



## Influence of physical exercise on the accuracy of continuous glucose sensors in children and adolescents with Type 1 Diabetes mellitus

*Influência do exercício físico na precisão do monitoramento contínuo de glicose em crianças e adolescentes com Diabetes mellitus Tipo 1*

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Received: 13-02-25

Accepted: 14-10-25

### How to cite in APA

Vaz Alves, L., Fornari Laurindo, L., Villa Chagas, H., Portero Sloan, K., dos Santos Haber, J. F., Maria Barbalho, S., Almeida Gabriel Filho, L. R., & Baisi Chagas, E. F. (2026). Influence of physical exercise on the accuracy of continuous glucose sensors in children and adolescents with Type 1 Diabetes mellitus. *Retos*, 74, 371-382. <https://doi.org/10.47197/retos.v74.113751>

### Abstract

**Introduction and Objective:** The objective of this study was to analyze the effect of duration, intensity and time of day of physical exercise on the accuracy of continuous blood glucose monitoring (CGM) sensors in children or adolescents aged 6 to 19 years with DM1.

**Methodology:** An observational study with a short follow-up (7 days) was carried out. Exercise was assessed using a physical activity report.

**Results:** The accuracy of the CGM was analyzed by %MARD considering cutoff points < 10%, ≤ 18% and ≤ 28%. The increase in time in minutes per week of physical exercise was related to the increase in the percentage of %MARD inadequate for clinical decision making for all cutoff points used. However, for the cutoff point of %MARD ≤ 28%, it was observed that days of physical exercise lasting >60 minutes increase inadequate %MARD (20.8%) for clinical decision-making when compared to <60 minutes of exercise on the day (15.2%) and days without exercise (10.4%).

**Conclusion:** Increasing the time of physical exercise per week can reduce the accuracy of the CGM blood glucose estimate, making it necessary to use capillary blood glucose measurements, especially in the presence of symptoms of hypoglycemia.

### Keywords

Biomedical technology; clinical medicine; diabetic complications; hypoglycemia; life style; self care.

### Resumo

**Introdução e Objetivo:** O objetivo deste estudo foi analisar o efeito da duração, intensidade e horário do dia do exercício físico sobre a acurácia dos sensores de monitoramento contínuo da glicose (CGM) em crianças e adolescentes de 6 a 19 anos com diabetes mellitus tipo 1 (DM1).

**Metodologia:** Foi conduzido um estudo observacional com curto período de acompanhamento (7 dias). A prática de exercício físico foi avaliada por meio de um relatório de atividade física.

**Resultados:** A acurácia do CGM foi analisada pelo %MARD, considerando os pontos de corte <10%, ≤18% e ≤28%. O aumento do tempo semanal de exercício físico (em minutos) esteve associado ao aumento do percentual de %MARD inadequado para a tomada de decisão clínica em todos os pontos de corte utilizados. Entretanto, para o ponto de corte %MARD ≤28%, observou-se que os dias com exercício físico de duração superior a 60 minutos apresentaram maior %MARD inadequado (20,8%) para a tomada de decisão clínica, quando comparados a dias com menos de 60 minutos de exercício (15,2%) e a dias sem exercício (10,4%).

**Conclusão:** Conclui-se que o aumento do tempo semanal de exercício físico pode reduzir a acurácia da estimativa de glicose obtida pelo CGM, tornando necessária a utilização de medições capilares de glicose, especialmente na presença de sintomas de hipoglicemia.

### Palavras chave

Tecnologia biomédica; medicina clínica; complicações diabéticas; hipoglicemia; estilo de vida; autocuidado.

## Introduction

Diabetes mellitus is a disease characterized mainly by resistance and/or deficiency in insulin production, leading to chronic hyperglycemia, which in turn is identified as the main factor related to complications of the disease (Kırkgöz et al., 2024). In type 1 diabetes mellitus (DM1), autoimmune destruction of pancreatic  $\beta$  cells leads to the need for the administration of exogenous insulin to maintain blood glucose levels. Epidemiological estimates suggest that in 2021, there were 355,900 new cases of DM1 worldwide among children and adolescents from 0 to 19 years, with incidence estimates for 2050 of approximately 476 thousand new cases (Stene & Haynes, 2022).

Although different therapeutic resources for insulin treatment and blood glucose monitoring are available, it has been observed that most patients with DM1 have inadequate glycemic control. The importance of glycemic control, even in children and adolescents, is due to its relationship with the increase in the risk of developing cardiovascular disease (CVD), which is increased in patients with DM1. However, other important complications are related to the lack of glycemic control, such as nephropathy, retinopathy, and peripheral arterial disease (Mao & Zhong, 2024).

Therefore, blood glucose monitoring must be carried out continuously, both by analyzing glycosylated hemoglobin (HbA1c) and by self-monitoring of capillary blood glucose or using continuous glucose monitoring systems (GMS) (Kolasa et al., 2023). Although GMS systems provide additional data for clinical practice and easier self-control glycemia, HbA1c remains the main clinical indicator in DM1 control (Foti Randazzese et al., 2024). However, the use of GMS systems has been associated with a decrease in glycosylated hemoglobin (HbA1c) values, contributing to better glycemic control and the risk of complications (Bernabe-Ortiz et al., 2023).

GMS estimates blood glucose through interstitial glucose, and although capillary and interstitial blood glucose may differ, GMS is recommended for blood glucose control and clinical decision-making. It provides information on average glycemia and glycemic variability coefficient, as well as the percentage of time and times of hyperglycemia, hypoglycemia, and glycemia within the therapeutic target (Dovc & Battelino, 2021), which has contributed to improved glycemic control (Cho et al., 2023).

The accuracy of GMS is assessed by MARD (mean absolute relative difference), which compares data from the GMS sensor with reference measurements of capillary blood glucose. Considering that the MARD is expressed as a percentage and represents the absolute error, the lower the MARD value, the greater the precision of the blood glucose estimates provided by the GMS (Bailey & Alva, 2021). Although GMS has greater application in the outpatient context, it has also been used for pediatric patients in hospitals who present acceptable MARD values for clinical decision-making and insulin administration (Waterman et al., 2024). For the use of GMS data in clinical decision making, a MARD value  $<10\%$  has been recommended (Heinemann et al., 2020), although MARD values  $<20\%$  are considered acceptable (Freckmann, 2020).

However, different factors can influence the accuracy of MSG blood glucose estimates by MARD analysis (Huang et al., 2022). Abrupt variations in blood glucose are one of these factors and may contribute to the increase of the difference between the estimates of interstitial blood glucose and capillary blood glucose, which are related to the rise in MARD (Heinemann, 2018). Physical exercise is one of these situations because the change in the circulation of subcutaneous tissue, muscle contraction in the region of the sensor, increase in body temperature, and change in oxygen levels in the blood can influence blood glucose values and their flow to interstitial tissue (Moser, Riddell, et al., 2020; Muñoz Fabra et al., 2021).

Although physical exercise is widely recommended for patients with DM1, as it helps to improve glycemic control (Moser, Eckstein, et al., 2020) and contribute to reducing complications (Huerta-Uribe et al., 2023; Farooqui et al., 2025), the accuracy of MSG blood glucose estimates during exercise may be reduced, particularly during continuous moderate-intensity exercise (Da Prato et al., 2022). Therefore, high MARD values can contribute to a greater risk of hypoglycemia and compromise the patient's decision-making regarding glycemia correction actions. Thus, the study's objective was to evaluate whether the practice of physical exercise, duration of exercise, intensity of exercise, and period of the day during which physical exercise is performed influence the percentage of absolute mean difference (MARD) in children or adolescents with DM1.



## Method

### Procedure

This longitudinal observational study has a short follow-up (7 days). The data were obtained in two situations, one in the initial assessment to obtain data that characterize the sample and another during using the iPro 2 continuous glucose monitoring (GMS) sensor for seven days. During a routine consultation at the medical outpatient clinic of the Interdisciplinary Center for Diabetes (CENID) patients were invited to participate in the study; after acceptance, a clinical assessment was carried out during a medical consultation, anthropometric assessment, and scheduling for placement and guidance on the use of the GMS sensor (iPRO2- medidtronic) and filling out the Bouchard activity log(Lima et al., 2017).

### Participants

The sample was a non-probabilistic convenience sample consisting of 64 children and adolescents aged 6 to 19 years with a diagnosis of type 1 diabetes mellitus for at least 12 months, treated at the CENID of the specialty medical outpatient clinic at Hospital Beneficente Unimar (HBU) from the University of Marília (UNIMAR), which receives patients from the Unified Health System (SUS) referred by the Municipal Health Department via CROSS. Patients who had a physical disability with poor functioning or paralysis of the upper and/or lower limbs that limited physical activity behavior, as well as those with some cognitive disability with limitations in understanding and recording physical activity records, were not included in the study.

#### *Physical Activity Quiz*

The data were obtained with the authorization of the patient and their legal guardian after signing the Free and Informed Assent Form and Free and Informed Consent Form. The procedures used in this research complied with the Ethics Criteria for Research with Human Beings as per resolution no. 466/12 of the National Health Council. The project was approved by the Ethics and Research Committee of the University of Marília (opinion: 3.606.397/2019).

### Data analysis

Data on age, sex, anthropometry, insulin administration method, and maturation stage were obtained through a medical consultation carried out on the day of the first consultation. The maturational stage was obtained using the Tanner sexual maturation scale and was stratified into pre-pubertal, pubertal, and post-pubertal. Regarding the method of insulin administration, patients were grouped into patients using the Continuous Insulin Infusion System (CIISCIIS- insulin infusion pump) and patients using multiple doses of insulin (MDI). Anthropometric body mass and height data were used to estimate the BMI z-score.

The physical activity level (PAL) was obtained through the physical activity recall proposed by Bouchard (Lima et al., 2017) during the seven days of use of the GMS sensor. The physical activity record is divided into 96 periods of 15 minutes per day, and physical activity is categorized on a scale of 1 to 9 categories of energy expenditure by MET's relative to the intensity of the activity performed. Category 4 was considered for light intensity, category 6 (six) for moderate intensity, and categories 8 (eight) and 9 (nine) for vigorous intensity to analyze the performance of physical exercise and its intensity. From the records of physical activity categories, days with or without physical exercise were identified, the duration of exercise per day (minutes), the period of the day in which physical exercise was performed (morning, afternoon, or night), the intensity of physical exercise per day (no exercise, light, moderate and vigorous) and the total number of minutes of physical exercise per week (minutes/week).

The duration of physical exercise per day was categorized as  $\leq 60$  minutes per day and  $> 60$  minutes per day. The time in minutes per week of moderate and vigorous intensity physical exercise (categories 6, 8, and 9) was used to classify the physical activity level (PAL) for the week of use of the GMS sensor. Thus, PAL was categorized into "Little active" ( $< 150$  minutes of physical exercise per week), "Active" (150 to 300 minutes of physical exercise / week), and "Very active" ( $>$  minutes of physical exercise per week)(Bull et al., 2020). For each patient, 7 days of physical exercise were recorded corresponding to the days of use of the GMS sensor and 448 days of data recording for analysis.



MARD percentage was used to estimate the accuracy of blood glucose estimates. The data were obtained using continuous glucose monitoring equipment (GMS) and a professional iPro2 model (MEDITRONIC®) with an Enlite sensor. Data were extracted using CareLink iPro® software. To calibrate blood glucose estimates and calculate the %MARD, the iPro2 uses capillary blood glucose measurements that were carried out four times a day with a minimum interval of 4 hours and a maximum of 12 hours (Moser et al., 2019). To avoid bias in capillary blood glucose measurement due to the equipment, all patients measured capillary blood glucose using the Roche brand Accu-check Active glucose monitor and strips provided by the research team. To analyze the accuracy (precision) of the blood glucose estimate, the iPro2 system generates a report with the calculations of the parameters of the number of valid calibrations and percentage of mean absolute difference (%MARD) per day and for the total period of seven days of sensor use. Only capillary blood glucose values between 40 and 400 mg/dl (2.2 and 22.2 mmol/l) were considered for calibration.

MARD percentage indicates the difference between the capillary measurement and the interstitial blood glucose estimate made by the sensor in percentage values. MARD values were categorized considering three cut-off points to analyze the adequacy of the accuracy of blood glucose estimation for clinical decision-making. The cut-off point of %MARD < 10% was used as the main reference criterion (Heinemann et al., 2020); however, the cut-off points recommended by the manufacturer of MARD ≤ 18% for blood glucose values <100 mg/dL and %MARD ≤ 28% for blood glucose values ≥100 mg/dL were also used (Pepper et al., 2012).

Qualitative variables were characterized by their absolute frequency (*f*) and relative frequency (%), while quantitative variables were described through the mean, standard deviation, median, minimum value, and maximum value. Normality distribution was assessed using the Komogorov-Smirnov test with Lilliefors correction. Associations among qualitative variables were examined using the Chi-square test, while correlation between quantitative variables was assessed using Pearson's test. Differences in means between two independent groups were analyzed employing the Student's t-test, with homogeneity of variances checked using Levene's test. When necessary, comparisons of means among more than two independent groups were conducted through the one-way ANOVA test, followed by the Bonferroni post-hoc test. Throughout these analyses, SPSS version 19.0 for Windows software was utilized, with a significance level of 5% applied.

## Results

The sample did not show a significant difference in the distribution of sex ratio, PAL, and maturation stage. The largest proportion of the sample uses multiple doses of insulin (MDI) as a method of insulin administration (Table 1).

Table 1. Absolute (*f*) and relative (%) frequency distribution of the qualitative variables that characterize the sample.

		<i>f</i>	%	p-value
Sex	Male	30	46.9	0.617
	Female	34	53.1	
PAL	< 150 min/week	18	28.1	0.444
	150 a 300 min/week	26	40.6	
	>300 min/week	20	31.3	
Maturation stage	Pre-pubescent	15	23.4	0.137
	Pubescent	21	32.8	
	Post-pubertal	28	43.8	
Insulin administration method	CIIS	23	35.9	0.024*
	MDI	41	64.1	

Physical Activity Level (PAL); Continuous insulin infusion system (CIIS); Multiple doses of insulin (MID); Continuous blood glucose monitoring (GMS); \* indicates a significant difference in proportion distribution using the Chi-square test.

The sample characteristics, mean blood glucose, and MARD% were compared in relation to the PAL presented during the week of sensor use (GMS). No significant difference was observed between the different activity behaviors for age, time of diagnosis, HbA1c<sup>0</sup>, mean glycemia, and MARD% (Table 2).

The MARD% values presented in Table 2 refer to the average values for the seven days of use of the GMS.

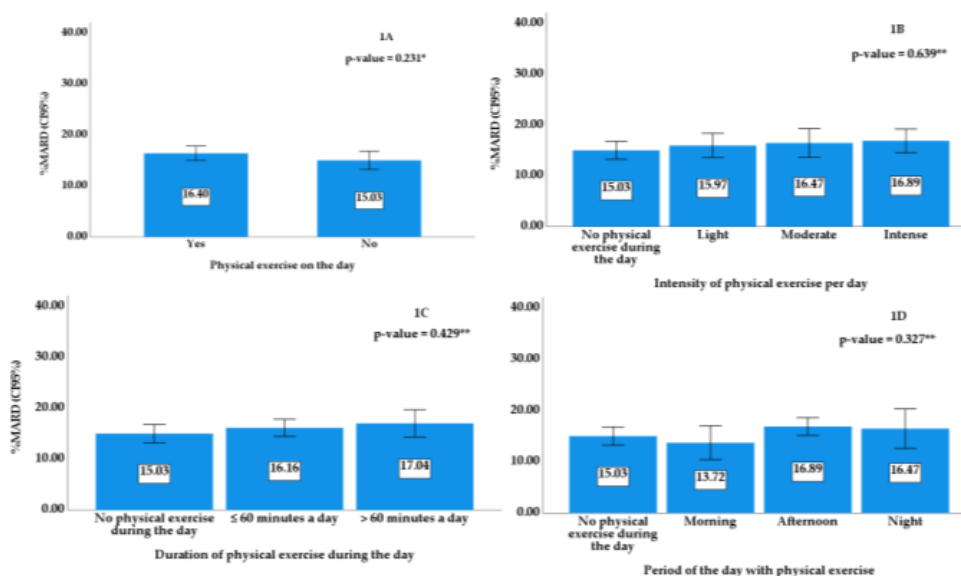
Table 2. Comparison of sample characteristics means in relation to Physical Activity Level (PAL).

Variable	PAL						p-value			
	< 150 min/week (n=18)			150 a 300 min/week (n=26)				>300 min/week		
	Mean	Min	Max	Mean	Min	Max	Mean	Min	Max	
Age (years)	12.1	7	18	13	6	19	12.5	6	17	0.628
Diagnosis time (years)	4.7	1	11	4.7	1	13	5.7	1	15	0.54
BMI z-score	0.68	-1.38	3.01	0.54	-2.6	4.36	0.42	-2.08	2.32	0.847
Average blood glucose (mg/dL)	177.2	126	257	162.5	105	256	162	103	229	0.275
HbA1c (%)	8.5	6.5	16.9	8.3	6.3	11.5	8.4	6.6	13	0.930
MARD (%) total	13.8	4.5	27.9	16.5	2.8	36.6	18.4	7.4	33.7	0.149

Physical activity level (PAL); Minutes per week (min/week); Minimum (Min); Maximum (Max); Glycated hemoglobin (HbA1c); Relative absolute Mean Difference (MARD); p-value calculated by one-way ANOVA. %MARD total indicates the average value for the 7-day period of sensor use.

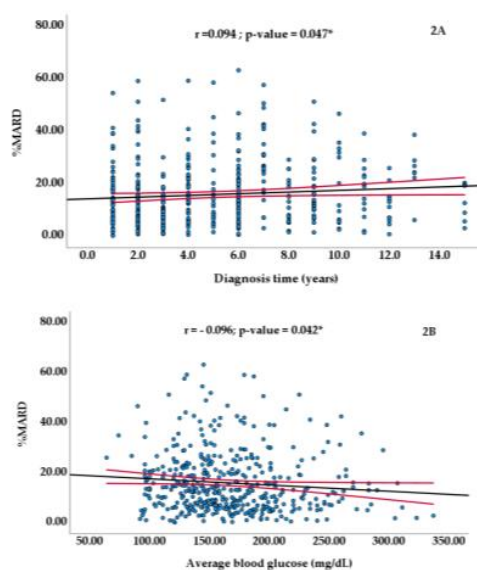
Figure 1 shows the effect on the day of exercise (yes or no), the intensity of exercise on the day (no exercise, light, moderate or vigorous), the duration of exercise on the day (no exercise,  $\leq 60$  minutes and  $> 60$  minutes) and period of the day during which the exercise was performed (no exercise, morning, afternoon or night) on the total %MARD during the period of sensor use; however, no significant effect of these exercise parameters on the MARD values was observed.

Figure 1. Comparison of the Mean and 95% confidence interval (95% CI) of the MARD percentage per day with exercise (1A), by exercise intensity (1B), duration of exercise on the day (minutes) (1C) and period of exercise on the day (1D). Mean absolute relative difference (MARD); significance level of 5% (p-value  $\leq 0.05$ ); \* p-value calculated by the Student t-test for independent samples; \*\* p-value calculated by the one-way ANOVA test.



A correlation analysis of MARD per day was performed with age, time since diagnosis, BMI z-score, HbA1c, and average blood glucose during the period of sensor use. There was no significant correlation between MARD and age, BMI z-score, and HbA1c (values not shown). However, a significant correlation was found between MARD and diagnosis time (Figure 2A) and average blood glucose during sensor use (Figure 2B). The increase in diagnosis time was related to the rise in MARD values. On the other hand, the increase in average glycemia was related to the reduction in MARD% values. It is worth highlighting that, although significant, the observed correlation coefficients indicate a low correlation.

Figure 2. Analysis of the correlation of MARD percentage per day with diagnosis time (2A) and Mean glycemia during sensor use (2B). Mean absolute relative difference (MARD percentage); Glycemia Mean (GL Mean); Pearson correlation coefficient (r); \* indicates significant correlation using the Pearson test for a significance level of 5% (p-value  $\leq$  0.05).



In Table 3, %MARD data was categorized into <10% and  $\geq$ 10% for comparison with sample characteristics and exercise parameters during sensor use. For this analysis, the MARD percentage value per day was considered. A significant association between %MARD and PAL was observed during the week of sensor use. Subjects with longer periods of exercise, considering moderate (150 to 300 min/week) and vigorous (>300 min/week) PAL had a higher percentage of %MARD >10%.

Table 3. Analysis of the association of sample characteristics and physical exercise behavior with the frequency distribution of MARD <10%.

Variables	Category	MARD (%)		p-value
		<10% n=171 (38.2%)	$\geq$ 10% n=277 (61.8%)	
Sex	Male	89 (42.4%)	121 (57.6)	0.085
	Female	82 (34.5%)	156 (65.5%)	
Maturation stage	Pre-pubescent	50 (47.6%)	55 (52.4%)	0.054
	Pubescent	52 (35.4%)	95 (64.6%)	
	Post-pubertal	69 (35.2%)	127 (64.8%)	
Insulin administration method	CIIS	56 (36.4%)	98 (63.3%)	0.569
	MDI	115 (39.1%)	179 (60.9%)	
Exercise in the day	Yes	101 (36.7%)	174 (63.3%)	0.429
	No	70 (40.5%)	103 (59.5)	
Exercise intensity per day	No exercise	70 (40.5%)	103 (59.5%)	0.133
	Light	48 (41.7%)	67 (58.3%)	
	Moderate	24 (34.8%)	45 (65.2%)	
	Intense	29 (31.9%)	62 (68.1%)	
Duration of exercise per day	No exercise in the day	70 (40.5%)	103 (59.5%)	0.388
	<60 minutes	74 (37.4%)	124 (62.6%)	
	> 60 minutes	27 (35.1%)	50 (64.9%)	
Exercise time of day	No exercise in the day	70 (40.5%)	103 (59.5)	0.386
	Morning	15 (42.9%)	20 (57.1%)	
	Afternoon	66 (35.4%)	121 (64.7%)	
	Night	20 (37.7%)	33 (62.3%)	
PAL (week)	Mild (<150 min/week)	57 (47.5%)	63 (52.5%)	0.006*
	Moderate (150-300 min/week)	69 (37.9%)	113 (62.1%)	
	Vigorous (>300 min/week)	45 (30.8%)	101 (62.9%)	

Mean Absolute Relative Difference (MARD); Continuous insulin infusion system (CIIS); Multiple doses of insulin (MID); Physical activity level (PAL); p-value calculated by the Chi-square test for association. \* Indicates a significant difference in proportion distribution for p-value  $\leq$  0.050.

Table 4 categorized the MARD percentage values per day according to the manufacturer's recommendations as  $\leq$  18% and > 18%. This cut-off point is suggested when Mean blood glucose values are below

100 mg/dL. A significant association between sex and the maturation stage was observed. A higher proportion of MARD values > 18% was observed in females and the post-pubertal maturational stage. Patients with more physical exercise time per week related to moderate and vigorous PAL also had higher proportions of MARD >18%.

Table 4. Analysis of the association of sample characteristics and physical exercise behavior with the frequency distribution of MARD ≤18%.

Variables	Category	MARD (%)		p-value
		≤ 18% n=309 (69.0%)	>18% n=139 (31.0%)	
Sex	Male	159 (75.7%)	51 (24.3%)	0.004*
	Female	150 (63.0)	88 (37.0%)	
Maturation stage	Pre-pubescent	78 (74.3%)	27 (25.7%)	0.046*
	Pubescent	106 (72.1%)	41 (27.9%)	
	Post-pubertal	125 (63.8%)	71 (36.2%)	
Insulin administration method	CIIS	102 (66.2%)	52 (33.8%)	0.365
	MDI	207 (70.4%)	87 (29.6%)	
Exercise in the day	Yes	184 (66.9%)	91 (33.1%)	0.234
	No	125 (72.3%)	48 (27.7%)	
Exercise intensity per day	No exercise	125 (72.3)	48 (27.7%)	0.189
	Light	79 (68.7%)	36 (31.3%)	
	Moderate	46 (66.7%)	23 (33.3%)	
	Intense	59 (64.8%)	32 (35.2%)	
Duration of exercise per day	No exercise in the day	125 (72.3%)	48 (27.7%)	0.124
	< 60 minutes	136 (68.7%)	62 (31.3%)	
	> 60 minutes	48 (62.3%)	29 (37.7%)	
Exercise time of day	No exercise in the day	125 (72.3%)	48 (27.7%)	0.143
	Morning	28 (80.0%)	7 (20.0%)	
	Afternoon	120 (64.2%)	67 (35.8%)	
	Night	36 (67.9%)	17 (31.2%)	
PAL (week)	Mild (<150 min/week)	91 (75.8%)	29 (24.2%)	0.012*
	Moderate (150-300 min/week)	128 (70.3%)	54 (29.7%)	
	Vigorous (>300 min/week)	90 (61.6%)	56 (38.4%)	

Mean Absolute Relative Difference (MARD); Continuous insulin infusion system (CIIS); Multiple doses of insulin (MDI); Physical activity level (PAL); p-value calculated by the Chi-square test for association. \* indicates a significant difference in proportion distribution for p-value ≤ 0.050

In Table 5, MARD values were categorized according to the manufacturer's recommendations as ≤ 28% and > 28%. This cut-off point is suggested when mean glycemia is greater than or equal to 100 mg/dL. A higher proportion of MARD >28% was observed in females. The increase in exercise duration per day was found to be related to the increase in the proportion of MARD >28%. Concerning the PAL of the week, the main factor in the rise in the proportion of %MARD > 28% was the vigorous PAL.

Table 5. Analysis of the association of sample characteristics and physical exercise behavior with the frequency distribution of MARD ≤ 28%.

Variables	Category	MARD ≤ 28%		p-value
		≤ 28% n=384 (85.7%)	>28% n=64 (14.3%)	
Sex	Male	188 (89.5%)	22 (10.5%)	0.031*
	Female	196 (82.4%)	42 (17.6%)	
Maturation stage	Pre-pubescent	89 (84.8%)	16 (15.2%)	0.734
	Pubescent	126 (85.7%)	21 (14.3%)	
	Post-pubertal	169 (86.2%)	27 (13.8%)	
Insulin administration method	CIIS	128 (83.1%)	26 (16.9%)	0.256
	MDI	256 (87.1%)	38 (12.9%)	
Exercise in the day	Yes	229 (83.3%)	46 (16.7%)	0.063
	No	155 (89.6%)	18 (10.4%)	
Exercise intensity per day	No exercise	155 (89.6%)	18 (10.4%)	0.132
	Light	96 (83.5%)	19 (16.5%)	
	Moderate	57 (82.6%)	12 (17.4%)	
	Intense	76 (83.5%)	15 (16.5%)	
Duration of exercise per day	No exercise in the day	155 (89.6%)	18 (10.4%)	0.027*
	< 60 minutes	168 (84.8%)	30 (15.2%)	
	> 60 minutes	61 (79.2%)	16 (20.8%)	
Exercise time of day	No exercise in the day	155 (89.6%)	18 (10.4%)	0.051
	Morning	32 (91.4%)	3 (8.6%)	



	Afternoon	152 (81.3%)	35 (18.7%)	
	Night	45 (84.9%)	8 (15.1%)	
PAL (week)	Mild (<150 min/week)	108 (90.0%)	12 (10.0%)	0.012*
	Moderate (150-300 min/week)	160 (87.9%)	22 (12.1%)	
	Vigorous (>300 min/week)	116 (79.5%)	30 (30.5%)	

Mean Absolute Relative Difference (MARD); Continuous insulin infusion system (CIIS); Multiple doses of insulin (MID); Physical activity level (PAL); p-value calculated by the Chi-square test for association. \* indicates a significant difference in proportion distribution for p-value  $\leq$  0.050.

## Discussion

When analyzing the percentage of MARD values in the data set (per day), it was found that 38.2% had MARD values <10%. MARD values <10% indicate high reliability for clinical decision-making based on glycaemia data provided by the GMS. However, MARD values <10% are used to validate the use of the equipment through comparison with blood glucose measurements by reference method (Siegmund et al., 2017).

Therefore, when considering that during the use of the GMS sensor, equipment calibration, and MARD estimates are carried out based on capillary blood glucose (performed and recorded by the user), the use of cut-off points to analyze MARD performance (%) suggested by the manufacturer can provide the patient with important information for decision-making regarding glycemia correction based on the glycemia values provided by the GMS. However, it is worth highlighting that although MARD is considered an important measure for analyzing the accuracy of GMS sensors, there are no clinical studies in people with diabetes that prove that this parameter can accurately differentiate between a safe and unsafe sensor or between a clinically more and less effective sensor (Vigersky & Shin, 2024).

Researchers point out many factors that can influence the accuracy of blood glucose estimation. Medication use is one of them (Cappon et al., 2019). However, this was not controlled in this study. For these reasons, differences in the equipment's brand, model, and conditions for measuring capillary blood glucose represent an important source of bias in the study, as they can lead to incorrect calibrations and estimates of the MARD percentage (Heinemann et al., 2020). To avoid this, in our research, capillary blood glucose measurements were carried out using equipment and tapes provided by the researcher to minimize bias.

Another factor that can contribute to incorrect estimates of blood glucose by the GMS and, consequently, inaccurate estimates of the MARD (%) is the blood glucose values. Considering that the GMS estimates blood glucose from interstitial glucose and the interstitial flux (IF) of glucose is dependent on the rate of diffusion of glucose from the plasma to the IF and the rate of glucose uptake by subcutaneous tissue cells, blood glucose values low levels can lead to incorrect blood glucose estimates by the GMS (Cengiz & Tamborlane, 2009). Therefore, to analyze the effect of physical exercise on the MARD percentage, both cut-off points suggested by the manufacturer were considered. The MARD value  $\leq$  18% is recommended for blood glucose values <100 mg/dL, and the MARD value  $\leq$  28% for blood glucose values  $\geq$  100 mg/dL. Although the data set, considering the weekly mean, did not present glycemia values below 100 mg/dL, when analyzing the data set per day, glycemia values below 100 mg/dL were verified, which justifies using both cut-off points for MARD analysis.

When considering MARD values  $\leq$  18%, it was found that 69% of the data set presented adequate MARD values for clinical decision-making and glycemia adjustment by the patient. However, when considering MARD values  $\leq$  28%, it was found that 85.7% of the data set provided safe glycemia estimates for clinical decision-making and glycemia correction. Although glycemia monitoring by GMS is accepted for monitoring and correcting glycemia when it is below 100 mg/dL and in physical activity conditions, the risk of hypoglycemia episodes is greater. It may require the use of capillary glycemia (Siegmund et al., 2017).

Regarding the influence of physical exercise on MARD, the main effect was verified in relation to the total number of minutes of physical activity during the week. For all cut-off points used, it was found that the increase in time in minutes of physical activity per week was related to the rise in the percentage of MARD values that were inadequate for clinical decision-making and glycemia corrections. In this sense, it is recommended that, with the increase in the time in minutes per week of physical exercise,

greater attention be paid to the symptoms of hypoglycemia, and the capillary blood glucose measurement is introduced into the routine when interstitial blood glucose values do not correspond to the symptoms. Aiming to minimize the impact of possible discrepancies between capillary and interstitial glycemia on the patient's decision-making regarding glycemia correction, GMS equipment currently provides feedback on the history of interstitial glycemia through trend arrows (Elbarbary et al., 2021).

Although the trend arrows provide complementary information about possible differences between interstitial and capillary blood glucose estimates, they are based on algorithms and may not be able to incorporate patients' individualities or provide sufficient data for adequate decision-making (Rodacki et al., 2021). The GMS estimation error is partly due to the time delay between the glucose value in the vasculature and the interstitial fluid, which is approximately 5 minutes in rest situations but can reach 24 minutes during and after physical exercise (Moser, Riddell, et al., 2020). For the other parameters used to analyze the influence of physical exercise on %MARD, no significant effect was observed between days with and without physical exercise, exercise intensity on the day, and the period of the day in which the exercise was performed. However, there are indications that physical exercise performed on an empty stomach in the morning may contribute to an increase in blood glucose during exercise, but with a greater risk of hypoglycemia after exercise (Houlder & Yardley, 2018).

However, in a study that compared the effect of continuous moderate-intensity exercise and high-intensity interval exercise on the accuracy of glycemia estimation by different GMS sensors in young adults with DM1, continuous exercise contributes to higher MARD% values concerning high-intensity interval exercise. However, no significant difference was found between the sensors (Da Prato et al., 2022). Continuous moderate-intensity exercise predominates aerobic metabolism and is usually performed for more extended periods than high-intensity interval exercise, which predominates anaerobic metabolism. Moderate-intensity aerobic orientation exercise leads to more significant reductions in blood glucose during exercise. On the other hand, high-intensity anaerobic guidance exercise can increase blood glucose during exercise. However, both in the recovery period lead to reduced blood glucose (Adolfsson et al., 2022).

Thus, moderate intensity and long duration of physical exercise can contribute more expressively to reducing blood glucose quickly, increasing the risk of hypoglycemia, and contributing to the elevation of MARD. In this study, the increase in exercise duration on the day significantly affected the rise in the percentage of MARD > 28% values, indicating that MARD values are inadequate for decision-making to correct blood glucose from the values provided by the MSG sensor. High MARD values are related to incorrect estimates of glycemia by the GMS, especially in conditions with low glycemia values (< 100 mg/dL) for exercise, which increases the risk of hypoglycemia in conditions of physical exercise lasting longer than 60 minutes (Price & Walker, 2016).

In addition to physical exercise, the results showed other factors significantly influencing the MARD values. Although the observed correlation coefficient indicates a low correlation, the increase in diagnostic time and the reduction in mean glycemia for the day are related to the rise in MARD values. These results corroborate another study that observed an increased MARD in blood glucose levels < 70 mg/dL on the Dexcom G7 and FreeStyle Libre 3 sensors (Hanson et al., 2024). Although our study did not use other models and brands of sensors for comparison, which can be considered a limitation. These findings are similar to those of other studies concerning MARD and its increase during exercise (Biagi et al., 2018; Da Prato et al., 2022). In addition, the mean values of %MARD for days with exercise (16.4 12.0) and without exercise (15.0 11.9) were similar to the findings of other studies with different types of sensors presented in a review study (Muñoz Fabra et al., 2021).

This research also verified that sex and stage of maturation, according to the Tanner scale, are also possible factors that influence the MARD. In females, a higher proportion of MARD percentage values were found to be inadequate for decision-making following the cut-off points suggested by the manufacturer. For the maturation stage, it was observed that the progression of maturation toward adulthood is related to the increase in the proportion of %MARD values > 18%. To the best of our knowledge, among the studies that analyzed the influencing factors on the accuracy of glycemia estimates by GMS by MARD (Huang et al., 2022), the effect of sex and maturation stage on the values of MARD so far.

An important point of this study's results is the included population. Only a few studies have evaluated the effect of physical exercise on the MARD in children and adolescents, but mainly on children aged 6



to 10 years in whom much of the time spent with physical activity occurs in non-systematized physical activities. Another relevant point concerns the analysis of different parameters of physical exercise in real-life conditions, which favors a closer approximation to clinical practice. However, studies that can evaluate the effect of exercise on MARD with monitoring of physical activity, both through recall recording and expenditure data through accelerometry and heart rate through telemetry, may bring new perspectives on the impact of physical exercise on the accuracy of glycemia estimation by GMS.

## Conclusions

The increase in the duration of physical exercise on the day and the increase in time in minutes per week of physical exercise contribute to the rise in the proportion of inadequate MARD values for clinical decision-making and the patient for corrections of blood glucose. These findings suggest that, during and after physical exercise, the presence of interstitial glycemia values by GMS that are discrepant from hyperglycemic symptoms, the patient should support decision-making to correct glycemia based on the trend arrows provided by the GMS equipment, as well as carrying out capillary blood glucose measurements to confirm blood glucose values.

## Aknowledgements

We would like to thank the University of Marília (UNIMAR), the Postdoctoral Program of São Paulo State University “Júlio de Mesquita Filho” – UNESP, the Coordenação de Aperfeiçoamento de Pessoal de Nível Superior (CAPES) for granting the Social Demand Scholarship to the author LV Alves, and the Conselho Nacional de Desenvolvimento Científico e Tecnológico (CNPq) for granting the Productivity Scholarship to the author LRA Gabriel Filho (Proc. 317061/2023-2).

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