Published in final edited form as:

Pediatr Diabetes. 2018 May ; 19(3): 375–380. doi:10.1111/pedi.12596.

Handgrip Strength Is Associated with Insulin Resistance and Glucose Metabolism in Adolescents: Evidence from NHANES 2011–2014

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Abstract

Background—Previous studies have reported that handgrip strength, a measure of muscular fitness, is associated with insulin resistance in children and adolescents, with conflicting results. Further, no studies have examined the association between handgrip strength with 2-hour glucose levels.

Objective—We tested the association of handgrip strength with measures of insulin resistance (fasting insulin and homeostasis model assessment of insulin resistance (HOMA-IR)) and glucose metabolism (fasting and 2-hour glucose levels) in adolescents from the National Health and Nutrition Examination Survey (NHANES) 2011–2014.

Methods—The study included 959 participants aged 12–19 years who underwent a handgrip test and a glucose tolerance test. General linear models were used to examine the associations between handgrip strength and the outcome variables.

Results—After adjustment for age, race, sex, body mass index, and physical activities, handgrip strength was inversely associated with fasting insulin levels ($P=0.017$) and HOMA-IR ($P=0.025$). Although there was no association between handgrip strength and fasting glucose levels ($P=0.77$), handgrip strength was inversely associated with 2-hour glucose levels ($P<0.0001$). Insulin and 2-hour glucose levels decreased linearly as handgrip strength increased from the bottom quartile to the top quartile (P for trend: 0.045 for fasting insulin levels and 0.004 for 2-hour glucose levels).

Conclusions—Muscular fitness, measured by handgrip strength, is associated with insulin resistance and glucose metabolism in adolescents, which indicates that increasing muscular fitness may have beneficial effects for early prevention of insulin resistance and type 2 diabetes.

Keywords

handgrip strength; glucose metabolism; insulin resistance; adolescents; NHANES

INTRODUCTION

Type 2 diabetes is a major public health challenge in the United States and around the world(1, 2). Numerous studies have demonstrated that childhood cardiometabolic risk factors, such as obesity and fasting glucose levels, are predictive of adult type 2 diabetes risk(3–5). As a result of the increasing trend in obesity prevalence(6, 7), more children and adolescents are at risk of developing type 2 diabetes in the future. In fact, age at onset of type 2 diabetes has gradually decreased such that pediatric type 2 diabetes has become less uncommon(8). Therefore, identifying at risk children and adolescents for future type 2 diabetes is important for early prevention and intervention.

Among risk factors for type 2 diabetes, cardiorespiratory fitness(9–11) and muscular fitness(9, 12) are important predictors for the development of type 2 diabetes in adults. In children and adolescents, an increasing body of evidence shows that both cardiovascular fitness and muscular fitness are associated with cardiometabolic health(13–16) or future mortality(17). Handgrip strength, measured by a commonly used handgrip test in epidemiological studies, is a measure of muscular fitness(13) and has been inversely associated with insulin resistance in children and adolescents(18–22). However, some studies reported that handgrip strength was positively associated with homeostasis model assessment of insulin resistance (HOMA-IR)(23), or suggested that the association between muscular fitness and cardiometabolic risk in children is not independent of obesity(24). Further, muscular fitness is not associated with fasting glucose levels in children and adolescents in most studies(18, 25–27); however, fasting glucose levels may not be sensitive for identifying compromised glucose metabolism in children and adolescents. So far, the association of handgrip strength with 2-hour glucose levels from an oral glucose tolerance test has not yet been examined.

Clarifying the association between muscular fitness and insulin resistance and glucose metabolism in children and adolescents can improve the understanding of the evolution of insulin resistance from childhood and will have implications for prevention of insulin resistance and type 2 diabetes in later life. To this end, we examined the associations of handgrip strength with measures of insulin resistance (fasting insulin and HOMA-IR) and glucose metabolism (fasting and 2-hour glucose levels) in 959 adolescents from the National Health and Nutrition Examination Survey (NHANES) 2011–2014.

Methods

Subjects

NHANES is a continuous program that examines a nationally representative sample of about 5,000 persons each year to assess the health and nutritional status of adults and children in the non-institutionalized general population of the United States (<http://www.cdc.gov/nchs/nhanes.htm>). Surveys include standardized physical examinations and other health related interviews. Information was self-reported during an interview on vigorous recreational physical activity (like running or basketball for at least 10 minutes continuously) and moderate recreational physical activity (such as brisk walking, bicycling, swimming, or volleyball for at least 10 minutes continuously) in a typical week (yes/no) and on time usually spent sitting on a typical day. Blood samples were collected for laboratory testing. In two survey cycles conducted between 2011 and 2014, a handgrip test was administered in participants aged 6 years or older. In the same surveys, levels of fasting plasma glucose, fasting serum insulin, and 2-hour glucose levels from a glucose tolerance test were measured in participants aged 12 years or older. A total of 959 adolescents aged 12–19 years (474 boys and 485 girls) met the following inclusion criteria for the current study: 1) data available on age, race, sex, fasting glucose, and fasting insulin; 2) fasting duration for at least 8 hours; 3) the handgrip test performed on both hands; and 4) no known diagnosed diabetes. Of the 959 participants, 840 (87.6%) had data on 2-hour glucose from an oral glucose tolerance test. The National Centers for Health Statistics Institutional Review Board reviewed and approved the study protocol.

Examinations

Body weight and height—Standardized measurement procedures were used for height and weight(7). Standing height was measured using a stadiometer with a fixed vertical backboard and an adjustable head piece, and weight on a standard digital scale with the participant wearing only underpants and a standard disposable examination gown. BMI was calculated as body weight in kilogram divided by height in meters squared (kg/m^2).

Handgrip test—Detailed descriptions of the protocol for handgrip strength examination are provided in the NHANES Muscle Strength/Grip Test Procedure Manual available on the NHANES website (<https://www.cdc.gov/nchs/nhanes/>). In brief, after preparation that included explanation and demonstration of the protocol, adjustment of the grip size of a dynamometer, and a practice trial, the participant was asked to use one of the hands to squeeze the dynamometer as hard as possible, exhaling while squeezing to avoid build-up of intra-thoracic pressure. Each hand was tested three times, alternating hands between trials with a 60-second rest between measurements on the same hand. The combined grip strength was calculated as the sum of the largest reading from each hand, and expressed in kilograms.

Oral glucose tolerance test (OGTT)—Detailed descriptions of the protocol for OGTT are provided and available on the NHANES website. In brief, after confirmation of fasting and other inclusion criteria, participants were asked to drink a calibrated dose (generally 75 grams of glucose) of Trutol™ and had blood sample drawn after 2 hours (plus or minus 15 minutes).

Laboratory measurements—Fasting and 2-hour plasma glucose concentrations were measurements by the Beckman UniCel® DxC800 Synchron system (Beckman Coulter Inc., Brea, CA) using a glucose oxidase method. Fasting serum insulin concentration was measured by a chemiluminescent “sandwich” immunoassay using ROCHE ELECSYS 2010 (Roche Diagnostics Corporation, Indianapolis, IN). Detailed descriptions of the protocols can be found in the NHANES Laboratory/Medical Technologists Procedures Manual available on the NHANES website.

Statistical Analysis

Descriptive results were presented as means (SDs) for continuous variables and percentage for categorical variables. Insulin resistance was assessed according to the HOMA-IR formula(28):

$$\text{HOMA-IR} = \text{fasting insulin } (\mu\text{U/ml}) \times \text{fasting glucose (mmol/l)}/22.5$$

Fasting insulin levels and HOMA-IR were log-transformed to increase normality for further analysis. General linear models were used to examine the associations between handgrip strength and outcome variables (fasting and 2-hour glucose, insulin, and HOMA-IR), adjusted for age, race, BMI, and physical activity (including vigorous and moderate activities as two separate variables). Least square means of outcomes that were significantly associated with handgrip strength was displayed by age- and sex-specific quartile of handgrip strength, adjusted for the covariates mentioned above. We also performed the following sensitivity analyses: 1) excluding those who were diabetic (fasting glucose levels ≥ 126 mg/dl, 2-hour glucose ≥ 200 mg/dl, or glycohemoglobin $\geq 6.5\%$) or had a BMI ≥ 40 kg/m², which led to a sample of 891 (448 boys and 443 girls); 2) handgrip strength adjusted for body weight (handgrip strength divided by body weight); and 3) further adjustment for daily sedentary time. In addition, interaction effects between handgrip strength and sex were explored in general linear models for the four outcome variables. All data analyses were performed using SAS 9.4 (SAS Institute, Inc., Cary, NC).

RESULTS

Among 474 boys with an average age of 15.3 years and 485 girls with an average age of 15.4 years (Table 1), boys reported engaging in more vigorous physical activity, had greater handgrip strength, higher levels of fasting glucose, and lower levels of fasting insulin and HOMA-IR.

After adjustment for age, race, sex, BMI, and physical activity levels, handgrip strength was inversely associated with fasting insulin levels ($P=0.017$) and HOMA-IR ($P=0.025$) (Table 2). As shown in previous studies, handgrip strength was not associated with fasting glucose levels ($P=0.77$); however, handgrip strength was inversely and significantly associated with 2-hour glucose levels ($P<0.0001$) (Table 2). The associations of handgrip strength with fasting insulin levels, HOMA-IR, and 2-hour glucose levels were all statistically significant ($P \leq 0.002$) in boys, but not in girls ($P>0.09$) (Supplementary Table).

There was a decreasing trend in fasting insulin and 2-hour glucose levels as handgrip strength increased from the bottom quartile to the top quartile (Figure 1). Mean 2-hour glucose levels in those with handgrip strength in the top quartile was 96.5 ± 1.7 (mean $\pm$ se) mg/dl, compared to 102.7 ± 1.7 mg/dl in those with handgrip strength in the bottom quartile.

The results remained essentially the same 1) if we excluded those who were diabetic or had BMI 40 kg/m^2 , 2) if handgrip strength was adjusted for body weight, or 3) if further adjustment for daily sedentary time was performed.

DISCUSSION

In this national sample of the US adolescents, muscular fitness, measured by a handgrip test, was inversely associated with fasting insulin resistance and 2-hour glucose levels. These associations were independent of BMI and physical activity and persisted in sensitivity analyses, indicating the robustness of these associations. The findings suggest that the first clinically identifiable marker for compromised glucose metabolism associated with low muscular fitness is elevated levels of postprandial rather than fasting glucose in adolescents.

The observed associations of handgrip strength with insulin resistance were robust against the potential confounding effects of obesity and physical activity. The robustness of these associations argues against the concept that the association of muscular fitness with cardiometabolic health in children is mediated by obesity(24). Similarly, the observed associations were independent of vigorous and moderate physical activities. Our findings support previous observations that muscular fitness is associated with insulin sensitivity but not fasting glucose levels(18, 25–27).

Noteworthy is that although handgrip strength was not associated with fasting glucose levels, it was with 2-hour glucose levels. This finding suggests that low muscular fitness is a risk factor for having impaired glucose tolerance, a strong risk factor for the development of type 2 diabetes(29). This novel finding suggests that fasting glucose levels are not a sensitive marker for impaired glucose metabolism in children and adolescents. A glucose tolerance test may be needed to identify those who have impaired glucose metabolism with low muscular fitness. The finding is consistent with previous knowledge that those with impaired glucose tolerance have predominantly muscle insulin resistance(30). With increased insulin resistance accompanied by impaired glucose tolerance, the risk of developing type 2 diabetes in children and adolescents with low muscular fitness may increase substantially.

The underlying mechanisms for the observed associations of muscular fitness with insulin resistance and glucose metabolism are yet to be well examined. Inflammation, an important factor for insulin resistance, is associated with low muscular fitness(31). It is also possible that impaired glucose metabolism associated with low muscular fitness is at least partially due to the intrinsic impaired muscle oxidative capacity(32). Insulin resistance may also linked to low muscular fitness by fat infiltration in the muscle as indicated by low muscle density(33–35). Low cardiorespiratory fitness associated with low muscular fitness may play a role, but studies have shown the adverse effects of low muscular fitness are independent of cardiorespiratory fitness(25). It is also possible that insulin-sensitive glucose transporter 4

(GLUT4) in plasma membrane in skeletal muscles cells is decreased in those with low muscular fitness(36). However, the precise mechanisms for the observed associations remain to be fully examined in future studies.

Findings from the current study have important implications. Adolescents with low muscular fitness may already have compromised glucose metabolism and increased insulin resistance, which makes them susceptible to future type 2 diabetes. Future studies should systematically examine the natural history of impaired glucose metabolism in youth and quantify the risk of type 2 diabetes associated with low muscular strength. If warranted, the utility of low muscular strength as an indicator for high risk of developing type 2 diabetes in youth should also be examined. Importantly, intervention programs to improve fitness are effective in reducing risk for type 2 diabetes in children and adolescents regardless of obesity status(36, 37). Vigorous physical activity, besides being a strong and independent predictor of fasting insulin levels and HOMA-IR(37), improves muscular strength and cardiorespiratory fitness and reduces fatness(14, 38–41). Further, the benefits of high muscular fitness are beyond cardiometabolic risk factors(42). Evidence from 498,135 UK-Biobank adult participants suggests that increasing physical activity may be particularly beneficial in those with low muscular strength(43). Of note, resistant training may also be of substantial benefit for improving insulin resistance, as shown by Shaibi et al(44). Therefore, promoting physical activity, in particular vigorous physical activity, should be a priority in adolescents with limited physical fitness, which is also supported by the findings in the current study that only vigorous physical activity was associated with insulin resistance.

We recognize that our study was cross-sectional in nature. Thus, causality of the observed associations cannot be established. However, combined with findings from previous studies, the observed associations in the current study support muscular fitness as an important identifier for children and adolescents who are at risk of developing type 2 diabetes. In addition, handgrip strength reflects only part of overall muscular fitness, and cardiorespiratory fitness measures were not available. We acknowledge that we did not have information on Tanner stage, which is particularly important for insulin resistance and glucose metabolism during puberty period. Finally, we acknowledge that information on physical activity was self-reported during an interview.

In conclusion, muscular fitness is associated with insulin resistance and glucose metabolism in US adolescents. Our study also suggests that fasting glucose levels may not be a sensitive marker for impaired glucose metabolism in youth. Findings of the current study have important implications for exploring new underlying mechanisms between glucose metabolism and muscular strength and for early prevention of adult cardiometabolic diseases, such as type 2 diabetes.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

Acknowledgments

Shengxu Li is partly supported by grant 13SDG14650068 from American Heart Association and grant 1P20GM109036-01A1 from National Institute of General Medical Sciences.

ABBREVIATIONS

BMI	body mass index
HOMA-IR	homeostasis model assessment of insulin resistance
NHANES	National Health and Nutrition Examination Survey
OGTT	oral glucose tolerance test

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Figure 1.

Log-transformed insulin levels and 2-hour glucose levels from a glucose tolerance test in adolescents from the National Health and Nutrition Examination Survey (NHANES) 2011–2014 by handgrip strength quartile. Handgrip strength quartile was age- and sex-specific. P values were adjusted for age, race, sex, body mass index, and physical activity.

Table 1

Characteristics of the study sample

Variable	Boys (n=474)	Girls (n=485)	P
Age (years)	15.3±2.3	15.4±2.3	0.69
Race (%)			0.55
Non-Hispanic White	27.0	25.8	
Non-Hispanic Black	29.0	25.1	
Mexican American	19.8	22.7	
Other Hispanic	8.2	9.9	
Other	16.0	16.5	
BMI (kg/m ²)	23.9±6.0	24.3±6.7	0.39
Vigorous PA (%)	66.7	42.1	<0.0001
Moderate PA (%)	49.8	48.9	0.77
Handgrip strength (kg)	72.7±20.0	53.5±10.6	<0.0001
Fasting glucose (mg/dl)	95.6±7.3	91.5±7.0	<0.0001
Fasting insulin (mU/l)	13.1±10.5	14.6±10.5	0.0004
HOMA-IR	3.1±2.8	3.3±2.4	0.02
2-hour glucose (mg/dl) *	99.0±24.4	100.1±24.1	0.56

Mean±SD is presented unless otherwise indicated.

HOMA-IR: Homeostasis model assessment of insulin resistance.

* : n=427 for boys and n=413 for girls

Table 2

Regression coefficients of handgrip strength and other covariates for glucose metabolism parameters

Independent variable	Dependent variable					
	Fasting glucose (mg/dl)		Fasting insulin [§]		HOMA-IR [§]	
	$\beta \pm SE$	P	$\beta \pm SE$	P	$\beta \pm SE$	P
Age (per year)	-0.43±0.12	<.0001	-0.072±0.008	<.0001	-0.077±0.009	<.0001
Female gender	-4.04±0.57	<.0001	0.033±0.039	0.39	-0.010±0.041	0.81
Race [§]						
Non-Hispanic Black	-1.54±0.62	0.013	0.070±0.042	0.10	0.053±0.044	0.23
Mexican American	2.00±0.66	0.002	0.132±0.045	0.003	0.153±0.047	0.001
Other Hispanic	0.44±0.86	0.61	0.053±0.058	0.37	0.057±0.061	0.35
Other	0.21±0.71	0.76	0.142±0.048	0.003	0.143±0.051	0.005
BMI (per kg/m ²)	0.19±0.04	<.0001	0.063±0.003	<.0001	0.065±0.003	<.0001
Vigorous PA (Yes)	0.05±0.47	0.91	-0.127±0.032	<.0001	-0.126±0.034	0.0002
Moderate PA (Yes)	0.01±0.46	0.99	-0.035±0.031	0.26	-0.034±0.033	0.29
Handgrip (per kg)	0.01±0.02	0.77	-0.003±0.001	0.017	-0.003±0.001	0.025

PA: physical activity; BMI: body mass index; HOMA-IR: homeostasis model assessment of insulin resistance

[§]: log-transformed;

[§]: relative to non-Hispanic white