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Type 2 diabetes in youth: A phenotype of poor cardiorespiratory fitness and low physical activity

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Abstract

Objective—The increased incidence of obesity and type 2 diabetes (T2D) among youth has prompted the development of guidelines for healthy cardiorespiratory fitness (CRF) and physical activity (PA) levels in the pediatric population. It is unclear whether youth with T2D meet these guidelines as previous research has not included type 2 diabetics. Therefore, the purpose of this investigation was to examine CRF and PA in youth with T2D and compare these results with recently published normative data for CRF and guidelines for PA in youth.

Methods—Forty adolescents (17 males and 23 females) with T2D were assessed for moderate-to-vigorous PA via the 7-day PA recall. CRF was determined by a progressive cycle ergometer test and indirect calorimetry. PA levels were compared with recently published guidelines for youth of 60 minutes per day, and CRF data were compared with age- and sex-adjusted normative values from the National Health and Nutrition Examination Survey 1999–2002.

Results—Only 17.6% (3/17) of boys and 21.7% (5/23) of girls met PA guidelines, while none of the participants met criteria for healthy CRF. When compared with normative CRF data for US youth, ~93% of boys and 95% of girls scored below the 10th percentile.

Conclusions—These results suggest that youth with T2D exhibit low levels of CRF and the majority do not participate in recommended amounts of PA. Practitioners working with type 2 diabetic youth need to emphasize the importance of regular PA to increase CRF and promote cardiovascular health in an effort to decrease long-term diabetes-related complications.

Keywords

Obesity; insulin resistance; exercise; VO₂ peak; children

Introduction

Pediatric obesity has reached epidemic proportions in most developed countries (1). In conjunction with the noted increase in adiposity among youth, type 2 diabetes (T2D) is an

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Declaration of interest

The authors report no conflicts of interest. The authors alone are responsible for the content and writing of the paper.

emerging clinical manifestation in this population (2). The etiology of obesity in youth is complex and the development of T2D is not well understood; however, it is hypothesized that poor cardiorespiratory fitness (CRF) coupled with a sedentary lifestyle may be contributory (3). As such, the assessment of CRF and physical activity (PA) in various populations of youth has received increased attention (4).

To better ascertain the CRF and PA levels across a representative sample of US youth, these measures were recently included in the National Health and Nutrition Examination Survey (NHANES). Using NHANES 1999–2002 data, Pate et al. (5) published normative values regarding the CRF of contemporary US youth. The authors reported several descriptive characteristics which significantly differentiated fit from unfit youth including: obesity, sex, PA levels, and sedentary behaviors (screen time). Additionally the authors found that approximately one-third of US adolescents aged 12 to 19 years failed to meet criterion referenced standards for acceptable CRF, as defined by the FITNESSGRAM (6). Other investigations have utilized CRF measures from the NHANES dataset to examine associations with T2D risk factors (insulin sensitivity and metabolic syndrome) in youth. Imperatore et al. (7) found CRF to be an independent predictor of insulin sensitivity in adolescents. Whereas, Janssen and Cramp (8) found CRF to be a significant determinant of the metabolic syndrome phenotype in youth. Given the predictive nature of both insulin resistance and the metabolic syndrome for T2D, it is plausible that low CRF may contribute to the development of T2D in youth. Unfortunately, children with T2D were not included in the NHANES analyses of Pate, Imperatore, or Janssen.

Although an increase in the incidence of T2D among youth has been reported, the prevalence remains far lower than that of type 1 diabetes (9). As a result, empirical data from studies of youth with T2D are limited. In fact, most studies examining CRF and/or PA in youth in relation to diabetes risk have not included youth with T2D (10,11). However, in adults, several studies have established a protective effect of both CRF and PA on T2D development (12). Therefore, the purpose of this study was to assess CRF and PA levels in a sample of youth with T2D and compare these findings to age-appropriate normative values for CRF and current pediatric recommendations for PA.

Research design and methods

Participants

Forty adolescent volunteers (age 13–18) with previously diagnosed T2D were invited to participate in this study. Youth were recruited through pediatric diabetes clinics where they were receiving regular care for T2D at the time of study. Participants who developed T2D secondary to treatment for another condition or medication were excluded. In addition, youth were also excluded if they had a known cardiac defect, or had delays in cognitive, psychological, or behavioral functioning. This study was approved by the Institutional Review Board at the University of Illinois at Chicago (UIC). Informed written consent and child assent were obtained from participants and families prior to any testing procedures.

Protocol

Participants were invited to the UIC General Clinical Research Center for collection of study measures. For standardization purposes, all testing occurred in the morning beginning between 08.00–09.00. Height (wall mounted stadiometer) and weight (medical balance beam scale) were measured in light clothing without shoes, and BMI and BMI percentiles were subsequently calculated according to the Centers of Disease Control and Prevention (13). Pubertal stages of maturation were determined during a physical examination (14) by a Pediatric Endocrinologist or Nurse Practitioner (pubic hair in boys and breast development

in girls) and T2D duration was determined by medical chart review with parent confirmation. Glycosylated hemoglobin (HbA1c) was determined using the Abbott IMx® assay method (Abbott Park, IL) for quantitative measurement of whole blood (CV < 5%). Upon completion of the clinical and metabolic testing, PA and CRF were subsequently assessed, as described below.

Physical activity

Moderate-to-vigorous PA (MVPA) was assessed by the Seven-Day PA Recall (7 day-PAR) developed by Sallis et al. (15). The 7 day-PAR is a structured interview, which has been shown to be a valid ($r = 0.55-0.72$) and reliable ($r = 0.77$) measure of PA in children and adolescents (16). Trained research staff asked participants to recall all activities participants undertook during the preceding 7 days. Activities were divided into light, moderate, hard, and very hard categories with examples for each provided for reference. Duration of activities was recorded in 10-minute blocks. Given the difficulty in quantifying short-bout activities of children, only bouts of at least moderate intensity performed for at least 10 minutes were used in the present analysis. The total amount and duration of MVPA (hard or very hard) was summed for the entire week and expressed as minutes per day of MVPA.

Cardiorespiratory fitness

Peak oxygen consumption (VO_{2peak}) was determined during an all-out progressive exercise test on a cycle ergometer. Expired gasses were collected and analyzed using a Sensormedics® VMAX29 integrated metabolic cart. The metabolic cart was calibrated prior to each testing session using medical grade gas mixtures of known concentrations and a 3.0 L syringe. Prior to testing procedures, participants were familiarized with the exercise equipment and instructed to maintain a cycling cadence of 50–60 revolutions per minute throughout the test. Each participant performed the McMaster cycle test protocol appropriate for adolescents (17). This protocol allows for sex- and height-specific workload adjustments in order to provide steady-state exercise increases in a linear fashion. Exercise testing was terminated when the participant could no longer maintain proper pedaling cadence despite verbal encouragement from research staff. VO_{2peak} was determined at the highest oxygen consumption obtained with a respiratory exchange ratio above 1.0.

Reference data and statistical analysis

PA levels were compared with age-appropriate guidelines and recommendations of at least 60 minutes of MVPA per day (18). CRF data were compared with available normative values for US youth, derived from exercise testing in 3 287 12–19-year-olds participating in NHANES 1999–2002 (5). Additionally, CRF data were compared with criterion-referenced standards of 42 ml/kg/min for males aged 12–19 and 35–37 ml/kg/min for females 12–19 years old (6).

Sex differences in CRF, MVPA, and descriptive characteristics were compared by independent sample t-test. Chi-squared analyses were used to examine sex comparisons with respect to meeting CRF or MVPA guidelines. All data were presented as means $\pm$ standard deviation or as percentages. Analyses were performed using SPSS version 15.0 with a type 1 error set at $P < 0.05$.

Results

Descriptive characteristics of the participants are presented in Table I. Boys were significantly taller and heavier than girls and the sample as a whole was obese. T2D duration was not different between sexes; however, boys tended to exhibited better T2D control than girls ($p = 0.06$).

Physical activity and cardiorespiratory fitness levels

Boys and girls reported performing similar amounts of MVPA (38.8 ± 27.2 vs. 32.3 ± 26.9 minutes/day; $p > 0.05$). When compared with current recommendations, only 17.6% (3/17) of boys and 21.7% (5/23) of girls reported performing at least 60 minutes of MVPA per day ($p > 0.05$ for sex comparison). CRF data were not available for five of the 40 participants (3 had blood glucose values > 250 mg/dl and were not tested as per our Data Safety and Monitoring Plan, 1 exceeded the weight limit of 300 pounds for the ergometer, and 1 refused to wear the nose clip and mouthpiece required for exercise testing). No significant MVPA differences were noted between youth who did and did not perform CRF testing (33.3 ± 23.4 vs. 47.1 ± 46.5 minutes/day; $p > 0.05$). CRF levels ($\text{VO}_{2\text{peak}}$) are presented in Figure 1. Boys exhibited ~19% higher CRF levels compared with girls (28.1 ± 5.7 vs. 22.0 ± 5.8 ml/kg/min; $p = 0.01$). CRF differences were accentuated when oxygen uptake data were expressed in absolute terms and BMI was statistically adjusted for (2.8 ± 1.1 vs. 1.9 ± 1.0 L/min, $p < 0.001$). Figure 2a and 2b display individual CRF and MVPA levels plotted against age- and sex-reference standards and recommendations for youth. Irrespective of sex, no participant met the criteria for healthy CRF levels. Furthermore, when data were compared with published CRF norms, ~93% of boys and 95% of girls scored below the 10th percentile for US youth ($p > 0.05$ for sex comparison).

Discussion

The incidence of T2D in youth has increased worldwide (2,19). Despite this increase, a dearth of empirical data exists from this population. Our findings suggest that this disorder co-exists with low CRF and low levels of MVPA. These results extend recent findings in healthy youth highlighting CRF and PA as significant determinants of T2D risk (20–22). The inclusion of youth diagnosed with T2D in the present analysis is novel and adds to the growing, but still limited, available data related to T2D in the pediatric population.

Regular PA is essential for promoting healthy growth and development of children (23). The increase in obesity among youth suggests that, as a whole, children are not obtaining sufficient levels of PA to match their caloric intake and thus excess energy is stored in the form of triglycerides (23). Over time, the accumulation of fat and further lack of PA will likely lead to reductions in CRF and increased risk for developing comorbidities, such as T2D (24). In our sample, MVPA was directly related to CRF levels ($r = 0.38$, $p = 0.03$), which suggests that youth who participated in greater MVPA had higher levels of CRF. However, the cross-sectional design of our study prohibits our ability to derive any causal relationship from this association. Nonetheless, when compared with contemporary US youth, the participants in the present investigation had profoundly low CRF levels. In addition to low CRF levels, these youth were considerably overweight with a mean BMI percentile for the entire sample consistent with the criteria for obesity. There is debate in the literature as to whether obesity *per se* impacts CRF levels in youth (25). To be consistent with the NHANES CRF data, we expressed CRF relative to total body mass. Therefore, it is difficult to parcel out whether the comparatively low CRF levels in our sample are the sole function of their high body mass and hence a larger denominator in the oxygen uptake equation or are a reflection of significant impairments in oxygen uptake and utilization. Towards this end, we have recently observed that boys with T2D had significantly lower CRF levels compared with BMI and age-matched non-diabetic controls (26).

It is likely that T2D is the end result of a complex etiology where obesity, CRF, and physical inactivity are key determinants. In terms of prevention, very few successful pediatric obesity treatment programs have been described in the literature (27). Therefore, as children become increasingly more overweight and present with clinical comorbidities, intervention efforts may be best served by focusing on MVPA in order to increase CRF and improve metabolic

health rather than focusing on adiposity (28). Clear evidence in adults supports the concept that higher CRF rather than obesity status is the primary determinant of health (29). Furthermore, the protective effect of CRF extends to active overweight adults with T2D who exhibit a lower all-cause mortality risk compared with lean sedentary diabetics (30). These findings suggest that exercise may reduce chronic disease risk independent of obesity and T2D.

Compared with the adult literature, the body of research in the pediatric population examining the associations between PA and T2D is limited. Most studies have focused on healthy or overweight youth at-risk for T2D. A recent study of ~1 700 9- and 15-year-old children from the European Youth Heart Study found that sedentary children were three times more likely to exhibit a clustering of chronic disease risk factors compared with the most active youth (22). Moreover, the weight status of the youth did not impact these odds. Although observational in nature, the findings from this large cohort underscore the importance of PA for preventing obesity-related diseases even in ostensibly healthy youth. In our dataset, we examined whether there was a cross-sectional association between CRF or MVPA and glucose control (HbA1c) as a proxy measure of overall metabolic health. We did not find either CRF ($r = -0.20$, $p = 0.27$) or MVPA ($r = -0.11$, $p = 0.49$) to be significantly correlated with HbA1c. Perhaps more salient than these cross-sectional findings are smaller scale exercise interventions in overweight youth, which have demonstrated significant improvements in T2D risk factors without changes in body composition (31,32). These studies suggest that PA can improve the metabolic health of overweight youth independent of changes in adiposity. Whether exercise can improve the health status of youth with type 2 diabetes is an important question that remains to be determined.

In addition to obesity and impaired glucose regulation, more than 90% of youth with T2D concurrently exhibit multiple cardiometabolic disease risk factors (33). Given that the leading cause of morbidity and mortality among individuals with T2D is cardiovascular disease (34), it is imperative for these youth to increase their MVPA levels, which may result in higher CRF, as these two constructs have important cardioprotective effects (35). Only 20% (8/40) of the total sample reported performing 60 minutes or more of MVPA per day and none reached the minimum threshold for healthy CRF levels. Our findings coupled with previous research highlighting that nearly 90% of pediatricians do not refer their patients diagnosed with T2D for PA (36) underscores the need to emphasize PA during diabetes education classes for youth.

The cross-sectional nature of our study limits any conclusions related to causality of poor CRF and low PA in the pathogenesis of T2D in our sample. However, the concept of mitochondrial dysfunction and hence impaired oxidative metabolism may be a mechanism underlying the pathogenesis of T2D and a critical precipitating factor, which may explain the low CRF levels in this population (37). This is supported by prospective work in adults, which has established that low CRF at baseline predicts the development of T2D (38). Furthermore, epidemiologic studies, reviewed elsewhere (39), and prospective lifestyle interventions (40) have shown that regular PA can effectively prevent the development of T2D. The protective mechanisms underlying PA may include improvements in peripheral insulin sensitivity (41) as well as improvements in total and regional adiposity (42). Longitudinal studies in children are necessary to examine whether decreases in CRF or PA patterns over time impact future risk of T2D.

We acknowledge several limitations of our study. The relatively small sample size may limit the generalizability of our findings. However, given the lack of available data and the low incidence of this disorder in the general pediatric population we believe that our report addresses a significant challenge, which warrants consideration by both the clinical and

research community. Our measure of PA was based upon self-report which is prone to recall error. An objective measure of PA, such as accelerometry would allow for a more accurate assessment of the frequency, intensity, and duration of PA and should be employed in future studies. We assessed CRF using a cycle ergometer whereas NHANES CRF data was measured by a treadmill. VO₂peak values are typically lower when assessed by an ergometer compared with treadmill. However, data in obese youth suggest that cycle ergometer and treadmill derived VO₂peak values are not significantly different (43). Lastly, we did not have complete data on all of our participants as 5 of the 40 youth did not perform CRF testing.

In conclusion, we have demonstrated that youth with T2D do not meet recommended guidelines for MVPA. Furthermore, the CRF levels of these youth are well below normative and published criterion values. These findings suggest that education programs for youth with T2D should emphasize the importance of a physically active lifestyle to increase CRF levels, support weight management, and improve cardiovascular health.

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Figure 1. Cardiorespiratory fitness (VO₂peak) in boys and girls with type 2 diabetes. Data are presented as Means $\pm$ standard deviation. *P < 0.05.

Figure 2.

Individual cardiorespiratory fitness levels (indicated by gray bars) and physical activity levels (indicated by large black dots) of boys (a) and girls (b). The dashed line represents minimum age and sex criteria for healthy cardiorespiratory fitness and the dotted line represents current pediatric recommendations for physical activity.

Table I

Physical characteristics of youth with type 2 diabetes (T2D).

	Boys (n = 17)	Girls (n = 23)	Total (n = 40)
Age (years)	15.8 ± 1.7	15.9 ± 1.8	15.8 ± 1.8
Tanner Stage (%)			
3	0	13%	7.5%
4	29.4%	8.7%	17.5%
5	70.6%	78.3%	75.0%
Ethnicity (%)			
AA	70.6%	100%	87.5%
Hisp	29.4%	0%	12.5%
T2D Duration (years)	2.5 ± 1.8	2.4 ± 2.2	2.5 ± 2.0
HbA1c (%)	7.7 ± 2.5	9.2 ± 2.3	8.6 ± 2.5
Height (cm)	175.7 ± 7.8	161.3 ± 6.7 [*]	167.4 ± 10.1
Weight (kg)	108.9 ± 39.1	86.2 ± 23.2 [†]	95.8 ± 32.6
BMI (kg/m ²)	34.8 ± 10.9	32.9 ± 7.9	33.7 ± 9.2
BMI Percentile	96.2 ± 5.8	94.6 ± 5.6	95.3 ± 5.7

Data presented are means ± standard deviation.

AA: African-American; Hisp: Hispanic; HbA1c: Glycosylated hemoglobin; BMI: Body mass index.

^{*} P < 0.05[†] P < 0.01 for sex comparison.