**Performance of the Dexcom G6 Continuous Glucose Monitoring (CGM) system during cardiac surgery using hypothermic extracorporeal circulation**

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**Twitter summary:**

Dexcom G6 CGM accuracy challenged during cardiac surgery with hypothermic extracorporeal circulation, with mean absolute relative difference of 23.8%. Accuracy improved post-surgery.

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**ABSTRACT**

*Background*

Continuous glucose monitoring (CGM) may be challenged by extreme conditions during cardiac surgery using hypothermic extracorporeal circulation (ECC).

*Research Design and Methods*

We evaluated the Dexcom G6 sensor in 16 subjects undergoing cardiac surgery with hypothermic ECC, of whom 11 received deep hypothermic circulatory arrest (DHCA). Arterial blood glucose, quantified by the Accu-Chek Inform II meter, served as reference.

*Results*

Intra-surgery mean absolute relative difference (MARD) of 256 paired CGM/reference values was 23.8%. MARD was 29.1% during ECC (154 pairs) and 41.6% immediately after DHCA (10 pairs), with a negative bias (signed relative difference: -13.7%, -26.6% and -41.6%). During surgery, 86.3% pairs were in Clarke error grid Zones A or B and 41.0% of sensor readings fulfilled the ISO 15197:2013 norm. Post-surgery, MARD was 15.0%.

*Conclusions*

Cardiac surgery using hypothermic ECC challenges the accuracy of the Dexcom G6 CGM although recovery appears to occur thereafter.

*Article Highlights:*

* This study tested the accuracy of the Dexcom G6 CGM sensor in patients undergoing cardiac surgery using hypothermic extracorporeal circulatory arrest.
* Our results showed limited performance during surgery and suggest a link to the hypothermia exposure. Of note, most sensors demonstrated adequate accuracy post-surgery.
* Cardiac surgery using hypothermic ECC challenges the accuracy of the Dexcom G6 CGM although recovery appears to occur thereafter.

**Introduction**

There is a growing interest in the use of continuous glucose monitoring (CGM) systems in the hospital setting1. The benefits are obvious: less labour-intensive finger-stick testing, provision of continuous glucose levels and customizable alerts.

Modern CGM systems displayed satisfactory performance in non-critical ill patients 2 and patients undergoing elective abdominal surgery 3 (mean absolute relative difference (MARD) <13%). However, because of the physiological effects of severe illness and specific medical interventions, more data related to the accuracy of CGM reading are required in these situations. One example of such a challenging condition is open cardiac surgery. To facilitate the operating environment, cardiac surgery is often combined with cardioplegia-induced cardiac arrest during extracorporeal circulation (ECC) 4. Hypothermia (32-34 °C) is often instated for organ protection 5. The most extreme conditions can be found during surgery of the ascending aorta and aortic arch, when only the brain is selectively perfused and blood flow to the rest of the body is halted at a core temperature between 15-22°C for a short period of time (termed deep hypothermic circulatory arrest [DHCA]) 6.

This study tested the accuracy of the Dexcom G6 CGM sensor in patients undergoing cardiac surgery using hypothermic ECC.

**Research Design and Methods**

In a prospective observational study, we evaluated the performance of the Dexcom G6 CGM sensor in adults (≥18 years) with or without diabetes undergoing scheduled cardiac surgery-induced hypothermic ECC. The Ethics Committee Bern approved the study (approval number 2020-01024) and all participants provided written informed consent.

Recruitment was performed at the pre-operative anaesthesia consultation. Participants were fitted with a Dexcom G6 CGM (Dexcom, San Diego, CA) on the lateral abdominal flank by the study team on the day of hospital admission. The CGM sensor was kept until discharge or end of sensor life (10 days). During hospitalization, reference glucose values were measured using the Accu-Chek® Inform II meter (Roche Diagnostics GmbH, Mannheim, Germany). A calibration was performed with arterial blood at the time of anaesthesia induction using the Accu-Chek® device. During surgery, blood for reference values was sampled every 20 minutes from the arterial line or the heart-lung machine during ECC, and immediately after cessation of DHCA, respectively. Post-surgery reference values were measured from capillary blood as part of usual care. Intraoperatively, core body temperature was monitored using a standard urinary catheter with temperature sensor. In addition, oesophageal temperature and mean arterial blood pressure were continuously recorded (Philips MX 700, Amsterdam, Netherlands). Blood gases (pO2, pCO2) were measured using a Radiometer (ABL 800, Brønshøj, Denmark). Patient characteristics and surgical details were obtained from the electronic health record and anaesthesia protocol.

CGM measurements were linearly interpolated on a 1-min temporal grid, except for CGM gaps larger than 10 min, which were not interpolated. Each reference measurement was paired with the closest in time interpolated CGM value and pairs with a time difference >5min were discarded. MARD was used as the main accuracy metric. Secondary accuracy metrics included signed relative difference (%, calculated as: [GlucoseCGM – GlucoseReference]/GlucoseReference\*100), the percentage of pairs in zone A and A+B of Clark Error Grid 7, the percentage of pairs within ±15 mg/dl or ±15% (15/15%) of references according to ISO 15197:2013 standards 8, and the percentage of pairs within 20/20% and 30/30% of the references. Accuracy metrics were calculated during surgery (defined from skin incision to closure), during ECC and immediately after cessation of DHCA as well as during the post-surgery follow-up (from end of surgery until hospital discharge or end of sensor life). In an exploratory analysis, we investigated the correlation of accuracy metrics with core body temperature. CGM accuracy outcomes were calculated using aggregated pairs from all study participants.

**Results**

Sixteen patients were included between 02.2021 and 03.2022. Procedures included four open coronary artery bypass graft surgeries (CABG) and 14 open aortic and 11 valve repair/replacement surgeries. Further patient/surgery characteristics are listed in the Supplementary Appendix.

In median, CGM was placed 22.8 hours [11.2, 79.4] ([min, max]) prior to surgery. The durations of surgery were 5.4±1.8 hours (mean±SD) including 3.0±1.1 hours of ECC. DHCA was performed in 11 patients (mean duration of 20.1±4.0 min). The minimal body temperature ranged between 20.9-32.0 °C. In all patients, myocardial protection was achieved with a glucose-containing cardioplegic solution, providing between 15.8-40.0 g of glucose during the surgery (mean 24.7±7.2 g).

Reference glucose levels ranged between 99.7±29.8 and 289.2±46.2 mg/dL during surgery and between 115.5±15.4 and 172.5±28.8 mg/dL during the post-surgical follow-up period. A total of 400 CGM/reference pairs were obtained (surgery: 256, ECC: 154, DHCA: 10, post-surgery: 144).

Figure 1A is an example of the CGM, reference glucose and temperature trajectory during surgery. MARD for the whole cohort was 23.8% during surgery, 29.1% during ECC and 41.6% immediately after DHCA, with a negative bias in all three periods (mean signed relative difference was -13.7%, -26.6% and -41.6%, respectively). During surgery, 86.3% pairs were in Clarke error grid Zones A or B (A, 51.6%). All accuracy metrics are reported in the Supplementary Appendix. The sensor accuracy was associated with body temperature (Pearson’s r=-0.57 and r=0.63, both p<0.001, for absolute and signed relative differences, respectively; Figure 1 C and D). The effect of body temperature on relative differences remained statistically significant (p<0.001) after adjustment for reference glucose, rate of glucose change (ROC) and time since sensor insertion, using linear mixed-effect modelling (Supplementary Appendix). Postoperatively, MARD was 15.0% with 95.4% pairs in Clarke error Grid Zones A or B (A, 73.6%).

Sensor readings were available 90.1% of the time during surgery and 97.6% of the time after surgery. One sensor required replacement in the postoperative period due to sensor failure, while in four patients, dropouts of CGM readings with sensor error alerts were transient and recovered. There were no adverse device effects.

**Conclusions**

We investigated the accuracy of the Dexcom G6 CGM during cardiac surgery using hypothermic ECC. Our results showed limited performance during surgery and suggest a link to the hypothermia exposure. Of note, most sensors demonstrated adequate accuracy post-surgery.

Our findings are in line with two recent studies performed by Emory University Investigators (Atlanta, GA, US) 9, 10. In a pilot study performed in 15 patients undergoing CAGB surgery (based on 149 CGM/reference pairs and without information on temperature exposure), the authors report a negative bias in Dexcom G6 glucose values 9. In a second study performed in the ICU setting in patients following cardiac arrest, a negative bias and frequent sensor signal losses were observed during hypothermia 10. Similar to our observations, sensor recovered post-surgery/hypothermia in both studies. We only identified one other study reporting CGM performance data during cardiac surgery. Of note, the study was performed in small children undergoing cardiac bypass surgery and with a different and older generation CGM system (Guardian RT, Medtronic Minimed). Whilst the authors provide no detailed information regarding the use of hypothermia and cardioplegia, they report a MARD of 16.6% during surgery but state that intraoperative sensor failure was experienced in 50% of the patients 11.

We observed a consistent rise in arterial blood glucose in all participants (mean±SD 168.5±49.4 mg/dL), which was likely caused to a considerable extent by the glucose-containing cardioplegic solution. Sensor measurement mostly failed to capture the initial rise in glucose (as seen in Figure 1A, upper), resulting in a large discrepancy between sensor and reference glucose. While we cannot rule out that the environmental conditions in the interstitium (such as a reduced partial oxygen pressure at the measurement site) may influence the sensing process, other factors more likely explain the observed discrepancy. For example, impaired microcirculation associated with lower temperature on ECC 12, 13 is likely to impair the equilibration between the vascular and interstitial compartment, thereby explaining the large discrepancies between arterial and interstitial glucose concentrations. This may be further compounded by rapid glucose dynamics14, which were induced by the glucose-containing cardioplegic solutions (peak glucose values of 289.2±46.2 mg/dL, max. ROC of 5.0±3.4 mg/dL/min, min ROC of -3.8±1.7 mg/dL/min). The recovery of the accuracy towards the end of the surgery, when blood glucose levels stabilize again, supports this hypothesis.

We acknowledge limitations of the present study. In particular, the number of patients is small, which results in a limited number of pairs (in particular for DHCA with only 10 CGM/ref pairs). Of note, the time dependence of body temperature and the collinearity with other variables such as glucose and the rate of glucose change in the present study do not allow conclusive results on the effects of body temperature on accuracy.

In conclusion, subcutaneous CGM values during cardiac surgery using hypothermic ECC and glucose-containing cardioplegic solutions do not adequately reflect glucose concentration in the vascular space. As diabetes technology continues to evolve in the inpatient perioperative setting, these limitations must be addressed to exploit the full potential of CGM use in the hospital.

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*Author contributions*

LB and APV designed and coordinated the study. LB, APV, AM, ACG, GK, LC, JR, DS and DPG were responsible for screening and enrolment of participants, arranged informed consent from the participants, and provided patient care. MV analysed the data and produced the display items. DH, AF and LB contributed to data analysis, including statistical analyses. DH and LB wrote the report. All authors contributed to the interpretation of the results, critically reviewed the report and approved the final manuscript. MV, DH and LB had full access to all the data in the study and take responsibility for the integrity of the data and the accuracy of the data analysis. All authors made the decision to submit for publication.

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*Conflict of interest statement*

The authors declare no competing interests associated with this manuscript.

*Data availability*

The datasets generated during and/or analyzed in the current study are available from the corresponding author upon reasonable request.

*Prior publication or presentation of the study*

This work was presented at Annual Meeting of the European Association for the Study of Diabetes (EASD) in September 2022.

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