






Do estimated metabolic equivalent and energy expenditure verify the physical effort of type-1 diabetics in resting and exercise situations? A randomized crossover trial

O equivalente metabólico estimado e o gasto energético verificam o esforço físico de diabéticos tipo 1 em repouso e exercícios? Um ensaio cruzado randomizado

¿El equivalente metabólico y el gasto energético estimados verifican el esfuerzo físico de los diabéticos tipo 1 en situaciones de reposo y ejercicio? Un ensayo cruzado aleatorio

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Keywords:

Metabolic equivalent;
Diabetes mellitus;
Physical exercise;
Video game.

ABSTRACT

To compare measured and estimated metabolic equivalent (MET) and energy expenditure (EE) in different situations with Type-1 diabetes (T1DM) patients. Ten T1DM patients performed three 30-minute sessions (resting, running-RS, and exergame-VS) at moderate intensity. MET and EE were measured by direct gas analyzer and estimated using the formula applying heart rate and $\dot{V}O_2$ peak. MET values (measured vs. estimated) were statistically different during RS (4.58 ± 1.11 vs. 7.59 ± 1.36) and VS (3.98 ± 0.84 vs. 5.77 ± 0.84) ($p < 0.001$). EE values were similar: RS (147 ± 43 vs. 246 ± 157) and VS (129 ± 33 vs. 184 ± 20) ($p < 0.001$). The error between the methods: 0.41, 1.51, and 1.07 METs and 20.1, 51.5, and 32.5 Kcals for resting, RS, and VS. Estimation could be used in resting and with caution for RS and VS.

Palavras-chave:

Equivalente metabólico;
Diabetes mellitus;
Exercício físico;
Videogame.

RESUMO

Comparar o equivalente metabólico (MET) medido e estimado e o gasto energético (EE) em diferentes situações em pacientes com diabetes tipo 1 (DM1). Dez DM1 realizaram três sessões de 30 minutos (Repouso, Corrida-RS e Exergame-VS) em intensidade moderada. MET e EE foram medidos por um analisador direto de gases e estimados pela fórmula usando frequência cardíaca e $\dot{V}O_2$ pico. Valores MET (medidos vs. estimados) foram estatisticamente diferentes durante o RS ($4,58 \pm 1,11$ vs. $7,59 \pm 1,36$) e o VS ($3,98 \pm 0,84$ vs. $5,77 \pm 0,84$) ($p < 0,001$). Semelhante em EE: RS (147 ± 43 vs. 246 ± 157) e VS (129 ± 33 vs. 184 ± 20) ($p < 0,001$). O erro entre os métodos: 0,41, 1,51 e 1,07 MET e 20,1, 51,5 e 32,5 Kcal para Repouso, RS e VS. A estimativa pode ser usada em repouso e com cuidado durante RS e VS.

Palabras-clave:

Equivalente metabólico;
Diabetes mellitus;
Ejercicio físico;
Videojuego.

RESUMEN

Comparar el equivalente metabólico (MET) y gasto energético (EE) medido y estimado en diferentes situaciones en diabéticos tipo-1 (T1DM). Diez T1DM realizaron tres sesiones de 30 minutos (Descanso, Running-RS y Exergame-VS) en intensidad moderada. El MET y EE se midieron con un analizador de gases y se calcularon con fórmula utilizando la frecuencia cardíaca y VO_2 pico. Valores MET (medidos frente a estimados) eran estadísticamente diferentes durante RS ($4,58 \pm 1,11$ vs. $7,59 \pm 1,36$) y VS ($3,98 \pm 0,84$ vs. $5,77 \pm 0,84$) ($p < 0,001$). Similar en EE: RS (147 ± 43 vs. 246 ± 157) y VS (129 ± 33 vs. 184 ± 20) ($p < 0,001$). El error entre los métodos: 0.41, 1.51 y 1.07 MET y 20.1, 51.5 y 32.5 Kcal para Reposo, RS y VS. La estimación podría usarse en reposo y con cuidado durante RS y VS.

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INTRODUCTION

Differing predominance of aerobic/anaerobic metabolism during exercise (e.g. interval running) has been exploited in treatments with the general population and with type-1 diabetics (T1DM) (Colberg et al., 2015; Carvalho et al., 2021). However, low adherence levels have been observed (Colberg et al., 2015; Theng et al., 2015). Active videogames (AVG or exergames) can motivate patients to exercise at high levels of enjoyment increasing the chances of successful adherence (Brito-Gomes et al., 2016; Levac et al., 2017; Mellecker et al., 2013) with metabolic benefits for the general population and type-2 diabetics (DeSmet et al., 2014; Perrier-Melo et al., 2015).

T1DM individuals, similar to type-2 diabetics, also need to control blood glucose levels daily, before and after exercise due to possible hypoglycemia or hyperglycemia (ADA, 2019; Colberg et al., 2016; Madhu, 2015). Moreover, without correct management, the disease can exacerbate secondary problems related to diabetes (Akturk et al., 2018; Hashimoto et al., 2014; Riddell and Perkins, 2009; Yardley and Colberg, 2018). In prescribing exercise, care management should consider the intensity of exercise prescribed by therapists for T1DM patients undertaking exercise (ADA, 2019; Colberg et al., 2016, 2015; Garber et al., 2011). Therefore, assessing metabolism using direct gas analysis (gold standard method) to verify oxygen consumption, energy expenditure and metabolic equivalent (MET) during physical effort is faithful to prescription and highly recommended to avoid problems in T1DM patients (e.g. hypoglycemia). However, gold standard equipment is difficult to obtain in real-life situations.

As such, alternative variables when prescribing can be used to substitute gold standard values. Heart rate (HR) is an interesting variable because it can be physiologically related to physical effort (ADA, 2019; Colberg et al., 2016; Garber et al., 2011). Several studies have used HR to estimate MET and energy expenditure (EE) under different conditions (e.g. real or virtual with AVG and resting/sitting situations) and intensities (e.g. 0-3 light, 3-6 moderate, and >6.0 vigorous) however, only with healthy individuals (Barbosa et al., 2017; Brito-Gomes et al., 2016; Pereira et al., 2017; Perrier-Melo et al., 2017). T1DM patients present a different metabolic condition which may not present consistent responses under differing conditions (ADA, 2019; Colberg et al., 2016).

There is a lack of literature regarding MET and EE estimations as an alternative to verify physiological effort in T1DM patients, a method that could represent a low-cost alternative for T1DM patients. Therefore, this randomized clinical trial aims to compare measured and estimated MET and EE values in resting, and real and virtual exercise situations for T1DM patients. Sedentary behavior (e.g. sitting activities) and exercise sessions can encourage different metabolic changes (Riddell and Perkins, 2009; Barbosa et al., 2017; Yardley and Colberg,

2018). As such, we hypothesize that estimated and measured MET and EE values during resting sessions would present no difference in T1DM patients. While, T1DM patients under stress during exercise situations would present differences.

METHODS

ETHICAL ASPECTS, DESIGN AND RANDOMIZATION

This research was approved by the ethics committee of the local university (protocol: 029770/2016) and is part of a randomized crossover clinical trial (n^o U1111-1194-370) which was conducted in acute responses over four different days: 1st day: baseline data collection and resting situation. 2nd day: blood analysis (24h after day 1). Next, randomization (allocation ratio 1:1) was performed 48-196h after the 1st day. Finally, 3rd and 4th days: A real and/or virtual session.

SAMPLE SIZE, PARTICIPANTS, INCLUSION AND EXCLUSION CRITERIA

An a priori sample size calculation was performed using G*Power 3.1.9 software (Franz Faul, University Kiel, Germany), given $\alpha = 0.05$, power $(1-\beta) = 0.9$, with a large-very large value for the effect size (ES: 0.8) with two tails. $\beta = 0.10$ and very-large ES were set to possibly increase the study's final actual power with a slightly larger cohort of participants than $\beta = 0.20$ being required. Thus, a minimum of nine participants per group was required to undertake the study considering 3 situations.

Inclusion criteria were: (I) having T1DM for a minimum of 1.5 years with regular insulin use over this period; (II) having no other comorbidity conditions; and (III) not using antidepressant medication (IV) and adequate glycated hemoglobin values (7.0-12.0%) to approximate real-life metabolic T1DM conditions. Exclusion criteria were: (I) participants who did not complete all the situation sessions; (II) taking medication or engaging in exercise therapy during the study or (III) those with osteoarticular injuries.

PRIMARY OUTCOMES

Metabolic equivalent measurement: Maximum oxygen uptake (Maximal test) was measured at the initial evaluation (day 1) using a computerized Cortex metabolic analyzer (QUARK COSMED CPET, Minnesota, Germany) from a treadmill test (T150, COSMED, Minnesota, Germany or 10200, Imbramed, Porto Alegre-Brazil). The protocol consisted of a two-minute warm-up at 5km/h, after which the intensity was continuously increased by 1km/h until maximum voluntary fatigue was reached (Brito-Gomes et al., 2020). The test was discontinued based on the demonstration of at least two of the following criteria: (1) a plateau or decrease in $\dot{V}O_2$ with increasing load; (2) respiratory exchange coefficient

(RER) equal to or greater than 1.15; (3) 95% range of maximum predicted HR by age (220-age). Voluntary oxygen consumption ($\dot{V}O_{2\text{peak}}$) was adopted as the highest $\dot{V}O_2$ value observed before interrupting the test.

During all situations, MET and EE were monitored and a 30-minute-average was used for each T1DM patient in each situation.

Metabolic equivalent and exergy expenditure estimation: MET and EE were estimated using the following sequence of mathematical formulas (steps 1–3):

Step 1. Calculate $\dot{V}O_2$ intensity for each session using HR:

$$\text{Intensity of } \dot{V}O_2 \text{ max (\%IVO}_{2\text{max}}) = \frac{\text{average HR} - \text{resting HR}}{\text{maximal HR} - \text{resting HR}} \quad (1)$$

Step 2. Estimate the MET of the sessions after step 1

$$\text{MET} = \frac{\dot{V}O_2 \text{ peak (ml/kg/min}^{-1}) \times \%IVO_{2\text{max}}}{3.5 \text{ (ml/kg/min}^{-1})} \quad (2)$$

Step 3. EE calculation (Brito-Gomes et al., 2016; Heyward, 2004)

$$\frac{\text{Kcal}}{\text{min}} = \frac{(\text{Sessions' MET} \times \text{weight (kg)} \times 3,5)}{200} \times \text{duration's physical activity} \quad (3)$$

Recommendations were made to avoid the risk of bias and participants were asked: a) not to perform any vigorous physical activity at least 24h before or after beginning data collection; b) not to drink alcoholic, energetic or caffeine-containing beverages 24h prior to beginning data collection, and c) to maintain their regular dietary habits and participate while maintaining real-life nutritional conditions.

SECONDARY OUTCOMES

Capillary blood glucose (before and immediately after the session) was checked using a portable glucometer (Accu-Check Active, Roche, Brazil) following recommendations manufacture's before and after the sessions. Participants performed exercise sessions only if their capillary glycemia was between 100 to 250 mg/dL, with carbohydrates being consumed when necessary before exercising (100-139mg/dL). Otherwise, the exercise session was canceled and rescheduled within 48-72 h. After each session, participants only left the study location if their capillary glycemia presented normal values according to recommendations (ADA, 2019). The pre-post $\Delta\%$ blood glucose was used for metabolic change comparisons.

HR and QR were recorded for all situations and a 30-minute-average was determined for each T1DM patient in each situation.

INTERVENTIONS

Resting session: The resting situation took place in a comfortable chair without conversation, screen time, or other distractions. Participants remained

with both feet on the ground and were advised to relax but not to sleep. In this manner, HR, QR, and blood glucose would maintain stable levels.

The Real exercise session: The RS consisted of the treadmill running with 1:1 minute-ratio in moderate-intensity (45% vs. 59% $\dot{V}O_2$) according to the SBD (ADA, 2019) for 30 minutes. The maximum oxygen consumption achieved during the maximal test was used to determine the velocities of 45% and 59% $\dot{V}O_2$ (Garber et al., 2011). A three-minute warm-up was performed at 4-5 km/h to start the activity.

The Virtual exercise session: The virtual session (AVG session) is structured similarly to the RS situation, which has characteristics of an interval session. An Xbox 360[®] with Kinect console (Microsoft, USA), multimedia projector (Power Lite S10+, Epson, Japan) and sound amplifier (OCM 126 professional, Oneal, Brazil) was used. The *Kinect Adventures!* game[®] (Microsoft Game Studios, USA) was chosen because of the use of large muscle groups reaching intensity session values according to recommendations (Garber et al., 2011; Brito-Gomes et al., 2015a, b). Trials of the three most intense mini-games of *Kinect Adventures!* game[®] were performed (3×10 minutes): 1. River Rush, 2. Rally Ball, and 3. Reflex Ridge, respectively, to complete the 30-minute AVG session. Similar to the previous study, jumps, squats, and lateral shifts with vertical and horizontal shoulder extension (or a combination of these) were performed in all mini-games, collecting all possible pins (Brito-Gomes et al., 2019). Identical to the RS session, a three-minute free warm-up game was performed before starting the activity.

STATISTICAL ANALYSIS

The Shapiro-Wilk normality test was used and data were reported using the mean and standard deviation (SD). The paired *t*-test was used to compare measured vs estimated MET and EE values during resting RS, and virtual session situations. The repeated-measures ANOVA was performed to verify possible metabolic changes (QR, HR, and pre-post Δ Blood glucose) for all situations. Statistical differences were obtained presuming $P < 0.05$. The effect size (ES) was computed (Hopkins et al., 2009) with: 0.01-0.20 being considered small, $d = 0.21-0.50$ moderate, $d = 0.51-0.80$ large, and $d \geq 0.80$ very large.

The formulas used were:

$$\sqrt{\frac{F(df)}{F(df) + df}} \quad (4)$$

where "F" is the Anova value and "df" is the degree of freedom ($df = n - 1$).

The ES for t-tests were:

$$d = \frac{\bar{x}_t - \bar{x}_c}{\sqrt{\frac{(n_t - 1)s_t^2 + (n_c - 1)s_c^2}{n_t + n_c}}} \quad (5)$$

where “x” is the mean, “s” is the variance, “n” is the number of participants, “t” is the treatment group and “c” is compared/control group.

Finally, the Bland-Altman’s test was performed to verify the agreement of measured vs. estimated MET and EE values for each session. Moreover, linear regression was used to obtain the standard error for estimated MET and EE values for each session.

RESULTS

No drop-outs occurred prior to beginning the study protocol. The baseline characteristics and intervention values for T1DM patients are presented in Table 1. Statistical differences were found in metabolic-physiological variables among resting, RS, and VS exercise situations ($P < 0.05$). Large ESs were found.

The male vs female comparison was initially obtained, with no differences observed for either measured or estimated values for any situation ($p > 0.05$). Then, the whole cohort was analyzed ($n=10$) with the primary outcome data showing no statistical differences for MET resting values [measured: 1.13 ± 0.20 vs. estimated: 1.89 ± 1.57 ; $p = 0.170$; $d = 0.679$]. Statistical differences were observed during RS [4.58 ± 1.11 vs. 7.59 ± 1.36 ; $p < 0.001$; $d = 0.957$] and VS [3.98 ± 0.84 vs. 5.77 ± 0.84 ; $p < 0.001$; $d = 0.934$] sessions (Figure 1). Large and very large ESs were found.

Agreement between measured vs. estimated MET values for the sessions was verified using the Bland-Altman test. The MET estimation was fully calculated for resting [95%: -0.7 ($1.0, -3.7$)] and AVG [95%: -1.6 ($0.3, 3.5$)], with a single case outside the 95% confidence interval (inferior limit) being observed during the running session [95%: -2.8 ($-0.8, 4.9$)] (Figure 2). However, the linear regression for MET values showed a standard error of 0.41, 1.51, and 1.07 METs for resting, running, and AVG sessions.

Table 1. Baseline characteristics and intervention values with secondary outcome comparisons for type 1 diabetes patients ($n=10$).

Baseline characteristics			
Age (years)	24.9 ± 7.5		
Sex (♂ male ♀female)	$\text{♂ } 7 \text{ ♀ } 3$		
Lean Mass (kg)	45.4 ± 5.5		
Fat Mass (kg)	12.4 ± 2.9		
BMI ($\text{kg} \cdot \text{m}^{-2}$)	21.5 ± 2.0		
Glycated Hemoglobin (%)	8.6 ± 1.4		
$\dot{V}O_2$ Peak ($\text{ml} \cdot \text{kg} \cdot \text{min}^{-1}$)	37.4 ± 6.6		
Sessions			
	Resting	Real	Virtual
Maximal HR (bpm)	104 ± 14	$154 \pm 19^*$	$176 \pm 21^*$
Average HR (bpm)	83 ± 11	$133 \pm 14^*$	$132 \pm 12^*$
RER (value)	0.85 ± 0.09	$1.03 \pm 0.05^*$	$1.11 \pm 0.07^*$
Δ pre-post Blood glucose ($\text{mg} \cdot \text{dL}^{-1}$)	7 ± 24	$-59 \pm 31^*$	$-41 \pm 32^*$

Note: BMI: Body mass index. HR: Heart rate. $\dot{V}O_2$ Peak: Maximal Oxygen Consumption Measured by $\dot{V}O_2$ test. QR: Respiratory Coefficient. Δ : variation. $*P < 0.05$ compared to the Resting situation. Maximal HR: $P < 0.001$, and $d = 2.8$. Average HR $P < 0.001$ and $d = 3.3$; RER: $P < 0.001$ and $d = 6.2$. Δ pre-post Blood glucose: $P < 0.001$ and $d = 1.6$.

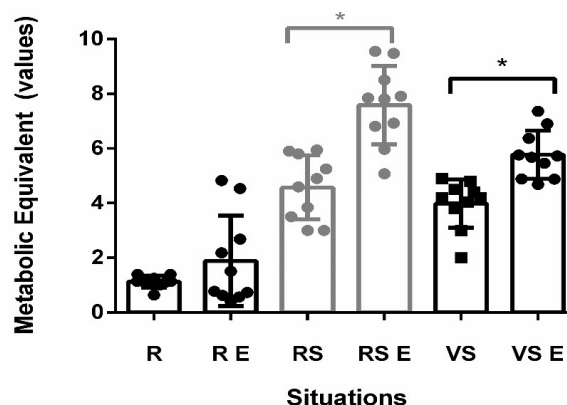


Figure 1. Measured and Estimated METs during the situations ($n=10$). Note 1 MET: R, Resting; RS – running exercise situation; VS – virtual exercise situation; E – Estimated. $*P < 0.05$ between measured and estimated MET values.

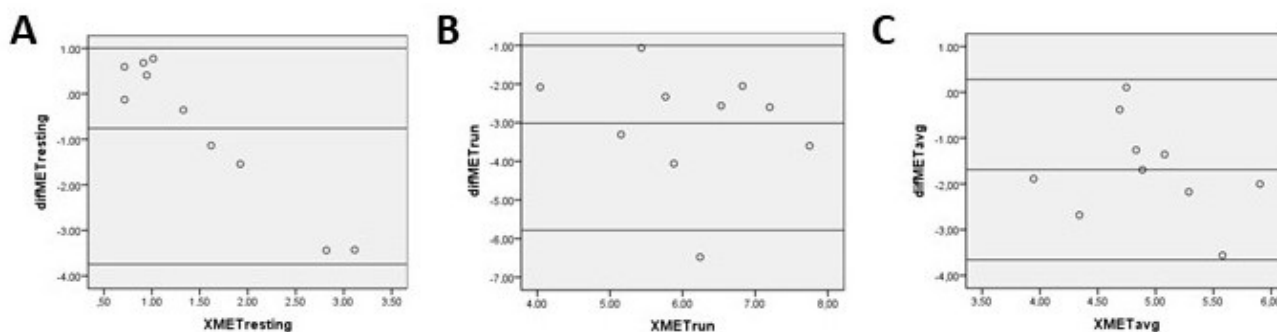


Figure 2. MET data verified by Bland-Altman for resting (panel A), running (panel B), and AVG (panel C) sessions.

Similar results in EE (kcal) without statistical differences for resting (measured vs. estimated) comparison [37±9 vs. 60±49; p=0.200; d=0.678] were observed. Furthermore, in exercise situations statistical differences were found during the RS [147±43 vs. 246±157; p<0.001; d=0.860] and VS [129±33 vs. 184±20; p<0.001; d=0.923] (Figure 3). Large and very large ESs were found.

Agreement between measured vs. estimated EE values for the sessions was determined using the Bland-Altman test. EE estimation was fully achieved for resting [95%: -21.4 (50.0, 120.0)] and AVG [95%: -49.4 (2.3, -101.0)], with a single case outside the 95% confidence interval (inferior limit) being observed for the running session [95%: -93.6 (-22.3, 164.9)] (Figure 4). The linear regression for EE showed a standard error of 20.1, 51.5, and 32.5 kcal for resting, running, and AVG.

DISCUSSION

This randomized clinical trial aims to compare measured and estimated MET and EE values in resting, running, and virtual exercise situations for T1DM patients. Our hypothesis was almost fully confirmed: *i*) Although the resting session presented no statistical differences

between measured and estimated MET and EE values, the active exercise situations for T1DM patients show statistical differences between measured vs. estimated values for MET and EE, *ii*) The MET and EE estimations by Bland-Altman test show the reasonable agreement limits for resting and VS sessions. A single case outside this interval was observed during the RS session. Finally, *iii*) The error between the methods: 0.41, 1.51, and 1.07 for MET and 20.1, 51.5, and 32.5 Kcal for resting, RS, and VS.

Several studies have adopted physiological variables to prescribe and verify physical effort under different conditions for healthy subjects. HR values have been used to estimate MET and EE values under different conditions including real exercise (e.g. running), virtual sessions with AVGs, and resting or sitting situations. Pereira et al. performed 15-minute real vs. virtual boxing with healthy subjects, finding statistical changes in MET (real: 4.9±1.4 vs. virtual: 4.1±1.4; p=0.005) and EE (real: 87.5±32.5 vs. virtual: 69.3±25.0; p=0.002) values. Otherwise, MET and EE values were estimated using HR and estimated VO₂ values by submaximal test, which may not reflect physiological metabolism.

Our study also performed moderate-intensity during real (4.58±1.11 METs) and virtual (3.98±0.84 METs) sessions when the gold standard method verifies metabolic changes (VO₂, MET, and EE). Otherwise, moderate-vigorous intensity was verified when the estimation was made, overestimating mean MET and EE values. This could be explained because the formula created other population and the diabetics metabolism was not included in this formula (ADA, 2019; Colberg et al., 2016).

It is important to note that regardless of whether it was a real (e.g. running) or virtual session, the measured secondary outcomes (HR, QR, and blood glucose) showed no statistical differences. Differences were only observed between active vs. the resting session. The similar metabolisms between active sessions could be explained due to the matched intensity and duration of the active sessions (Brito-Gomes et al., 2016; Carvalho et al., 2021). When verifying the resting session, the results showed no statistical differences between measured and estimated values, which is probably explained by the stability of the

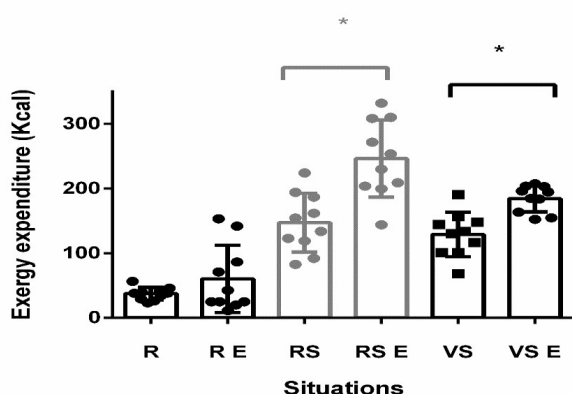


Figure 3. Measured and Estimated EEs during situations (n=10). Note: R, Resting; RS – running exercise situation; VS – virtual exercise situation; E – Estimated. *P<0.05 between measured and estimated EE values.

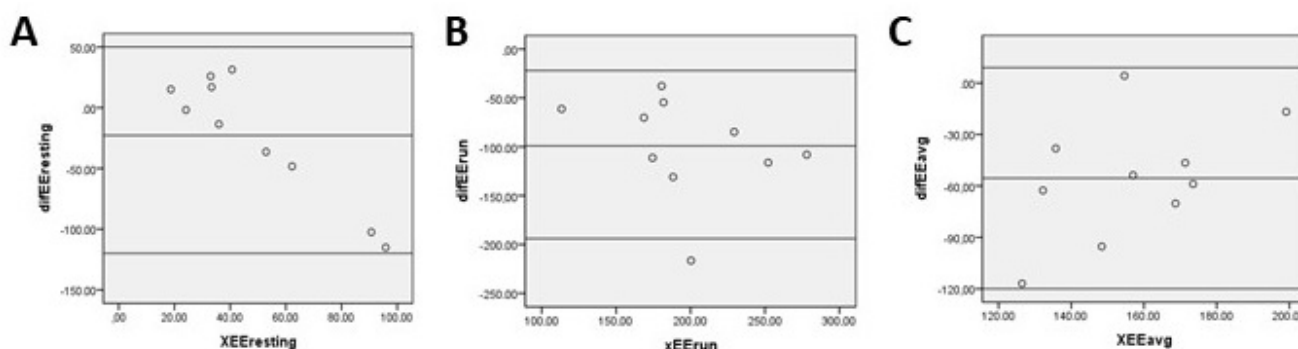


Figure 4. EE data verified by the Bland-Altman test for resting (panel A), running (panel B), and AVG (panel C) sessions.

resting session (ADA, 2019; Colberg et al., 2016; Riddell and Perkins, 2009).

While metabolic and secondary outcomes were similar between the exercise situations, they were statistically different from the resting session. Measured vs. estimated MET and EE values were statistically different for each active session. These differences could be due to different metabolic uptakes (e.g. respiratory coefficient, heart rate, and blood glucose) when observing resting (similar to basal metabolism) and active sessions (greater metabolic changes).

CLINICAL RELEVANCE, PRACTICAL APPLICATION, AND LIMITATIONS

Studies with T1DM patients are difficult mostly because of the small population size. However, this population performs exercises similar to non-diabetic individuals and as such requires scientifically reliable data. While we did consider the costs of metabolic assessment, unfortunately we should advise that the estimation of physical effort (MET and EE) during real or virtual sessions can over or underestimate values (t-test and Bland-Altman). Clinically, it is notable that previous crossover studies using MET and EE estimation have observed lower effect sizes ($d = 0.53 - 0.67$) (Pereira et al., 2017; Perrier-Melo et al., 2017) than our present crossover trial ($d = 0.68-93$) with T1DM patients.

The strong aspect of our study is that the MET and EE estimations were within agreement limits (Bland-Altman) for resting and VS sessions. However, a single case outside this interval was verified for the RS session and this data should be considered when health professionals or diabetics make use of these estimations. Therefore, for practical purposes, these formulas should be cautiously applied during active exercise sessions (especially RS) because measured moderate-intensity could over or underestimate MET and EE values. The error for these estimations could be around 0.41, 1.51, and 1.07 for MET and 20.1, 51.5, and 32.5 Kcal for resting, RS, and VS.

Study limitations include a possibly unrepresentative sample for specific metabolic control (7.5 to 11.5% Hba1C) due to the criteria adopted, despite having performed a sample size calculation, and an absence of sex-related data. Therefore, although sex comparisons present no statistical differences, future studies should analyze differences by sex for each situation. A single exercise intensity was verified (moderate). Finally, another glycosylated hemoglobin cohort should be studied (better control <7.0% and without control >12.0%).

CONCLUSION

The estimated MET and EE values should only be used for the resting situation and with care in the real and virtual situations because they can over or underestimate MET and EE values in T1DM patients.

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CONFLICTS OF INTEREST

Conflicts of interest declaration not received.

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