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Association of physical activity metrics with glucose variability in people with type 1 diabetes: A cross-sectional study

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Abstract

This study aims to investigate the association of physical activity metrics with measures of glucose variability in people with type 1 diabetes. From August 2019 to January 2022, people with type 1 diabetes, attending clinics or participating in ongoing research at the Dasman Diabetes Institute in Kuwait, were invited to participate in the study. Physical activity was measured over a 7-day period using a wrist-worn accelerometer, and glucose variability data were measured by continuous glucose monitoring (CGM) of the same period. Three hundred and eleven participants were recruited (age 33 (10) years, BMI 27(5) kg/m^2 and $n = 311$ (169 female and 142 male)). Overall physical activity levels were not associated with any measure of glucose variability. The intensity gradient, which measures the distribution of physical activity intensity, was negatively associated with mean glucose (−1.01(−0.28, −1.74) and $p = 0.007$), CONGA (−1.00(−0.28, −1.72) and $p = 0.007$), J-index (−11.7(−2.23, 21.2) and $p = 0.016$), HBGI (−2.73(−0.44, −5.02) and $p = 0.020$), GRADE (−2.27(−0.59, −3.95), $p = 0.009$) and GRADE – euglycaemia (−4.26(−0.46, −8.06) and $p = 0$–029) and the M-value (−4.41 (−0.05, −8.77) and $p = 0.049$). Overall physical activity remains important, but it may be worth recommending people with type 1 diabetes to spend proportionately more of their day doing moderate to higher intensity physical activity, although this remains to be confirmed in an appropriately designed trial.

KEYWORDS

exercise, glycaemic control, intensity, physical activity, type 1 diabetes

Highlights

- Physical activity is recommended to people with type 1 diabetes due to its broad health benefits.
- The relationship between physical activity and glucose variability is unclear.
- The current study shows that overall physical activity levels are not associated with measures of glucose variability, but spending proportionately more of their day doing moderate to higher intensity physical activity was associated with better glucose variability.

1 | INTRODUCTION

Worldwide, there are currently 537 million adults (20–79 years) living with diabetes, with a current prevalence of 10%, predicted to rise to 643 million by 2030 and 784 million by 2045 (International Diabetes Federation, 2021). In 2021, 6.7 million deaths were due to diabetes (International Diabetes Federation, 2021) Around 5%–10% of people with diabetes have type 1 diabetes, with prevalence of an upwards trajectory, which results in an increase in risk of microvascular and cerebrovascular disease (Daneman, 2006; de Ferranti et al., 2014; Pambianco et al., 2006). Indeed, people with type 1 diabetes have a 5–10-fold increase in risk of having a coronary heart disease (CHD) event (Livingstone et al., 2012), with the risk even higher if onset occurs at a younger age (Rawshani et al., 2018). At the age of 20 years, the life expectancy of people with type 1 diabetes is around 12 years lower, with around 1/3 of this excess risk due to cardiovascular disease (Livingstone et al., 2015), compared to people without diabetes. Kuwait has the third highest incidence of type 1 diabetes in the world (Shaltout et al., 2017).

It is established that physical activity has wide-ranging benefits in people with type 1 diabetes including a reduction in macrovascular risk, mortality, insulin resistance and blood lipids alongside improvements in cardiorespiratory fitness, endothelial function and well-being (Chimen et al., 2012), although evidence for effects on glycaemic control, as measured by HbA1c, is less clear (Kennedy et al., 2013). Physical activity is, therefore, recommended for people with type 1 diabetes (Colberg et al., 2016) although care must be taken as blood glucose responses to physical activity are highly variable (Biankin et al., 2003) with the potential to increase the risk of hypoglycemia. This is often cited as a barrier to participation in physical activity in people with type 1 diabetes (Cockcroft et al., 2020), although this has been made easier with continuous glucose monitoring (CGM) systems (Moser et al., 2020).

Previous research has shown that acute exercise, both aerobic and high intensity interval exercise, will reduce blood glucose levels in people with type 1 diabetes (Tonoli et al., 2012) and possibly influence glucose variability (Manohar et al., 2012; Reddy et al., 2019; van Dijk et al., 2016). Whilst these data are extremely useful, it does not represent the real-world association of physical activity with glycaemic control in people with type 1 diabetes. A study (n = 10) in adolescents reported an inverse relationship between glucose variability and moderate-vigorous physical activity (MVPA) (Jaggers et al., 2023). Another small study (n = 35) of young adults with type 1 diabetes found that overall physical activity levels were not associated with one measure, SD, of glucose variability (Martyn-Nemeth et al., 2017). Whilst overall physical activity levels are important, they do not provide any information about how the intensity of physical activity is distributed. The novel physical activity metric, the intensity gradient, which provides information on the intensity distribution of physical activity, can be used alongside overall physical activity levels to provide a full description of the activity profile. The intensity gradient has been shown to be associated with body fatness and muscle strength, independently of overall physical activity levels, in adolescent girls and in people with type 2 diabetes (Rowlands et al., 2018). To our knowledge, there are no studies which have investigated the association of overall physical activity and the intensity gradient with indices of glucose variability in people with type 1 diabetes.

The aim of the current study, therefore, is to investigate the associations of wrist-worn accelerometer-derived metrics of overall physical activity, intensity gradient and MVPA with measures of glucose variability in people with type 1 diabetes.

2 | MATERIALS AND METHODS

2.1 | Study setting and participants

From August 2019 to January 2022, people with type 1 diabetes aged ≥18 years, attending clinics or participating in ongoing research at the Dasman Diabetes Institute in Kuwait, were invited to participate in the study. All patients had documented diagnosis of type 1 diabetes (per ADA 2022 definition/criteria). This was confirmed by an undetectable C-peptide level at diagnosis and the presence of autoantibodies consistent with the diagnosis of type 1 diabetes. All patients graduated from the Dose Adjustment for Normal Eating (DAFNE) programme, which is a highly skilled structured education programme for type 1 diabetes. For the current study, demographic and clinical data were collected, and a CGM device and an accelerometer were worn for the same 7-day period. The study was fully explained to the participants, both orally and in writing, prior to providing them written informed consent. The study was approved by the Dasman Diabetes Institute Ethical Review Committee and followed the guidelines set out in the Declaration of Helsinki.

2.2 | Demographics

Age was calculated from participants' date of birth, clinical history was recorded and measurements of body mass, height, BMI and waist circumference were made. We collected the HbA1c, total cholesterol, HDL cholesterol, LDL cholesterol and triglycerides from the patients' electronic health records.

2.3 | Accelerometry

Participants were issued with a GENEActiv (Activinsights Ltd, UK) original wrist-worn accelerometer and instructed to wear this 24h per day for a 7-day period on the wrist of the dominant hand. The accelerometer was set to record at 100 Hz. Collected acceleration data were calibrated to local gravity using the methods established by van Hees et al. (van Hees et al., 2014). Data

extraction and processing was performed using GGIR defaults (version 2.8.2) which includes detection of sustained high values, nonwear detection and calculation of the average magnitude of acceleration corrected for gravity (Euclidean Norm minus 1g, ENMO) averaged over 5-s epochs (mg) (Migueles et al., 2019). Physical activity levels were quantified using methods previously described (Sabia et al., 2014; van Hees et al., 2013) with the intensity gradient calculated according to Rowlands et al. (2018). Overall acceleration (ENMO) was used as a measure of overall physical activity. The time spent in MVPA was considered as unbouted physical activity, to reflect updates to the physical activity recommendations, above 100 mg. The intensity gradient is derived from a plot of time accumulated (log – *y* axis) and activity intensity (log – *x* axis), and it is the gradient of this line, which is always negative which reflects the fact that there is less time spent at higher intensities. It depicts how activity intensity is distributed over a 24-h period. Lower values (more negative) indicate a larger portion of the day spent at high activity intensity, while a higher (less negative) value indicates more time spread across the different intensities. This is visually demonstrated in supplementary Figure S1. As per GGIR recommendations a valid day was defined as having >16 h of data in it, and we excluded participants with less than 3 valid days of data or if wear data were not present for each 15-min period of the 24-h cycle (van Hees et al., 2013). Data outputs were checked for calibration errors (>0.01 g) and if present data were excluded ($n = 0$).

2.4 | Continuous glucose monitoring

Glucose monitoring was via the Abbott Freestyle Libre Flash system (Abbott Diabetes Care) for the same 7-day period as the accelerometer was worn. Data were extracted and processed using the EasyGV Version 9.0 (Hill et al., 2011) for the calculation of measurements of glycaemic variability: mean glucose, standard deviation (SD), continuous overall net glycaemic action (CONGA), lability index (LI), J-index, low blood glucose index (LBGI), high blood glucose index (HBGI), glycaemic risk assessment diabetes equation (GRADE), GRADE % hypoglycemia, GRADE % euglycaemia, GRADE % hyperglycemia main of daily differences (MODD), average daily risk range (ADRR), mean amplitude of glycaemic excursions (MAGE), M-value and mean average glucose (MAG). Each of these terms is briefly described in supplementary Table S1. Those with less than 70% of wear time during the study period were excluded ($n = 7$) and not included in the participant numbers; no data imputation was carried out.

2.5 | Statistical analysis

General demographics, CGM and physical activity descriptive data are presented as mean (SD). Multiple linear regression analysis was employed to investigate the association of overall daily acceleration and the intensity gradient slope (exposures) with glycaemic variability metrics (outcome). Models were as follows: 1: unadjusted, 2: adjusted for sex, age and BMI and 3: model 2 plus adjustment for overall daily acceleration or intensity gradient slope (when not the exposure). The statistical analysis was conducted by using SPSS version 29, and a *p*-value ≤0.05 was considered statistically significant.

3 | RESULTS

3.1 | Participant characteristics

The current study includes 311 participants, 169 female and 142 males. The clinical and general demographics are presented in Table 1.

3.2 | Association of physical activity metrics with glycaemic variability

CGM and physical activity data are presented in Table 2. Across all models, there was no association of average daily acceleration, as a measure of overall physical activity, with any measures of glycaemic variability (Table 3). On the other hand, in model 1 (unadjusted), the intensity gradient slope (Table 4) was negatively associated the Mean Glucose, CONGA, J-index, GRADE – % Eugly, MAGE and ADRR. In model 2 (adjusted for sex, age and BMI), the intensity gradient slope remained negatively associated with Mean, CONGA, J-index, GRADE, GRADE – % Eugly and ADRR, but was no longer associated with MAGE. Furthermore, in model 2 the intensity

TABLE 1 General characteristics in people with type 1 diabetes included in the current study ($n = 311$).

	Mean (SD)
Age (years)	33.05 (9.69)
Diabetes duration (Years)	18 (8.6)
Height (cm)	164.75 (9.70)
Weight (kg)	73.65 (15.06)
BMI (kg/m^2)	27.05 (4.51)
Waist circumference (cm)	88.96 (14.12)
HbA1c (mmoL/moL)	63.8 (15.7)
Total cholesterol (moL/L)	4.56 (1.04)
HDL cholesterol (mmoL/L)	1.55 (0.39)
LDL cholesterol (mmoL/L)	2.63 (0.95)
Triglycerides (mmoL/L)	0.95 (0.80)
Bolus insulin dose (U/kg/day)	0.34 (0.16)
Basal insulin dose (U/kg/day)	0.31 (0.13)
Total insulin dose (U/kg/day)	0.64 (0.23)

TABLE 2 Glycaemic variability metrics derived from 7-day CGM and overall physical activity and the intensity gradient derived from 7-day accelerometry in people with type 1 diabetes (n = 311).

	Mean (SD)
Mean glucose (mmoL/L)	9.30 (1.44)
SD	3.73 (0.87)
CONGA	8.29 (1.43)
LI	7.84 (3.02)
J-index	56.47 (19.68)
LBGI	4.41 (2.12)
HBGI	11.69 (4.67)
GRADE	8.00 (3.28)
GRADE – %Hypo	4.43 (5.61)
GRADE – %Eugly	6.18 (2.78)
GRADE – %Hyper	89.39 (6.47)
MODD	4.06 (1.05)
MAGE (mmoL/L)	6.58 (2.17)
ADRR	32.40 (9.94)
M-value	15.52 (9.43)
MAG	2.50 (0.43)
Overall physical activity (mg)	25.21 (7.19)
Intensity gradient slope	−2.18 (0.29)

gradient slope was negatively associated with HGBI and was positively associated with GRADE – %Hyper. In the final model, adjusted for age, sex, BMI and average daily acceleration, the intensity gradient slope was negatively associated with Mean, CONGA, J-index, HGBI, GRADE, GRADE – % Eugly and M-value. Similar data were found for MVPA (Supplementary Table S2). Across all models there was no association between MVPA and any measures of glycaemic variability.

4 | DISCUSSION

The current study has demonstrated that overall physical activity levels are not associated with any of the currently employed measures of glucose variability in people with type 1 diabetes. On the other hand, several aspects of glucose variability were associated with the novel intensity gradient, which measures the distribution of physical activity intensity. Our data does not mean that overall physical activity should not be recommended, as it should, but that for glycaemic control, the distribution of physical activity intensity should be considered for physical activity prescription guidelines.

The current study found that overall physical activity was not associated with measures of glucose variability. This is perhaps not surprising as previous research has shown that, in people with type 1 diabetes, exercise training does not reduce glycaemic variability (Kennedy et al., 2013). A small study of Martyn-Nemeth

TABLE 3 Associations of overall daily acceleration with glycaemic variability in people with type 1 diabetes (n = 311).

	Unadjusted		Adjusted for sex, age and BMI		Adjusted for sex, age, BMI and intensity gradient slope	
	B-coefficient (95% CI)	p-value	B-coefficient (95% CI)	p value	B-coefficient (95% CI)	p-value
Mean	−0.004 (0.02, −0.028)	0.757	−0.006 (0.019, −0.031)	0.622	0.015 (0.044, −0.014)	0.306
SD	0.003 (0.017, −0.011)	0.711	0.001 (0.016, −0.014)	0.891	0.007 (0.024, −0.01)	0.453
CONGA	−0.007 (0.017, −0.031)	0.594	−0.01 (0.014, −0.034)	0.421	0.011 (0.039, −0.017)	0.444
LI	0.033 (0.086, −0.02)	0.211	0.034 (0.087, −0.019)	0.203	0.041 (0.104, −0.022)	0.200
J-index	−0.027 (0.287, −0.341)	0.869	−0.064 (0.255, −0.383)	0.693	0.182 (0.555, −0.191)	0.341
LBGI	0.023 (0.06, −0.014)	0.221	0.026 (0.063, −0.011)	0.174	0.013 (0.057, −0.031)	0.547
HBGI	0.001 (0.077, −0.075)	0.979	−0.009 (0.068, −0.086)	0.822	0.048 (0.138, −0.042)	0.294
GRADE	0.001 (0.056, −0.054)	0.978	−0.001 (0.056, −0.058)	0.968	0.046 (0.112, −0.02)	0.171
GRADE – %Hypo	0.006 (0.059, −0.047)	0.829	0.01 (0.065, −0.045)	0.719	−0.016 (0.046, −0.078)	0.627
GRADE – %Eugly	−0.073 (0.056, −0.202)	0.271	−0.081 (0.052, −0.214)	0.235	0.002 (0.153, −0.149)	0.982
GRADE – %Hyper	0.067 (0.181, −0.047)	0.245	0.071 (0.186, −0.044)	0.229	0.014 (0.145, −0.117)	0.838
MODD	0.005 (0.038, −0.028)	0.787	0.009 (0.043, −0.025)	0.589	−0.011 (0.03, 0.08)	0.624
MAGE	−0.02 (0.019, −0.059)	0.312	−0.02 (0.02, −0.06)	0.330	0.001 (0.05, 0.12)	0.958
ADRR	0.141 (0.476, −0.194)	0.412	0.189 (0.522, −0.144)	0.270	−0.04 (0.38, 0.96)	0.851
M-value	−0.004 (0.139, −0.147)	0.956	−0.021 (0.13, 0.33)	0.779	0.071 (0.24,0.56)	0.416
MAG	0.005 (0.013, −0.003)	0.203	0.005 (0.01, 0.02)	0.007	0.005 (0.01, 0.02)	0.121

TABLE 4 Associations of intensity gradient with glycaemic variability in people with type 1 diabetes (n = 311).

	Unadjusted		Adjusted for sex, age and BMI		Adjusted for sex, age, BMI and average daily acceleration	
	B-coefficient (95% CI)	*p*-value	B-coefficient (95% CI)	*p*-value	B-coefficient (95% CI)	*p*-value
Mean	−0.72 (−0.11, −1.33)	0.02*	−0.81 (−0.2, −1.42)	0.011*	−1.01 (−0.28, −1.74)	0.007*
SD	−0.16 (0.21, −0.53)	0.408	−0.18 (0.2, −0.56)	0.349	−0.27 (0.17, −0.71)	0.234
CONGA	−0.75 (−0.15, −1.35)	0.016*	−0.85 (-0.24, −1.46)	0.006*	−1 (−0.28, −1.72)	0.007*
LI	0.18 (1.5, −1.14)	0.796	0.24 (1.59, −1.11)	0.728	−0.31 (1.28, −1.9)	0.698
J-index	−8.3 (−0.41, −16.19)	0.040*	−9.29 (−1.27, −7.31)	0.024*	−11.75 (−2.28, −21.22)	0.016*
LBGI	0.63 (1.55, −0.29)	0.178	0.77 (1.71, −0.17)	0.110	0.59 (1.7, −0.52)	0.301
HBGI	−1.86 (0.05, −3.77)	0.058	−2.08 (−0.14, −4.02)	0.037*	−2.73 (-0.44, −5.02)	0.020*
GRADE	−1.54 (−0.14, −2.94)	0.032*	−1.64 (−0.22, −3.06)	0.025*	−2.27 (−0.59, −3.95)	0.009*
GRADE – %Hypo	0.93 (2.27, −0.41)	0.174	1.13 (2.5, −0.24)	0.108	1.32 (2.89, −0.25)	0.102
GRADE – %Eugly	−3.58 (−0.34, −6.82)	0.032*	−4.24 (−0.93, −7.55)	0.013*	−4.26 (−0.46, −8.06)	0.029*
GRADE – %Hyper	2.65 (5.48, −0.18)	0.068	3.12 (6, 0.24)	0.035*	2.95 (6.25, −0.35)	0.082
MODD	0.78 (1.83, −0.27)	0.148	0.82 (1.86, −0.22)	0.130	1.02 (2.35, −0.31)	0.137
MAGE	−0.99 (−0.01, −1.97)	0.048*	−0.99 (0.02, −2)	0.057	−1.01 (0.19, −2.21)	0.102
ADRR	10.64 (20.97, 0.31)	0.047*	10.97 (21.23, 0.71)	0.040*	11.74 (24.86, −1.38)	0.084
M-value	−3.09 (0.53, −6.71)	0.096	−3.45 (0.24, −7.14)	0.069	−4.41 (−0.05, −8.77)	0.049*
MAG	−0.01 (0.18, −0.2)	0.921	0.02 (0.21, −0.17)	0.862	−0.08 (0.15, −0.31)	0.498

(Martyn-Nemeth et al., 2017) found no association between total physical activity and blood glucose SD. As acute exercise has been demonstrated to alter glucose levels and, in some instances glucose availability, it is not immediately clear why no association between overall physical activity and glycaemic variability was seen, as also found in the current study. This may be due to the role of other factors, such as dietary patterns, and may also reflect that more structured exercise is required to alter glucose variability.

The current study is the first to investigate the association between the novel intensity gradient physical activity metric and glucose variability in people with type 1 diabetes. Our data demonstrated that the distribution of physical activity intensity is negatively associated with mean blood glucose, J-index, HGBI, CONGA, GRADE and M-value. This means that a higher (i.e., less negative) intensity gradient, which would indicate a more even spread of time spent across the intensity range, may be beneficial from the point of view of glucose control. Interestingly, the intensity gradient was not associated with all aspects of glucose variability (SD, LI, LBGI, GRADE-%Hypo, MODD, MAGE, ADRR and MAG); this may be due to the relatively small sample size of the current study or simply that these aspects of glycaemic control are not susceptible to modulation by physical activity. The M-value (Schlichtkrull et al., 1965) and the J-index (Wójcicki, 1995) are measures which incorporate both the mean glucose levels plus its variability which indicates that the intensity distribution of physical activity may be associated with both aspects of glycaemia. This is supported by the fact that both mean blood glucose levels and CONGA (Mcdonnell et al., 2005), which is a measure of intra-day glucose variability, were negatively associated with the intensity gradient. The negative association between mean glucose and intensity gradient, may partly be attributed to lower time spent in the hyperglycaemic range, also reflected by the negative association of intensity gradient with the HGBI. The negative association that we observed between the intensity gradient and GRADE (Hill et al., 2007) indicates that more time spent across the physical activity intensity range may reduce the clinical risk associated with the glucose profile, particularly within the euglycemic range. As mentioned above, why the intensity gradient is not associated with the other measures of mean glucose and glucose variability is not clear but is an area worthy of further study. Secondly, the absence of significant associations between MVPA and our measures of glucose variability suggests that it is the entire intensity distribution that is important, and not simply the amount of time spent at higher intensities.

From a practical perspective, the current data do not mean that the overall amount of physical activity is not useful and that it should not be recommended. In fact, as mentioned previously, the benefits of physical activity in general go beyond glucose variability (Chimen et al., 2012), and increasing overall physical activity should still be encouraged. On the other hand, our data do indicate that to aid with the management of glucose variability it may be prudent to consider the distribution of physical activity intensity in physical activity recommendations for people with

type 1 diabetes. Specifically, strategies to improve the intensity gradient may include increase in the amount of physical activity performed in the moderate to high intensity domains. Our data suggests that a higher (less negative) intensity gradient is most beneficial for glucose variability. To achieve this, it would mean a more even spread of time spent at different activity intensities, which as mentioned, would mean increasing time spent at the higher intensites and less time at the lower intensities whilst maintaining overall activity levels. This redistribution of time spent at different physical activity intensities could be achieved without necessarily increasing the total amount of activity, and our data indicates that this would be of benefit for people with type 1 diabetes. This is interesting as new data indicates that exercise at higher intensities may an effective and preferred choice of exercise for people with type 1 diabetes (Scott et al., 2019, 2020). Further work is needed to establish how to implement this in practice and investigate the feasibility and subsequent efficacy of interventions targeting the distribution of time spent at different activity intensities.

The current study is not without limitations. Primarily, the current study is a cross-sectional analysis and, although physical activity and blood glucose variability were measured at the same time, we cannot be certain about causality in this relationship. The continuous glucose monitors employed in the current study were unblinded, and so, there is the possibility that participants may have modified their dietary and self-care routines, although this effect is likely to be minimal as participants were regular users of these devices, and so, data likely reflects a normal week. Furthermore, although the current sample is larger than previous studies in this area, it is still relatively small. The dietary patterns of participants will interact with physical activity levels, and this was not accounted for in this analysis. On the other side, the current study is an analysis under free living conditions and reflects the pragmatic association between physical activity and glucose variability. Finally, the current sample was taken from Kuwait, where the prevalence of type 1 diabetes is particularly high, and whether similar findings would be seen in other countries remains to be investigated.

In conclusion, the current study has shown that overall physical activity is not associated with measures of glucose variability, but the intensity distribution of physical activity is associated with several, but not all, measures of glucose variability. Overall physical activity should continue to be promoted for health, but it may be prudent to consider recommending to people to have a more even intensity distribution of their physical activity, although this remains to be confirmed in an appropriately designed trial.

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CONFLICT OF INTEREST STATEMENT

The authors declare no conflicts of interest. The results of the study are presented clearly, honestly, and without fabrication, falsification, or inappropriate data manipulation.

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SUPPORTING INFORMATION

Additional supporting information can be found online in the Supporting Information section at the end of this article.