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Accuracy of two continuous glucose monitoring devices during aerobic and high-intensity interval training in people with type 1 diabetes

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ABSTRACT

Background: This study aimed to evaluate the accuracy of the Dexcom G6 (DG6) and the FreeStyle Libre-2 (FSL2) during aerobic training and HIIT in individuals with type 1 diabetes (T1D).

Methods: Thirty-nine males (mean age 29.5 ± 6.2 years and mean duration of diabetes 15.2 ± 6.2 years) participated in this study. Interstitial glucose levels were measured using DG6 and FSL2, while plasma glucose levels were measured every 10 min using the YSI 2500 as the reference for glucose measurements in this study. The measurements began 20 min before the start of exercise and continued for 20 min after exercise. Seven measurements were taken for each subject and exercise.

Results: Both DG6 and FSL2 devices showed significant differences compared to YSI glucose data for both aerobic and HIIT exercises. Continuous glucose monitoring (CGM) devices performed better during HIIT than aerobic training, with DG6 showing a mean absolute relative difference (MARD) of 17.28% versus 30.60%, respectively. When comparing the two devices, the FSL2 performed significantly better than the DG6 for aerobic training, but its performance was similar to DG6 during HIIT.

Conclusions: The findings suggest that the accuracy of DG6 and FSL2 deteriorates during and immediately after exercise, but it remains acceptable with both devices during HIIT. However, accuracy is compromised with DG6 during aerobic exercise. This study is the first to compare the accuracy of two CGMs, DG6 and FSL2, during two exercise modalities using plasma glucose YSI measurements as the gold standard for comparisons.

INTRODUCTION

Type 1 diabetes (T1D) is a chronic disease characterized by autoimmune loss of pancreatic insulin secretion and subsequent disruption of glucose homeostasis.[1,2] Its global prevalence is approximately 9 million individuals and is projected to double in the next 20 years.[3,4] Over the years, the management of T1D has significantly improved due to continuous advancements in pharmacological and technological approaches.[5,6] Presently, intensive insulin therapy combined with regular glucose monitoring[7] remains the cornerstone of T1D treatment, essential for achieving optimal glycemic control.[8]

Until the past decade, the predominant method for checking blood glucose levels was self-monitoring of capillary blood glucose using a glucometer.[9] However, more recently, continuous glucose monitoring (CGM) devices have gained increasing popularity. These devices continuously estimate glucose levels from the interstitial fluid using electrochemical glucose sensors.[10,11] The adoption of CGM among individuals with T1D has been facilitated by reimbursement policies implemented by most Western governments (e.g., Spain, France, Italy) and private insurance providers (e.g., US, Switzerland).[11] CGM devices are classified as real-time CGM (rtCGM)[12] or intermittent scanning CGM (isCGM).[13,14] The former provides continuous blood glucose information, while the latter requires an interaction (scanning) between the sensor and a device, such as a mobile phone or a reader.[15] Both rtCGM and isCGM have demonstrated improvements in glycemic control and a reduction in hypoglycemia with some cost reductions,[18] primarily by decreasing expenses related to the management of hypoglycemia events.[16,17]

Physical exercise has been strongly recommended to improve cardiovascular health and glycemic control in individuals with T1D.[18,19] Exercise has been shown to enhance insulin sensitivity and improve body composition, endothelial function, and blood lipid profile.[20] However, to exercise safely, it is crucial that CGM devices offer high accuracy in glucose measurements, even during the frequent glycemic variations associated with physical activity.[21] Previous reports have examined the accuracy of specific CGM models, with the Dexcom G4 Platinum and FreeStyle Libre (FSL) being the most frequently evaluated to date.[22] These reports found significant inaccuracies when faced with rapid and unexpected changes in glucose levels during exercise.[22,23] Consequently, as suggested in these studies, further research is needed to better understand why accuracy is partially

lost during exercise and to identify the best compensation strategies to mitigate this issue.[22,24]

Two of the most popular forms of exercise for individuals with T1D are aerobic and high-intensity interval training (HIIT).[25,26] While both interventions have shown some positive effects on glycemic control,[27,28] they differ in their impact on glycemic regulation.[29] It is known that aerobic exercise is associated with a more pronounced and longer decrease in glycemic levels.[30] Therefore, considering the distinct characteristics of each exercise modality and the importance of evaluating the performance of CGM devices during exercise activities, this study was designed to assess the accuracy of two of the most recent and widely used CGM devices: the Dexcom G6 (DG6) and the FreeStyle Libre-2 (FSL2) in individuals with T1D. Currently, DG6 is widely regarded as the most accurate rtCGM device,[31] while the FSL2 is the CGM device most commonly used by T1D patients in Spain, particularly those using multiple daily injections.[32]

RESEARCH DESIGN AND METHODS

Patients and experimental design

Thirty-nine male participants were recruited for this study from the Diabetes Reference Unit at the Clinic University Hospital of Valencia, Spain. The inclusion criteria were as follows: (1) age between 18 and 40 years, (2) T1D with a diabetes duration of over 2 years, (3) glycated hemoglobin (HbA1c) levels below 8.5% (below 69 mmol mol^{-1}), (4) a stable insulin regimen with less than a 20% change in the total daily insulin dose over the past 6 months, (5) multiple daily injections, and (6) engagement in at least 90 min of physical activity per week, but not participating in any sport as amateurs or professionals. Participants were excluded if they had clinical conditions or were taking medications (other than insulin) known to affect glycemic control, such as oral or parenteral steroids or metformin, among others. All patients were provided with detailed information regarding the potential risks and benefits of the study and signed an informed consent form. The study protocol received approval from the Ethics Committee of the University of Valencia, Spain (1587001).

Study measures

Interstitial glucose levels were measured using two CGM devices: DG6 (Dexcom Inc., San Diego, CA, USA) and FSL2 (Abbott Diabetes Care, Alameda, CA, USA) devices. Both devices were inserted into the back of the upper arms 72 h before the first exercise session and were worn for a minimum of 48 h after completing the exercise. While all participants followed the protocol conditions and wore the DG6, some of them did not wear the FSL2 device provided by the Spanish health system, that is, all participants with FSL2 also wore the DG6 at the same time. The placement arm of both sensors (i.e., left or right) was randomized.

During aerobic training and HIIT sessions, a nurse inserted a catheter to collect forearm venous blood samples throughout the exercise sessions. Plasma glucose levels were measured every 10 min using the YSI 2500 STAT Plus analyzer (Yellow Springs, OH), serving as the reference glucose measurements in this study. In turn, this device, considered the gold standard for measuring plasma glucose, checks between measurements the correct functioning of the glucose measurement membranes using a calibrated liquid with a concentration of 2.5g/L Dextrose. The measurements began 20 min before the start of exercise and continued for 20 min after exercise, with adjustments made for the difference in duration between aerobic training and HIIT sessions (Figure 1).

Furthermore, heart rate was continuously monitored during both sessions via chest belt telemetry using a Polar H10 heart rate monitor. All exercise sessions were conducted in the Clinical Research Laboratory of the Physiotherapy Department at the University of Valencia, Spain, under the supervision of a physiotherapist specifically trained in this type of exercise methodology.

Figure 1 about here

Exercise protocol

Before being randomized to separate sessions of aerobic training and HIIT, each study participant completed an exercise incremental test. These sessions were scheduled at least 3 days apart to prevent potential interactions between them. Prior to commencing the tests, sociodemographic and anthropometric data were collected for each participant.

An incremental exercise test was conducted to determine the working power for the aerobic session on the cycle ergometer. The test began with a 3-minute period during which patients remained seated on the cycle ergometer at 0 W. This was followed by a 3-minute warm-up period during which the participants cycled at a workload of 60 W. Subsequently, the workload was increased by 40 W every 3 min until volitional exhaustion. Finally, a 3-minute active recovery phase at 40 W was performed, followed by a 3-minute passive recovery phase at 0 W, both on the cycle ergometer. The lactate turn point 1 (LTP1) and power at that level were determined during the incremental test to prescribe the exercise intensity.

Additionally, patients participated in a habituation session with elastic bands. During this session, they performed two sets of twelve repetitions for each exercise. The purpose of this session was to help participants adapt to the exercises and become familiar with the technique using the elastic bands.

The aerobic training session started with a 3-minute resting period during which participants remained seated quietly on the cycle ergometer at 0 W. This was followed by a 3-minute warm-up period at 60 W. Subsequently, the exercise intensity was increased in a stepwise manner by 20 W per minute to reach the power determined during the incremental test at the LTP1. This target workload was maintained for a duration of 30 min. The active and passive recovery periods, lasting 3 min each, were the same as those performed during the incremental test.[33]

On the other hand, the HIIT session was a modified version of the HIIT protocols used by previous authors,[34,35] replacing body weight exercises with exercises using TheraBand CLX (The Hygenic Corporation, Akron, OH, USA).[36] The exercise program was designed to engage large muscle groups and simulate conventional bodybuilding exercises by applying external resistance through the elastic bands. A total of eight exercises were selected: four involving the upper limb (bench press, seated dumbbell, shoulder press, and seated row) and four involving the lower limb (squats, stiff-legged

deadlifts, hamstring curl exercise, and quadriceps curl exercise). These exercises were alternated in the program to avoid performing two consecutive exercises targeting the same area.[37] All exercises were performed with both legs simultaneously or with the dominant arm (as the other arm had a catheter in place).

Prior to the HIIT session, participants carried out a warm-up that consisted of 3 min at 60W on the cycle ergometer and 15 no-load shoulder flexo-extensions. The HIIT session comprised two 4-minute series of interval workouts, with a 3-minute rest period between cycles (total duration 11 min). During each cycle, the eight aforementioned exercises were performed, lasting 20 seconds each with 10 seconds of rest in between (totaling 4 min). Participants were instructed to select a grip width on the elastic band that would require maximum effort during the 20-second duration of each exercise. They were encouraged to complete as many repetitions per interval as possible while maintaining correct form.

If blood glucose levels were equal to or less than 60 mg/dL at any time, the incremental test or exercise session was either not initiated or halted to prevent hypoglycemia.[38] In the event of mild hypoglycemia (above 70 mg/dL), participants were given 200 mL of orange juice containing 10.4 g of carbohydrates per 100 mL. Blood glucose levels were checked after 10 min. If the glucose levels did not rise above 70 mg/dL, an additional half serving of juice was consumed, and glucose levels were rechecked after another 10 min.

Statistical analysis

MATLAB Version 9.12.0.2009381 (R2022a) from The MathWorks Inc., Natick, Massachusetts, and its Statistics and Machine Learning Toolbox Version 12.3 were used for statistical programming. Reported *p*-values are double-sided and were not adjusted for multiple testing. Unless stated otherwise, statistical analyses were conducted using all available data for each exercise, employing a two-sample *t*-test. For the *before-after* exercise comparison, a paired-sample *t*-test was performed. The mean absolute relative difference (MARD) was employed to assess the accuracy performance of the devices in relation to the following criteria:

$$MARD := \frac{\sum_i^n \frac{YSI_i - CGM_i}{YSI_i}}{n}$$

Where YSI_i stands for the i-th YSI measurement, CGM_i stands for the i-th G6 or FSL2 sensor reading and n is the number of paired YSI-CGM samples in each exercise branch or glucose sensor used.

Delays between signals were calculated computing the cross-correlation between the data shifting one of the time streams forward or backward to simulate random delays. The time shift that maximizes the cross-correlation is considered as the observed delay between those two signals .

The Clarke error grid analysis was utilized to visualize the data and quantify the clinical accuracy of the system, providing an estimation of safe and unsafe glucose measurements compared to reference values.

Additionally, Bland-Altman plots were used to visually depict the data distribution and quantify the bias, defined as the difference between paired CGM device readings (i.e., DG6 or FSL2) and YSI glucose values.

RESULTS

Patients' characteristics

Patients' characteristics are presented in Table 1. The mean age was 29.5 (± 6.2) years, and the duration of diabetes was 15.2 (± 6.2) years. None of the patients were obese. All FLS2 subjects performed all sessions also with DG6 on.

Table 1 about here

CGM error

To ensure that the differences are significant and the computed errors are meaningful, Table 2 presents the average glucose values of the available YSI-CGM data pairs at various times during exercise, along with the statistical significance of the reported variances. Both the DG6 and FSL2 devices, as well as aerobic and HIIT exercises, exhibited significant differences in YSI and CGM glucose data.

Table 2 about here

Regarding the magnitude of the significant differences reported above, Table 3 presents the MARD for each exercise bout (before, during, and after) and sensor, along with the corresponding *p*-values comparing the MARD values between devices for the same type of exercise. Both CGM devices demonstrated better performance during HIIT compared to aerobic training. However, the MARD differences between both exercises for the same device were notably larger for DG6 (30.60% vs. 17.28%), which was also statistically significant. When comparing the two devices, the FSL2 exhibited significantly better performance than the DG6 for aerobic training, but its performance was similar to the DG6 during HIIT.

Table 3 about here

The data are presented in Table 3, which includes both sampled pairs *before* the start of exercise (BD1, BD2, and BD3 in Figure 1) and sampled pairs of data during and immediately *after* exercising. Table 4 displays the differences in MARD between devices and sessions, categorized by before and during exercise and immediately after.

Table 4 about here

The MARD values were higher with exercise samples compared to those obtained before the onset of physical activity. Notably, CGM errors for both devices were significantly worse for aerobic training. However, this difference was not found to be statistically significant for HIIT.

Glucose trends during each exercise period are illustrated in Figure 2. Solid lines represent the median values of the data at each time sample, while the shaded areas represent the interquartile ranges. During exercise, both CGM devices tended to overestimate glucose concentration compared to YSI.

Figure 2 about here

Considering the possibility of a consistent time delay between the signals of CGM and YSI, we calculated the maximum correlation time lag between the data of all patients and summarized it in Figure 3. The most common delay observed for all types of exercise and CGM devices was 0 min, with approximately 30% of patients showing a 10-minute delay for CONT and DG6. No other relevant non-zero delay was observed for EB-HIIT data or FS2 CGM.

Finally, supplementary material expands on the nature of the error distribution. Figure 1S displays Clarke Error Grids for all four combinations of data pairs representing both types of exercise, using either DG6 or FSL2 devices. The black dots on the grid correspond to the data pairs (horizontal axis for YSI and vertical axis for CGM) obtained during or immediately after exercise, while the hollow diamonds represent the points of data collected before the onset of exercise. The number of points falling within each region of the Clarke error grid (A, B, C, D, or E) is summarized in Table 1S. Alternatively, Bland-Altman plots are shown in Figure 2S, which include the mean and $\pm 1.96 \cdot SD$ lines. The data collected *before* exercise are represented by red diamonds, while the data obtained

during and after exercise are depicted as blue circles. All Bland-Altman plots indicate a negative sensor bias in all cases, both for pre- and post-exercise data. Moreover, all biases are statistically significant. The largest bias was observed for DG6 post-aerobic exercise points, with a value of -30.23 (p<0.001), while the smallest bias corresponds to the DG6 post-HIIT exercise.

DISCUSSION

This study was designed to evaluate changes in CGM values using DG6 during two different types of exercise, namely aerobic training and HIIT, in males with T1D. As some patients were also using FSL2, we were able to simultaneously compare the accuracy of DG6 and FSL2 before, during, and after each exercise. The main findings of our study were as follows: (1) both devices exhibited lower accuracy during aerobic training compared to no exercise or HIIT, and (2) surprisingly, FLS2 demonstrated better accuracy than the DG6 during aerobic training.

When comparing glucose values from CGM devices with their corresponding YSI values, which served as our gold standard, we observed significantly higher values with glucose sensors for both exercise modalities. One possible explanation for these findings is that glucose concentrations are measured in different tissues: venous blood by YSI and interstitial fluid by CGMs. Over the decades, researchers have studied differences in glucose concentrations depending on their origin (i.e., arterial, venous, or capillary) or whether it is whole blood or plasma.[39,40] Therefore, since plasma and interstitial fluid exhibit different dynamics in glucose changes, they should be considered as two separate glucose compartments, and their glucose values may not always align perfectly.[40] To address these differences, adjustments in the software of CGM devices have been implemented. However, in situations where rapid changes in glucose concentrations are expected, such as during exercise, differences in glucose levels obtained from alternate sites may be considerable due to fluctuations in blood flow.[40] Consequently, it is expected that CGMs will display the greatest disparity in glucose values during exercise.[22] This may explain why, in the data presented in this study, greater differences between CGMs and YSI values were found in aerobic training rather than in HIIT, as aerobic exercise tends to lead to greater variations in glucose levels.

Furthermore, we observed significant differences in accuracy between the two CGM devices when compared to the reference method. In our study, DG6 exhibited larger disparities than the FSL2, especially during aerobic training. If the difference between interstitial and plasma glucose alone contributed to the error in the analyzed devices, one would anticipate similar differences in the MARD between the devices. However, our MARD findings indicate noteworthy distinctions between both devices (DG6 30.6% vs FSL2 22.9%). Specifically, during aerobic training, FSL2 outperformed DG6 and proved to be more accurate.

In contrast to the findings reported by Guillot *et al.*, which suggested no influence of exercise (including aerobic and HIIT) on the accuracy of the DG6, our study has demonstrated that both types of exercise had a significant impact on sensor accuracy.[31] Guillot *et al.* reported average MARD values of approximately 13% during exercise, which appear to be considerably lower than the average values of 18.9% and 35.4% observed in our study.[31] One possible reason for this discrepancy might be the difference in glucose reference methods used in each study: Guillot *et al.* relied on capillary measurements to estimate sensor accuracy, while our study protocol used plasma glucose measured by YSI, which is considered the gold standard for glucose measurement accuracy.

Our findings on the time delay of CGM sensors suggest that average delay of both sensors has been reduced to less than 10 minutes. Indeed, the average delay between signals, and the most common subject-level delay, was 0 minutes, but considering that the YSI sampling rate was 10 minutes, it may be possible that delays between branches and CGM were different and lower than 10 minutes, which our protocol was unable to detect. It is worth mentioning that more patients (about 30%) showed a 10 minute delay for CONT exercise and the DG6 sensor, which was not appreciated for EB-HIIT or FS2.

Previous studies have utilized the Clarke error grid to assess CGM accuracy during exercise from a clinical impact perspective, focusing on the percentage of values falling within Zones A and B to determine clinical safety.[41] This percentage has typically been set around 95–100%,[42–44] similar to the criteria established in ISO 15197:2013 of 99%.[45] While our findings for HIIT were closely similar between the two devices, falling within the 98% range, there was a significant disparity during aerobic training, with DG6 at 80.9% and FSL2 at 90%. These results differ from those reported for DG6 by Guillot in

his study, where the authors found 100% accuracy using the same device for both aerobic and HIIT exercises.[31] The 19.1% discrepancy in accuracy during aerobic training between our findings and Guillot's study is somewhat unexpected. However, this difference could be attributed to methodological variations, particularly our controlled aerobic training based on an incremental test, as opposed to its absence in Guillot's study, as well as the utilization of plasma glucose measurements with YSI in our study versus capillary measurements with a glucometer. Therefore, caution should be exercised when interpreting the accuracy results of DG6 due to this inconsistency. On the other hand, as FSL2 values have been examined for the first time in our study and are slightly higher than those of DG6, a clinical implication of our results is that the FSL2 may be a safer option than DG6 when used as a CGM device during exercise.

There are several strengths in this study. One major strength lies in implementing a standardized exercise protocol, where the intensity during aerobic training was regulated based on a previous incremental test. This approach allows individual exercise adaptation to each subject using a validated method. Another strong aspect of this study was including an additional HIIT protocol with elastic bands, which can be easily adopted in clinical settings and requires affordable and portable equipment. Additionally, the sample size, which included many patients performing both exercises, may have further contributed to reduced data variability. Moreover, data collection was conducted in a well-controlled clinical setting, using two different CGM devices simultaneously, alongside plasma glucose YSI measurements, which served as the reference measure instead of capillary glucose, thus enhancing the reliability of the findings.

However, we acknowledge that our study has several limitations. One potential limitation is the unequal sample size of patients using the two devices, which may introduce constraints in interpreting results. We only performed paired-sample tests for the *before-after* comparison, and although our results support the finding that CGM glucose values during HIIT are more accurate for both devices, enhancing user safety, this was not observed during aerobic training. Another limitation of the study is that exercise bouts were restricted to a duration of 30 min for aerobic training and 11 min for HIIT. Consequently, changes associated with longer durations of exercise cannot be predicted based on our findings. Additionally, the post-exercise window in this study was limited to 20 min, while previous studies using the Medtronic Paradigm Enlite-2 CGM have

shown a return of CGM accuracy 1 h after exercise cessation.[42] Unfortunately, we could not assess a longer post-exercise period in this study. Since, in general, time delay between CGM and YSI is in the order of five to ten minutes, the 10-min sampling rate for YSI stated in the clinical protocol may have hindered our ability to appropriately measure delays shorter than ten minutes.

In summary, our findings suggest that the accuracy of both DG6 and FSL2 deteriorates during and immediately after exercise, but it remains similar and acceptable with both devices during HIIT, while it is compromised with DG6 during aerobic exercise. This is the first study to compare the accuracy of two CGMs, DG6 and FSL2, during two exercise modalities, using plasma glucose YSI measurements as the gold standard for comparisons.

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Figure legends

Fig. 1. Moments of blood sampling time (BD) in the exercise sessions.

Fig. 2. Median and interquartile range for YSI and both CGM devices, for aerobic training (top panel) and HIIT (bottom).

Fig. 3. Histogram of the measured delay for the data of each subject visit. Top panels show the delays of the CONT visits, and the EB-HIIT visits are shown in the two bottom panels. Left panels correspond to the DG6 delay, and the right panels to the FS2.

Table 1. Baseline characteristics of patients.

	Patients with DG6	Patients with FSL2
n	39	26
Age (years)	29.5 (6.2)	29.3 (6.3)
Diabetes duration (years)	15.2 (6.2)	14.9 (6.1)
Weight (kg)	78.76 (13.79)	80.80 (13.38)
BMI (kg/m^2)	25.01 (3.61)	25.08 (3.53)
HbA1c (%)	7.3 (0.9)	7.2 (1.0)
Insulin total daily dose	51.4 (16.1)	52.7 (16.0)
(U/kg/day)	0.65 (0.19)	0.66 (0.20)

Mean values and SD
DG6: Dexcom G6; FSL2: FreeStyle Libre-2

Table 2. Mean and statistical comparison of the data pairs YSI-CGM glucose values for each exercise type and CGM devices.

	DG6				FSL2			
	YSI	*CGM*	*n*	*p-value*	*YSI*	*CGM*	*n*	*p-value*
Aerobic	126.94	148.98	291	<0.001*	126.18	144.28	191	<0.001*
HIIT	153.58	163.82	271	<0.001*	159.60	175.71	145	<0.001*

CGM: continuous glucose monitoring; DG6: Dexcom G6; FSL2: FreeStyle Libre-2; HIIT: High-Intensity Interval Training

Table 3. Comparison between measurement errors (MARD) for each exercise type and device.

	MARD (%)		p-value
	DG6 [n]	*FSL2 [n]*	*DG6 vs FSL2*
Aerobic	30.60 [36]	22.88 [25]	0.027
HIIT	17.28 [37]	21.09 [21]	0.265
p-value Aerobic vs HIIT	0.001	0.646	

MARD: mean absolute relative difference; DG6: Dexcom G6; FSL2: FreeStyle Libre-2; HIIT: High-Intensity Interval Training

Table 4. Measurement errors of the samples before each exercise bout and during the time of exercise.

		MARD (%)		
		Before exercise	*During and immediately after exercise*	*p-value*
DG6	*Aerobic*	23.24	35.44	0.001
(n=35)	*HIIT*	15.98	18.86	0.163
FSL2	*aerobic*	17.90	24.24	0.029
(n=21)	*HIIT*	19.21	22.52	0.123

MARD: mean absolute relative difference; DG6: Dexcom G6; FSL2: FreeStyle
Libre-2; HIIT: High-Intensity Interval Training