the use of CGM in hospitalized patients is a reasonable alternative to standard care to achieve the goal of reducing exposure to healthcare professionals. However, further research is needed to verify the safety, accuracy and efficacy of the technology. The monitoring device is Continuous Glucose Monitoring (CGM).

The seventh relevant article identified in 2021. The study looked into the effect of real-time continuous glucose monitoring (rtCGM) on glucose management in critically ill patients based on the status real-world data are needed(Agarwal et al., 2021). This study looked into evidence on continuous glucose monitoring (rtCGM) on glucose management in real-world. The evidence was generated by 11 patients, the results showed that CGM reduced POC testing by ~60% for patients on insulin infusion (CII). The usage of CGM is early feasibility, considerable accuracy, and meaningful reduction in the frequency of POC glucose testing. The findings of this plot study support the use of rtCGM on critical patients to achieve the glycemic goals.

The eighth relevant article is also a plot study on real-time continuous glucose monitoring (rtCGM) on glucose control and the perceptions of the healthcare providers. The author Kenneth W et al(Chow, Kelly, Rieff, et al., 2021) proposed this retrospective article aimed to assessed the clinical utility and accuracy of rtCGM in managing diabetes patients. The data was analyzed by 11 patients and the results showed a significant glucose decreased by using the rtCGM and a reduction of POC measurements was also be detected. Besides, the majority of nurses reported that rtCGM was helpful for improving care during the COVID-19 pandemic, and it can reduce the use of personal protective equipment (PPE). The study provides a strong rationale to increase clinician awareness for the adoption and implementation of rtCGM systems in the ICU. Results are summarized in tables 1.1 and 1.2.

## Discussion

The eight included articles put forth the following evidence.

First, during the pandemic, all the studies showed continuous glucose monitoring (CGM) proved a considerable benefit in glucose control for critical patients although the evidence is from a small sample patient. The continuous glucose monitoring can track blood glucose levels automatically. Healthcare providers and patients can review the glucose changes over a few hours or days directly to see the trends so as to make more informed decisions to maintain the glucose level.

Second, four studies concerned the accuracy. Although

FDA-approved CGMs (Dexcom G and Freestyle Libre) for nonadjunctive use in the hospital settings because of the pandemic, there are specific concerns that several factors may affect CGM performance in the ICU, including changes in tissue perfusion or edema, hydration, acid-base balance, and medication interference(Faulds et al., 2021) and thus limited its usage in ICU. However, early feasibility and considerable accuracy were demonstrated and a rationale increase for the adoption and implementation of rtCGM systems in the ICU was recommended.

Third , some of the studies also mentioned other benefits such as meaningful reduction in the frequency of POC glucose testing, a reduction of nursing and staff workload as well as help conserve personal protective equipment and minimize unnecessary staff exposure in the setting of COVID-19.

Besides, devices were also identified. In 2021,2 CGMs (Dexcom G and Freestyle Libre) were FDA-approved for nonadjunctive use in the outpatient setting but no advice for inpatient. Six studies used the Dexcom G6 device and two studies only stated used a rtCGM devices with limited details.

However, the eight articles present some limitations.

One is that all of the studies come from the USA and the CGM device were mainly FDA-approved. The benefit of the usage of CGM in critical patients still need to be demonstrated in other countries and other devices.

Another limitation is that the number of patients included in each study was low with no more than thirty or even a case report which limits the reliability of the findings of each study. Further studies with larger sample size will be suggested. The small sample size may be related the limited usage of CGM in critical patients. Before the COVID-19 pandemic, the usage of CGM in ICU was under ongoing discussion but very few related studies were available. All of the included studies are primary research and they all provide important developments for the application of CGM intervention in critically ill patients, especially during the COVID-19 epidemic and provided considerable benefits.

Future research should seek to confirm the identified benefits in larger sample sizes, in other Countries besides USA, the use of other devices and add evidence on economic impacts.

| NO. | Article Title | Authors/Country | Year | Key Findings | Monitoring Device |
|---|---|---|---|---|---|
| 1 | Use of Continuous Glucose Monitoring to Assess Parenteral Nutrition–Induced Hyperglycemia in an Adult Patient With Severe COVID-19 | Kenneth W Chow, et al USA | 2020 | The usage of rtCGM in the critical COVID-19 patient can treat PN-induced hyperglycemia and help conserve personal protective equipment and minimize unnecessary staff exposure | Dexcom G6 |
| 2 | Continuous Glucose Monitoring in Critically Ill Patients With COVID-19: Results of an Emergent Pilot Study | Archana R Sadhu,Ivan Alexander et al USA | 2020 | CGM is feasible in critically ill patients and has acceptable accuracy to identify trends and guide intermittent blood glucose monitoring with insulin therapy | Medtronic Guardian Connect and Dexcom G6 CGM systems |
| 3 | Continuous Glucose Monitoring in the Operating Room and Cardiac Intensive Care Unit | Perez-Guzman MC, Duggan E, Gibanica S, Cardona S, et al USA | 2021 | CGM use is helpful in the ICU to guide therapy in patients that require contin- uous insulin infusion to maintain glucose control | Dexcom G6 CGM (Dexcom, San Diego, CA) |
| 4 | Use of Continuous Glucose Monitor in Critically Ill COVID-19 Patients Requiring Insulin Infusion: An Observational Study | Eileen R Faulds,Andrew Boutsicaris,Lyndsey Sumner,L et al USA | 2021 | CGM using a hybrid protocol is feasible, accurate, safe, and has potential to reduce nursing and staff workload | Dexcom G6 (San Diego, CA) |

**Table 1.1 Continuous Glucose monitoring on Covid-19 patients and monitoring devices**

| NO. | Article Title | Authors/Country | Year | Key Findings | Monitoring Device |
|---|---|---|---|---|---|
| 5 | Remote Continuous Glucose Monitoring With a Computerized Insulin Infusion Protocol for Critically Ill Patients in a COVID-19 Medical ICU: Proof of Concept | Georgia M Davis,Eileen Faulds,Tara Walker,Debbie et al USA | 2021 | A hybrid protocol integrating real-time CGM and POC is helpful for managing critically ill patients with COVID-19 requiring insulin infusion | Dexcom G6) |
| 6 | Use and Accuracy of Inpatient CGM During the COVID-19 Pandemic: An Observational Study of General Medicine and ICU Patients | Rebecca Rick Longo,Heather Elias,Mehvish et al USA | 2021 | The use of CGM is a reasonable alternative to standard of care to achieve the goal of reducing healthcare professional exposure | Dexcom G6, Dexcom, San Diego, CA, USA) |
| 7 | Continuous Glucose Monitoring in the Intensive Care Unit During the COVID-19 Pandemic | Agarwal S, Mathew J, Davis GM, Shephardson A, Levine A,et al USA | 2021 | The use of rtCGM demonstrated early feasibility, considerable accuracy, and meaningful reduction in the frequency of POC glucose testing | G6 sensor |
| 8 | Outcomes and Healthcare Provider Perceptions of Real-Time Continuous Glucose Monitoring (rtCGM) in Patients With Diabetes and COVID-19 Admitted to the ICU | Kenneth W Chow,Danielle J Kelly,Mary C et al USA | 2021 | rtCGM was helpful for improving care for patients and reduced their use of personal protective equipment (PPE). | Dexcom G6 system (Dexcom, Inc., San Diego, California) |

**Table 1.2 Continuous Glucose monitoring on Covid-19 patients and monitoring devices**

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