Association Between Physical Activity Level and Cardiovascular Risk Factors in Adolescents Living with Type 1 Diabetes: A Cross-sectional Study

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Abstract

Background:

Type 1 diabetes (T1D) is associated with a high risk of cardiovascular disease (CVD) and an increased rate of premature mortality from CVD. Regular physical activity can improve overall health and wellbeing and plays an important role in primary and secondary prevention of CVD.

Methods:

This cross-sectional study assessed cardiovascular risk factors, physical activity, and fitness (and their associations) in young individuals living with T1D and healthy controls. Primary outcomes included blood pressure, lipid profiles, and physical activity (accelerometry). We included a total of 48 individuals living with T1D and 19 healthy controls, aged 12 to 17 years. Statistical differences between groups were determined with chi-square, independent-samples t-tests or analysis of covariance. The associations between aerobic fitness, daily physical activity variables and cardiovascular risk factors were assessed with univariate and multivariate linear regression analysis.

Results:

In comparison to healthy controls, youth living with T1D showed higher levels of total cholesterol (4.03 ± 0.81 vs. 3.14 ± 0.67 $mmol \cdot L^{-1}$, p = 0.001), low-density lipoprotein cholesterol (LDL-C) (2.31 ± 0.72 vs. 1.74 ± 0.38 $mmol \cdot L^{-1}$, p = 0.035), and triglycerides (0.89 ± 0.31 vs. 0.60 ± 0.40 $mmol \cdot L^{-1}$ p = 0.012), and lower maximal oxygen power (VO_2max) (35.48 ± 8.72 vs. 44.43 ± 8.29 $mL \cdot kg^{-1} \cdot min^{-1}$, p = 0.003), total physical activity counts (346.87 ± 101.97 vs. 451.01 ± 133.52 $counts \cdot min^{-1}$, p = 0.004), metabolic equivalents (METs) (2.09 ± 0.41 vs. 2.41 ± 0.60 METs, p = 0.033), moderate to vigorous intensity physical activity (MVPA), and the percentage of time spent in MVPA. The level of HDL-C was positively associated with METs (β = 0.29, p = 0.030, model R^2 = 0.17), and the level of triglycerides was negatively associated with physical activity counts (β = -0.001, p = 0.018, model R^2 = 0.205) and METs (β = -0.359, p = 0.015, model R^2 = 0.208) in persons living with T1D.

Conclusions:

Youth with T1D, despite their young age and short duration of diabetes, present early signs of CVD risk, as well as low physical activity levels and cardiorespiratory fitness compared to healthy controls. Regular physical activity is associated with a beneficial cardiovascular profile in T1D, including improvements in lipid profile. Thus, physical activity participation should be widely promoted in youth living with T1D.

Background

Type 1 diabetes is associated with high risk of microvascular and macrovascular complications, as well as other cardiovascular risk factors, including obesity, hypertension, hyperglycemia, dyslipidemia, insulin

resistance, and physical inactivity [1]. Cardiovascular disease (CVD) is the most frequent cause of premature death and disability in this population [2]. In a cross-sectional study, 76% of children and adolescents with T1D were found to have one or more cardiovascular risk factors [3]. Therefore, cardiovascular risk identification and prevention is essential in such a high-risk population.

Our recent systematic review and meta-analysis showed that exercise training can decrease risk factors of CVD by improving cardiorespiratory fitness, endothelial function, and vascular health in youth living with T1D [1]. Further, the review also demonstrated that exercise training can reduce the severity of CVD risk factors, such as obesity and body composition, high blood pressure, worsened lipid lipoprotein profile, and systemic inflammation [1]. The American College of Sports Medicine guidelines for exercise testing and prescription recommend that individuals living with T1D undertake 150 minutes of exercise at 40–59% of their oxygen uptake reserve (VO_2R) or 75 minutes of vigorous intensity exercise (60% – 89%VO_2R) per week, or 30 minutes or more of daily low to moderate intensity physical activity participation [4]. Moreover, the 2018 Diabetes Canada clinical practice guidelines recommend that even smaller amounts of physical activity can provide some health benefits [5]. However, children with T1D report lower physical activity levels than those prescribed in current recommendations [6] and less time spent in physical activity than their peers without diabetes [7]. In order to better promote physical activity in people living with diabetes, more evidence is needed regarding the association of objectively measured daily physical activity and CVD risk factors.

Therefore, the first objective of this study was to assess CVD risk factors in youth living with T1D in comparison with healthy controls. The second objective was to evaluate the relationship between physical activity levels and markers of CVD. We hypothesized that the CVD risk profile in youth with T1D would be proatherogenic compared with the profile of healthy controls, and that higher physical activity levels would be associated with improved CVD risk factors among youth with T1D.

Methods

Study Design and Participants

The study is a cross-sectional study including 48 adolescents living with T1D (World Health Organization (WHO) criteria) and 19 heathy participants aged 12 to 17 years old. The study was performed at the Sport Science Research Center, Ji’nan, China. The participants with T1D were all Chinese recruited from Ji’nan Centeral Hospital. Individuals living with T1D for at least 6 months with hemoglobin (HbA1c) greater than or equal to 7.5% in the last three months, with normal renal function and free from previous CVD and chronic kidney disease were eligible for participation. Participants with significant diabetic complications (diabetic foot, retinopathy, severe neuropathy), uncontrolled hypertension, diabetic keto-acidosis, CVD (defined as any form of clinical coronary heart disease, stroke or peripheral vascular disease), severe hypoglycemia episodes within the past 3 months were excluded. Participants on lipid lowering therapy were excluded. The selection of healthy control participants was based on the same criteria, except for the criterion that concerned the diagnosis of T1D.

Anthropometric measurements

Height was measured in bare feet to the nearest 0.1 cm using a wall-mounted stadiometer. Body mass was measured in light clothing to the nearest 0.1 kg using BC-418 segmental body composition analyzer (Tanita, Tokyo, Japan). Body mass index (BMI) was calculated as weight (kg) divided by height squared (m^2) and adjusted for age and sex to give a BMI standard deviation score (BMI z-score). BMI z-score was calculated using the WHO Reference 2007 growth data for the age group 5–19 years with SPSS software (https://www.who.int/growthref/tools/en/). Waist circumference was measured in triplicate with a flexible tape at the midpoint between the lower margin of the last palpable rib and the top of the iliac crest following WHO [8]. Blood pressure was measured after 10 minutes of rest in the seated position and the average of 3 measurements taken one minute apart was used in the analysis. The cuff was chosen to be of the appropriate size for the adolescent's upper arm, with a bladder width that is at least 40% of the arm circumference at a point midway between the olecranon and the acromion and a bladder length to cover 80–100% of the circumference of the arm.

Body composition assessment

Body composition measurements were performed by dual energy X-ray absorptiometry (DXA) using the iDXA instrument (GE Medical Systems, Madison, WI) with Encore 2011 software (version 13.6). All study participants underwent a whole-body scan (Lunar iDXA, GE Healthcare, WI), in which the participant was placed in the supine position, centralized in the DXA scan table.

Puberty and diabetes assessment

Puberty was assessed via self-report using pubertal staging images and the children were categorized as prepubertal (Tanner 1), in early puberty (Tanner 2), mid puberty (Tanner 3–4) or post puberty (Tanner 5) (Rasmussen et al., 2015). Participants were asked to complete a questionnaire upon arrival at the testing location, which included: diabetes history, age, duration of diabetes, complications, insulin regimen, medications, and physical activity levels.

Biochemical investigations

All participants were studied after a 12-h overnight fast and, in the case of T1D individuals, before their morning insulin injections. Fasting capillary (fingertip) blood glucose samples were taken for analysis of glycosylated hemoglobin (HbA1c), total cholesterol, LDL-C, HDL-C, and triglycerides. Total cholesterol, LDL-C, HDL-C and triglycerides were analyzed using the Cardiochek PA Blood Analyser (Polymer Technology Systems Inc., Indianapolis, IN, USA) and HbA1c were analyzed using the A1cNow+ (Metrika Inc., Sunnyvale, CA, USA). Both devices have been validated previously [9, 10].

Physical activity assessment

Physical activity levels were objectively measured using accelerometers. The ActiGraph wGT3x-BT triaxial accelerometers (ActiGraph LLC, Pensacola, FL, USA) were used to assess bodily movements 24 h per day. Participants were asked to wear the accelerometers on their non-dominant wrist for seven consecutive days (5 weekdays), except in the water, as the device is water-resistant, but not waterproof. We collected data at 50 Hz, as this sampling frequency has shown to sufficiently capture body movement and allow for five weekdays and two weekend days of data collection [11]. Participants were given a paper calendar-style tracking log on which they were instructed to write down the time they put the accelerometer on and the time they removed it in order to support wear-time compliance.

Data were downloaded with the manufacturer's software (ActiLife Version 6) and processed using 60-second epochs to derive the following daily physical activity parameters: metabolic equivalent of task (METs, $kcal \cdot h^{-1} \cdot kg^{-1}$; as an index of the intensity of activities), total daily physical activity counts ($counts \cdot min^{-1}$), the percentage of time spent in sedentary behaviour, daily average time spent in light intensity physical activity, daily average time spent in moderate to vigorous intensity physical activity (MVPA), and the percentage of time spent in MVPA. Sedentary behaviour period (≤ 100 counts-per-minute [CPM]), light intensity physical activity (101–2295 CPM), moderate intensity physical activity (2296–4011 CPM) and vigorous intensity physical activity (≥ 4012 CPM) established cut-offs were used [12]. Moderate to vigorous intensity physical activity time accumulated in bouts (prolonged periods) of 10 or more consecutive minutes following physical activity guidelines was also derived [13]. Sedentary time accumulated in bouts of 20 or more consecutive minutes, which has been shown to have a negative effect on cardio-metabolic biomarkers [14], was also derived. The non-wear period was defined as a minimum of 60 min of continuous zero counts according to ActiLife's default option and at least 600 minutes of wear time per day without excessive counts (> 20,000 CPM) was required to be considered valid [15]. At least three valid wear days were required to be included in the analysis.

Resting energy expenditure was estimated from accelerometer counts and age-specific prediction equations to derive the metabolic equivalent of MET intensity levels. The equation was: METs = 2.757 + (0.0015*CPM) - (0.08957*age) - (0.000038*CPM*age) [16].

Physical fitness assessment

Participants were screened for any cardiovascular complications and readiness for exercise testing using the Physical Activity Readiness Questionnaire for Everyone (PAR-Q+) [17] prior to physical fitness test. The Leger 20-metre shuttle run test was used for aerobic fitness assessment. Participants are required to run back and forth on a 20-m course and must reach the 20-m line at the same time that a sound signal is emitted from a prerecorded tape. The frequency of the sound signals increases in such a way that running speed is increased by 0.5 $km \cdot h^{-1}$ catch minute from a starting speed of 8.5 $km \cdot h^{-1}$. The test stops when the participants are no longer able to follow the set pace. If patients experienced

hypoglycemia during their laboratory stay, a 15 g carbohydrate bolus was administered (Glucose drinks, Henan Three Connaught food Co., LTD, China). Hypoglycemia was defined as a blood glucose concentration of ≤ 3.9 mmol·L^{-1} and hyperglycemia ≥ 10.9 mmol·L^{-1} [18].

Statistical analysis

All statistical analyses were performed using the SPSS 20 for Windows (Statistical Package for the Social Sciences). Data were screened for normal distribution. The chi-square test was used for comparison of proportion (categorical variable including gender and pubertal status) between groups, and independent-samples t-tests were used for comparison of the continuous variables (age, height, body mass, body composition, BMI, cardiovascular risk factors and daily physical activity variables) between groups. Analysis of covariance (ANCOVA) was used for statistical differences between groups while blood pressure, daily physical activity variables, lipid profiles, and aerobic fitness were adjusted for BMI z-score. The non-parametric test (Mann-Whitney) was used to compare time spent in MVPA and the percentage of time in MVPA among groups as the distributions were not normal. Results were summarized using means and standard deviation (SD) for normally distributed variables, medians and 25–75th quartile for non-normally distributed variables and using frequencies and percentages for categorical variables.

The associations between aerobic fitness, daily physical activity variables and cardiovascular risk factors were assessed with univariate linear regression analysis (Step 1), and multivariate linear regression analysis (Step 2) adjusting for age, gender, insulin dose, and pubertal stage. The probability was considered to be statistically significant at P value < 0.05.

Results

The demographic characteristics and laboratory results of individuals with T1D and healthy controls are presented in Table 1. Specific descriptive data in youth with T1D are presented in Table 2. No significant differences were shown between groups for age, gender, pubertal stage, body fat percentage, BMI, waist circumference, and blood pressure (all p 0.05). T1D participants showed significantly higher values of total cholesterol (4.03 ± 0.81 vs. 3.14 ± 0.67 mmol·L^{-1}, p = 0.001), LDL-C (2.31 ± 0.72 vs. 1.74 ± 0.38 mmol·L^{-1}, p = 0.035), triglycerides (0.89 ± 0.31 vs. 0.60 ± 0.40 mmol·L^{-1}, p = 0.012) compared to the healthy controls.

Individuals living with T1D had significantly lower VO_2max (35.48 ± 8.72 vs. 44.43 ± 8.29 mL·kg^{-1}·min^{-1}, p = 0.003), total daily physical activity counts (346.87 ± 101.97 vs. 451.01 ± 133.52 CPM, p = 0.004), and daily light physical activity (335.93 ± 120.16 vs. 449.33 ± 89.55 min, p = 0.002), while higher percentage of time spent in sedentary behaviour (36.34 ± 11.04 vs. 28.86 ± 12.56, p = 0.04) compared with healthy participants. In persons living with T1D, median MVPA [(53.19 (35.68–63.16) vs 89.57 (61.00- 124.14) min, p = 0.001] and median percentage of time spent in MVPA [(8.56 (6.18–10.12) vs 11.91 (7.74–16.22)

%, p = 0.038] was significantly lower compared to healthy controls. Because of the observed differences in BMI z-score, the P value of main outcomes adjusted for the differences were also calculated (Table 1).

Table 1
Comparison of descriptive data between young people with type 1 diabetes (T1D) and healthy control participants

	T1D (n = 48)		**Healthy controls (n = 19)**			
	Mean	SD	Mean	SD	p	Adjusted p
Gender (male/ female) (%)	37.5/62.5		42.1/57.9		0.129	
Pubertal stage (n)					0.543	
Stage 1 (Not started)	18		7			
Stage 2 (Barely started)	8		1			
Stage 3 (Definitely underway)	12		6			
Stage 4 (Seems completed)	5		1			
Stage 5 (Completed)	5		4			
Ages (yr)	14.02	2.89	13.58	3.46	0.601	
Body mass (kg)	49.48	12.56	52.34	15.45	0.452	
Height (m)	1.60	0.13	1.59	0.13	0.772	
BMI ($kg \bullet m^{-2}$)	18.97	3.10	20.38	3.32	0.119	
BMI-Z score	-0.27	1.16	0.50	1.01	0.018*	
Body fat (%)	29.28	9.54	28.42	6.61	0.765	0.084
Waist circumference (cm)	67.63	7.96	73.65	8.22	0.055	0.151
Systolic blood pressure (mmHg)	106.07	16.72	107.07	15.45	0.837	0.778
Diastolic blood pressure (mmHg)	65.24	11.65	65.75	9.88	0.878	0.821
Total cholesterol ($mmol \bullet L^{-1}$)	4.03	0.81	3.14	0.67	0.001*	0.001
HDL-C ($mmol \bullet L^{-1}$)	1.48	0.28	1.29	0.42	0.078	0.184
LDL-C ($mmol \bullet L^{-1}$)	2.31	0.72	1.74	0.38	0.005*	0.008

Data are presented as means and standard deviation (SD). T1D, type 1 diabetes; N, number; yr, year; BMI, body mass index; HDL-C, high-density lipoprotein cholesterol; LDL-C, low-density lipoprotein cholesterol; VO_2max, maximal aerobic power; METs, metabolic equivalent; CPM, counts-per-minute.

*Statistically significant difference ($p < 0.05$) between type 1 diabetes and healthy controls;

	T1D (n = 48)		Healthy controls (n = 19)			
Triglycerides ($mmol \bullet L^{-1}$)	0.89	0.31	0.60	0.40	0.012*	0.007
Estimated VO_2max ($mL \bullet kg^{-1} \bullet min^{-1}$)	35.48	8.72	44.43	8.29	0.003*	0.003
METs ($kcal \bullet h^{-1} \bullet kg^{-1}$)	2.09	0.41	2.41	0.60	0.066	0.075
Physical activity counts (CPM)	346.87	101.97	451.01	133.52	0.004*	0.033
Light physical activity ($min \bullet day^{-1}$)	335.93	120.16	449.33	89.55	0.002*	0.003
Percentage of time spent in Sedentary behaviour (%)	36.34	11.04	28.86	12.56	0.04*	0.095

Data are presented as means and standard deviation (SD). T1D, type 1 diabetes; N, number; yr, year; BMI, body mass index; HDL-C, high-density lipoprotein cholesterol; LDL-C, low-density lipoprotein cholesterol; VO_2max, maximal aerobic power; METs, metabolic equivalent; CPM, counts-per-minute.

*Statistically significant difference ($p < 0.05$) between type 1 diabetes and healthy controls;

Table 2
Specific descriptive data in young people living with type 1 diabetes

	Type 1 diabetes (n = 48)	
	Mean	SD
Diabetes duration (years)	3.64	2.29
Pubertal Stage (n)		
Prepubertal (Tanner 1)	18	
Early puberty (Tanner 2)	8	
Mid-puberty (Tanner 3-4)	17	
Post-puberty (Tanner 5)	5	
MDI	30	
CSII	18	
CGM	26	
SMBG	22	
HbA1c ($mmol \bullet mol^{-1}$)	61	9
HbA1c (%)	7.70	2.47
Insulin dose ($unit \bullet kg^{-1} \bullet day^{-1}$)	0.87	0.29

Data are presented as means and standard deviation (SD). MDI, multiple daily injection; CSII, continuous subcutaneous insulin infusion; CGM, Continuous Glucose Monitoring; SMBG, self-monitoring of blood glucose; HbA1c, Glycosylated hemoglobin.

We investigated the within-group relationships between CVD risk factors (blood pressure, HbA1c, HDL-C, LDL-C, total cholesterol, and triglycerides) and physical fitness or daily physical activity variables with bivariate analysis. For participants with T1D, a significant relationship between HDL-C and METs ($r = 0.41$. $p = 0.030$) was shown. Also, there is a significant relationship between triglycerides and METs ($r = -0.46$, $p = 0.015$), time spent in sedentary behaviour ($r = 0.395$, $p = 0.042$), and physical activity counts ($r = -0.453$, $p = 0.018$). No similar relationships were shown in healthy participants ($p > 0.05$).

Linear regression models are presented in Table 3 and showed that HDL-C in persons with T1D were positively associated with METs ($\beta = 0.29$, $p = 0.030$, model $R^2 = 0.17$), but the results changed after adjusting for age, sex, pubertal stage, BMI z-score ($\beta = 0.305$, $p = 0.195$, model $R^2 = 0.54$). Linear regression models adjusted for age, sex, pubertal stage, BMI Z-score, and insulin treatment showed that there was a trend for a negative association between HDL-C in T1D and time spent in sedentary

behaviour (β = -0.002, p = 0.060, model R^2 = 0.60). HDL-C in healthy controls was not significantly associated with daily physical activity variables and VO_2max. Triglycerides were negatively associated with daily physical activity counts (β = -0.001, p = 0.018, model R^2 = 0.205) and METs (β = -0.359, p = 0.015, model R^2 = 0.208) in persons with T1D, but the results changed to non-significance after adjusting for age, sex, pubertal stage, BMI z-score (Table 4).

Table 3
Linear regression model examining the association between HDL-C and physical activity variables after adjusting by potential confounders in young people living with type 1 diabetes

dependent variable: HDL-C						
Independent variables	β	95%CI		p	Adjusted R^2	R^2
Physical activity counts (CPM)						
Step 1 (unadjusted)	0.001	0.000	0.002	0.091	0.075	0.110
Step 2(adjusted†)	0.001	-0.001	0.002	0.350	0.275	0.526
Sedentary behaviour ($min \bullet day^{-1}$)						
Step 1 (unadjusted)	-0.001	-0.003	0.001	0.201	0.027	0.065
Step 2(adjusted†)	-0.002	-0.003	0.000	0.060	0.383	0.597
HDL-C, high-density lipoprotein cholesterol; β, estimated value; CI, confidence interval; R^2, coefficient of determinations; † adjusted for age, gender, insulin dose, and pubertal stage						

Table 4
Linear regression model examining the association between Triglycerides and physical activity variables after adjusting by potential confounders in young people living with type 1 diabetes

dependent variable: Triglycerides						
Independent variables	β	95%CI		p	Adjusted R^2	R^2
Physical activity counts (CPM)						
Step 1 (unadjusted)	-0.001	-0.003	0.000	0.018	0.173	0.205
Step 2(adjusted †)	-0.001	-0.002	0.001	0.344	0.178	0.463
METs ($kcal \bullet h^{-1} \bullet kg^{-1}$)						
Step 1 (unadjusted)	-0.359	-0.641	-0.077	0.015	0.178	0.208
Step 2(adjusted†)	-0.272	-0.839	0.295	0.326	0.202	0.468
METs: metabolic equivalents; β, estimated value; CI, confidence interval; R^2, coefficient of determinations; † adjusted for age, gender, insulin dose, and pubertal stage						

Discussion

An increased risk for CVD was found in youth living with T1D compared with those without diabetes in this cross-sectional study. A significant correlation among physical activity levels and components of lipid profile was found. Our findings emphasize the importance of promoting daily physical activity among youth living with T1D.

Adults living with T1D have a high prevalence of dyslipidemia [19, 20]. Corroborating this, our results showed that youth living with T1D have increased total cholesterol, LDL-C, and triglycerides compared to healthy controls. Similarly, a previous study showed that youth with T1D (5–15 years) had elevated values of total cholesterol and LDL-C compared to healthy controls [21]. Lipids levels are very important in predicting adverse cardiovascular outcomes [22]. Previous studies showed that LDL-C independently correlated with abnormal plethysmography responses [23], endothelial dysfunction [24], carotid intimal medial thickness [25], and aortic intimal medial thickness [26] in youth living with T1D. Of note, the median duration of diabetes in our study was less than 4 years, which suggests that the functional changes in lipid profiles start very early in the course of the disease and likely deteriorate to over time, previous studies have similarly demonstrated atherogenic lipoprotein profiles in youth with a short duration of diabetes [20], which highlights the importance of optimizing the management of T1D in youth for lifelong habits.

Our results showed no significant associations between daily physical activity variables and HbA1c in youth with T1D. Similar results have been demonstrated in previous studies. Ligtenberg et al. found that glycemic control was not associated with physical activity in adults (18 and 45 years of age) living with

T1D [27]. Wieliczko et al. reported that there was no correlation between the time spent every week participating in sports and glycated hemoglobin levels in children and adolescents with T1D [28]. On the contrary, Herbst et al. found increasing physical activity was associated with better HbA1c levels in 23,251 children living with T1D [29]. Valerio et al. have reported that regular physical activity was associated with better metabolic control and lipid profile in 138 children and adolescents with T1D [30]. One of the possible reasons for the inconsistency could be differences in sample size between studies, with larger sample sizes being required to find significant findings. The other reasons could be possible variation in carbohydrate intake and insulin dosage (for avoiding hypoglycaemia episodes that caused by exercise), stress or stricter medical monitoring, which may all influence glycaemic status.

Regular exercise, physical activity participation, and reduced sedentary behaviour are important for CVD risk management [31]. The latest guidelines published in 2018 by the International Society for Paediatric and Adolescent Diabetes (ISPAD) recommended that children (aged 5–11 years) and adolescents (aged 12–17 years) should aim for 60 minutes or more per day of MVPA physical activity and minimize sedentary time, and participate in vigorous intensity exercise, muscle and bone strengthening exercise at least three times a week [32]. In our study, individuals living with T1D did not achieve the minimal time of daily MVPA (60 minutes). Moreover, total daily physical activity count and the time spent in MVPA were significantly lower in individuals with T1D than healthy controls (mean difference − 36 minutes). Reduced physical activity during childhood is an important risk factor for CVD and insufficient physical activity during childhood is a key risk factor for CVD [33]. Results of an observational study of children and adolescents (4 to 18 years of age) demonstrated associations between increased time spent in sedentary activities with decreased levels of physical activity and related cardiovascular risk factors [34]. Furthermore, cardiorespiratory fitness was significantly reduced in individuals with T1D compared with healthy controls in our study. Similarly, previous research also found that adolescents with T1D have a lower aerobic exercise capacity when compared with normal controls [7, 35]. However, well-documented evidence of randomized controlled trials showed that there was improvement in cardiorespiratory fitness with exercise training [36–39]. These results highlight the importance to engage in regular physical exercise for persons living with T1D. Importantly, very small volumes of physical activity appear to have significant health benefits [1, 31].

A positive association between HDL-C and METs, and a trend for a negative association between HDL-C and time spent in sedentary behaviour was found in the T1D group. Furthermore, triglycerides were negatively associated with daily physical activity counts and METs in youth with T1D, while these relationships were not shown in the healthy controls. These results are in agreement with previous studies in youth with T1D that regular physical activity was associated with improved metabolic control and lipid profile in adolescents with T1D [30, 40]. However, age, sex, pubertal stage, BMI z-score, and insulin treatment may affect an individual's physical activity variables and lipid profiles. Therefore, it is expected in multivariable analyses that potential confounding factors (age, sex, pubertal stage, BMI z-score, and insulin treatment) would decrease the association with physical activity variables and lipid profiles. Martin and colleagues revealed that each MET (approximately 3.5 $mL \cdot kg^{-1} \cdot min^{-1}$) increase in

cardiorespiratory fitness was associated with a 25% point reduction in all-cause mortality [41]. Furthermore, in a systematic review and meta-analysis of physical activity and major chronic diseases showed that increased exercise, from achieving 11.25 MET-hours per week (675 MET-minutes per week), may be effective to decrease incidence and mortality of cardiovascular disease by 17% and 23%, respectively [42]. Therefore, our observation suggests that increased daily physical activity has positive effects on CVD risk factors.

Limitations

The major strengths of the study include a well characterized cohort of youth living with T1D and healthy controls and the use of an objective and reliable method to assess the physical activity levels and aerobic fitness. There were some potential limitations with our study. First, because of the single-centre design and small sample size, our study might have been underpowered to detect significant changes in some variables. Second, wGT3x-BT triaxial accelerometers are water-resistant, but not waterproof, participants were required to remove the device when they engaged in aquatic activities such as swimming, which would lead to a potential underestimation of total physical activity levels. We only measured physical activity for one week, and this may not reflect the annual physical activity pattern. Third, the cross-sectional nature of this study does not allow determining causality, though it provides enough data to draw significant association between CVD risk factors and physical activity levels in youth living with T1D. A randomized controlled trial including a structed exercise training program would be required. Furthermore, there was a potential for selection bias since not all individuals who were approached agreed to participate in the study. It is possible that the individuals who were more sedentary may have been less willing to participate in the study.

Conclusions

Our findings provide evidence that youth living with T1D, despite their young age and short duration of diabetes, exhibit proatherogenic lipid profiles characterized by higher total cholesterol, LDL-C, and triglycerides. Furthermore, youth living with T1D showed lower physical activity levels and VO_2max compared to healthy controls. Being physically active reduced the risk for CVD in youth living with T1D. Accordingly, this study provides compelling evidence supporting the promotion of physical activity in youth living with T1D to reduce the risk for cardiovascular morbidity and premature mortality.

Abbreviations

T1D: Type 1 diabetes

CVD: cardiovascular disease

LDL-C: low-density lipoprotein cholesterol

HDL-C: high- density lipoprotein cholesterol

VO_2max: lower maximal oxygen power

METs: metabolic equivalents

MVPA: moderate to vigorous intensity physical activity

VO_2R: oxygen uptake reserve

BMI: Body mass index

WHO: World Health Organization

DXA: dual energy X-ray absorptiometry

SD: standard deviation

CPM: counts-per-minute

MDI: multiple daily injection

CSII: continuous subcutaneous insulin infusion

CGM: Continuous Glucose Monitoring

SMBG: self-monitoring of blood glucose

HbA1c: Glycosylated hemoglobin

CI: confidence interval

ISPAD: International Society for Paediatric and Adolescent Diabetes

Declarations

Ethics approval and consent to participate

The study protocol received approval from, and was executed in exact accordance with, the ethical guidelines set forth by the University of British Columbia's Clinical Research Ethics Board for research involving human participants (H18-03355). The experimental procedures and risks were explained to participants both verbally and in writing, and written informed consent and assent were obtained from parents and child prior to study participation.

Consent for publication

Not applicable

Availability of data and materials

The datasets used and/or analysed during the current study are available from the corresponding author on reasonable request.

Competing interests

The authors declare that they have no competing interests.

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Authors' Contributions

N.W. contributed to study design, data collection, data analysis and writing of the manuscript. S.S.D.B. contributed to the methodology. S.S.D.B., V.K.J., M.S.K., and D.E.R.W. contributed to critical review and editing of the manuscript. Y.G. contributed to data collection, statistical analysis and reviewing the manuscript. E.M.S. contributed to reviewing and editing the manuscript. Y. L. and J.L. contributed to coordinating the study implementation. N.W. and D.E.R.W. is the guarantor of this work and, as such, had full access to all the data in the study and takes responsibility for the integrity of the data and the accuracy of the data analysis. All authors were involved in revising the manuscript critically for important intellectual content and have read and agreed to the published version of the manuscript.

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