Original Article

The relationship between dietary inflammatory index (DII) and muscle mass and strength in Chinese children aged 6-9 years

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Background and Objectives: The dietary inflammatory index (DII®) is a measure of the overall inflammatory potential of a person's diet. However, there have been no studies looking at the effect of DII on measures of muscle mass and strength. We aimed to examine the association between DII and skeletal muscle mass and strength in Chinese children. **Methods and Study Design:** A total of 466 children aged 6-9 years completed the study. Total body skeletal muscle mass (TSM), appendicular skeletal mass (ASM) and appendicular lean mass (ALM) were determined using Dual-energy X-ray absorptiometry. TSM/Height², TSM/Weight, ASM/Height² and ASM/Weight were calculated. The residual method was applied to compute ALM index (ALMI) adjusted for height and body fat. Hand grip strength was measured using hand dynamometer. DII scores were calculated from a 79-item food frequency questionnaire. **Results:** Fully adjusted linear regression models showed a statistically significant negative relationship between DII and ASM, ASM/Height², ASM/Weight, ALMI, TSM, TSM/Height², and TSM/Weight (*p*: 0.019–0.014). The analysis of covariance indicated that the percentage differences in the extreme quartiles (Q4 vs Q1) of DII for the above-mentioned measures ranged from -1.04% to -4.36% (*p*-trend: <0.001–0.013). When boys and girls were analyzed separately, similar findings were observed for boys but not for girls. No significant associations were detected between DII and hand grip strength. **Conclusions:** DII score was inversely associated with skeletal muscle mass in boys but not in girls aged 6-9 years old. No significant associations were observed between DII and hand grip strength.

Key Words: dietary inflammatory index, skeletal muscle mass, muscle strength, children, Guangzhou

INTRODUCTION

Skeletal muscle mass plays a pivotal role in the maintenance of metabolic homeostasis, affecting the pathogenesis of obesity, diabetes, and other diseases. It also serves as the primary reservoir for amino acids to maintain protein synthesis in vital tissues and organs.[1] Muscular strength has been increasingly recognized in the pathogenesis and prevention of chronic diseases.[2] In younger populations, muscular fitness has been inversely related to insulin resistance,[3,4] clustered cardiometabolic risk,[5,6] as well as risk of hypertension[7] and incidence of metabolic syndrome.[8] In addition, muscle mass and strength achieved in later life are not only determined by the rate of muscle loss, but also reflect the peak attained in early life.[9] Thus, identifying the important modifiable risk factors of muscle mass and strength in pediatric populations is crucial to improve health.

Beyond aging, muscle wasting is also a feature associated with several pathological states or chronic diseases such as malnutrition, chronic kidney disease, burns, muscular dystrophies, inflammatory bowel disease, and immune disorders,[10] which are also reported in pediatric patients.[11,12] Most of the above-mentioned pathological

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conditions are linked with variable degrees of local and/or systemic chronic inflammation, a factor that could play a vital role in the onset of muscle wasting.[10] In vitro studies indicate that administration of interleukin 6 (IL-6) or tumor necrosis factor-α (TNF-α) in rats increases skeletal muscle protein breakdown, decreases the rate of protein synthesis, reduces the total skeletal muscle amino acid concentration, and induces muscle wasting.[13,14] Studies in both adults and adolescents have revealed that higher circulating levels of inflammatory markers such as IL-6, C-reactive protein (CRP) correlated with lower muscle mass and strength.[15-18] Muscle protein breakdown and the alteration of amino acid turnover may provide for potential mechanisms linking inflammation and poor muscle fitness. Dietary factors have been suggested to modulate inflammation status and, in turn, downstream health effects.[19] Specific dietary components, such as fiber and moderate amounts of ethanol, have been shown to have anti-inflammatory properties.[20] In contrast, some nutrients have been shown to be associated with higher levels of inflammation, e.g., saturated fatty acids (SFAs) and trans fatty acids.[21] The dietary inflammatory index (DII®) is a novel composite score developed by researchers at the University of South Carolina to estimate the overall inflammatory potential of the diet based on a range of nutrients and foods known to be associated with inflammation.[22] Higher DII scores, indicating greater inflammatory potential, have been proven to correlate with greater inflammatory biomarker levels, including C-reactive protein (CRP),[21] IL-6[23] and TNF-α[24] in adults. A recent study in pediatric group reinforced the fact that higher DII was also associated with increased levels of various inflammatory markers including TNF-α, IL-1, IL-2 and IFN-γ.[25] Cumulative evidence has suggested that unhealthy eating mostly starts during the period of childhood and/or adolescence, and progresses throughout life and thus contribute to the onset of various chronic diseases later in life,[26,27] including sarcopenia.[28] However, there have been no studies looking at the effect of DII on measures of muscle mass and strength, in either adults or children. We aimed to examine the association between the overall inflammatory potential of diet measured by the DII and skeletal muscle mass and strength in healthy Chinese children.

METHODS

Subjects

This cross-sectional study involved a total of 466 children (266 boys and 200 girls) between 6 to 9 years of age in urban Guangzhou city, China from December 2015 to January 2017 who were recruited as follows; A total of 1394 children were invited by sending invitation letters with detailed inclusion and exclusion criteria to their primary schools, 315 responded and agreed to participate in the study. A further two hundred and six children were enrolled by advertisements and referrals bringing the total number that agreed to enrol to 521. Only healthy, developmentally normal, aged 6–9 years, full-term singleton children were studied. We excluded 12 twins and 25 children born preterm, and 12 with childhood medical conditions that might have interfered with growth. These conditions included: thyrotoxicosis (2); diseases of the digestive tract (2); kidney stones or inflammation of the kidney (2); hepatitis (1); metabolic bone diseases (1); and anaphylactoid purpura (1). Six children did not complete muscle mass measurements. Thus, we based the analyses on 466 participants (Figure 1). The investigators confirmed the information regarding the children who agreed to participate in the study via phone call before they were invited for physical examination. A written consent was approved by each participant through his or her parent or legal guardian before enrollment. The study was conducted in accordance with the Declaration of Helsinki and was approved by the ethics committee of the School of

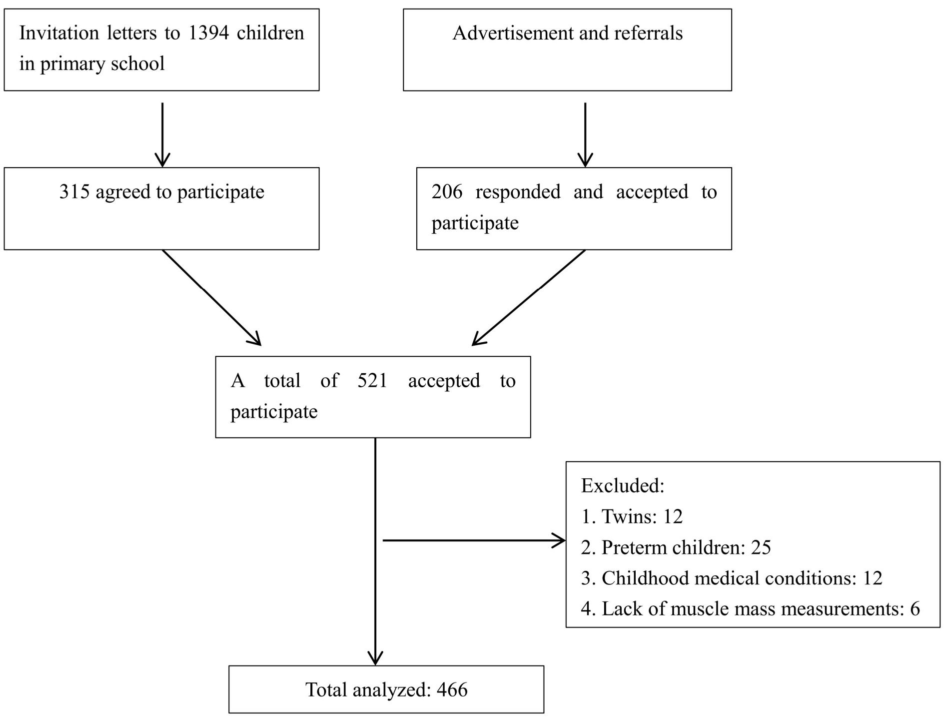

Figure 1. Flow chart for selection of study participants.

Public Health at Sun Yat-sen University (201549).

Data collection

Anthropometric measures

Weight was measured to the nearest 0.1kg using a Tanita MC-780A (Tanita Corporation, Tokyo, Japan) scale with participants wearing light clothes and no shoes. Height was measured to the nearest 0.1 cm using a portable fixed stadiometer, with the child in an upright position. Whole-body DXA scans were performed using Hologic Discovery W (Discovery W; Hologic Inc., Waltham, MA, USA), in accordance with the manufacturer's instructions, to determine total skeletal mass (TSM), appendicular skeletal mass (ASM) and appendicular lean mass (ALM). Reproducibility was assessed by replicating measurements for 34 randomly selected subjects on the same day after re-positioning. The *in-vivo* reproducibility values of muscle mass at total body and limbs were 0.77% and 1.56%, respectively; while that for lean mass at the limb was 2.68%. Skeletal muscle mass indices were calculated as TSM (kg) / Height $(m)^2$, TSM (kg) / Weight (kg) × 100, ASM (kg) / Height $(m)^2$ and ASM (kg) / Weight (kg) × 100. The residual method was applied to compute appendicular lean mass index (ALMI) by adjusting for height and body fat according to the model proposed by Newman et al[29] but with some slight modifications according to the formula below;

$$\text{ALMI} = \beta 1 \times \text{Body fat mean} + \beta 2 \times \text{Height mean} + \text{Constant} + \text{Residual};$$

where βi, constant and residual were derived from the linear regression model.

Hand grip strength measurement

In accordance with the European Working Group on Sarcopenia in Older People's criteria, handgrip strength was use to evaluate muscle strength [30] using the Jamar® Plus+ Hand Dynamometer (JAMAR® Hydraulic Hand Dynamometer, Sammons Preston, Bolingbrook, IL, USA) with standard test posture according to the manufacturer's instructions. Grip strength was measured while children were in a sitting position with shoulder adducted and neutrally rotated elbow at 90°flexion, and the forearm and wrist in neutral positions. The handle of the device was set to the second position for all participants. Children were instructed to squeeze the handle of the dynamometer as hard as they could and to sustain the effort for 5 seconds. Verbal encouragement (i.e., squeeze as hard as you can) was provided to children during testing. Children performed three trials for each hand, with one minute of rest between trials and alternating hands to minimize the effects of fatigue.[31] The mean values of these trials were recorded for muscle strength indices as right hand grip strength and left hand grip strength. Replicating measurements were performed in 28 randomly selected children within a time interval of about 30 minutes. The coefficient of variation in the left hand was 9.48%, and the right hand was 8.19%.

DII calculation

Usual dietary intake for the past one year was assessed by a validated 79-item food frequency questionnaire.[32] The parents and their children were asked to respond to the questionnaires together. Photographs of food portion sizes were provided to help estimate the amount of food consumption. For each food item, 5 possible frequencies (never, per year, per month, per week, and per day) and 1 quantitative (amounts) response were available. Daily mean nutrient and energy intakes were calculated using the Chinese Food Composition Table, 2009.[33] The flavonoid values were derived from two USDA databases of flavonoids[34] and proanthocyanidins,[35] and one Hong Kong database of isoflavones.[36] The consumption of vitamin D and β-carotene were calculated based on the USDA databases of carotenoids[37] and vitamin D.[38]

The exact derivation method of DII has been reported elsewhere.[22] Briefly, DII is a scoring algorithm based on an extensive review of the literature published from 1950 to 2010, linking 1943 articles to a total of forty-five food parameters. These dietary parameters were scored according to whether they increased (for a score of +1) or decreased (for -1) or had no effect (0) on six inflammatory biomarkers (Interleukin 1b (IL-1b), interleukin 4 (IL-4), IL-6, interleukin 10 (IL-10), TNF-α and C-reactive protein (CRP). To avoid over or under estimation of any one food parameter on the overall score, an individual's dietary intake was standardized to mean intakes from a global composite dataset created for this purpose and converted to proportions for the calculation of an overall DII score. For this study, 32 of the 45 food parameters were available for the construction of the DII: total energy intake, protein, carbohydrate, total fat, saturated fatty acids, cholesterol, vitamins A, B6, C, D, E, B-12, thiamin, niacin, riboflavin, magnesium, folic acid, monounsaturated fatty acid (MUFA), polyunsaturated fatty acid (PUFA), n-3 PUFA, n-6 PUFA, fiber, beta-carotene, anthocyanidins, flavan-3-ols, flavonols, flavones, flavanones, isoflavones, iron, selenium, and zinc. A total of 28 children and their parents completed 3-day dietary records and two FFQs (FFQ1 and FFQ2) over a 12-month interval. Reproducibility was estimated by comparing the intakes from FFQ1 and FFQ2. Intraclass correlation coefficients between FFQ1 and FFQ2 were significant for 28 out of 32 items that was included in the DII calculation and ranged from 0.31 to 0.78. Validity of the FFQ was evaluated by comparing the average of the 3-day dietary records with data of FFQ1. Pearson correlation coefficients between dietary intake estimates derived from the FFQ and the 3-day dietary records were significant for 26 out of 32 items used to calculate DII and ranged from 0.37 to 0.68.

Covariates

Face-to-face interviews were conducted by trained interviewers to collect essential parental information including age, height, weight, educational level and birth weight of their children. We classified parental current education level into four categories: primary or less, secondary, graduate, post graduate or above. A three-day physical activity questionnaire was made to obtain daily physical activities. Each day was divided into 96 blocks (15 minutes per block) of time between 0:00 and 24:00. Participants were asked to recall the types of activities in each block on 2 ordinary school days and 1 weekend day. Physical activity was calculated by combining the metabolic equivalent score (MET, kcal•kg-1•h-1) for each type

Table 1. Characteristics of the participants

Variables	Total (N=466)		Boys (N=266)		Girls (N=200)		p
	Mean	SD	Mean	SD	Mean	SD	
Age(years)	8.0	1.0	8.0	1.0	8.1	1.0	0.438
Height (cm)	128.7	8.1	128.9	8.3	128.5	7.8	0.642
Weight (kg)	26.5	7.1	27.4	8.0	25.4	5.5	0.003
BMI (kg/m^2)	15.8	2.7	16.3	3.0	15.2	2.4	<0.001
Birth Weight (kg)	3.3	0.4	3.3	0.4	3.2	0.4	0.002
Maternal BMI (kg/m^2)	21.8	7.2	22.2	9.4	21.3	2.5	0.215
Paternal BMI (kg/m^2)	23.7	2.8	23.7	3.1	23.7	2.6	0.926
Maternal educational level (%)							
Primary or less	2.8	-	3.4	-	2.0	-	0.141
Secondary	35.3	-	34.2	-	37.0	-	
Graduate	53.1	-	51.3	-	55.5	-	
Post graduate or above	8.6	-	11.0	-	5.5	-	
Paternal educational level (%)							
Primary or less	1.5	-	1.9	-	1.0	-	0.542
Secondary	39.1	-	38.7	-	39.7	-	
Graduate	45.7	-	54.8	-	47.7	-	
Post graduate or above	13.7	-	15.3	-	11.6	-	
Physical activity (MET.h/d)†	40.0	4.3	40.7	4.5	39.0	3.8	<0.001
Energy adjusted DII	1.40	1.42	1.91	1.75	1.93	1.57	0.863
Total Body Fat (kg)	7.5	3.7	7.6	4.1	7.4	3.0	0.629
Right Handgrip Strength (kg)	10.6	2.9	11.1	3.1	9.9	2.5	<0.001
Left Handgrip Strength (kg)	9.9	2.7	10.4	2.9	9.3	2.3	<0.001
ASM (kg)	7.5	1.8	7.9	1.9	7.0	1.4	<0.001
ASM/Height^2 (kg/m^2)	4.4	0.6	4.7	0.6	4.2	0.5	<0.001
ASM/Weight (%)	28.4	2.8	28.9	2.8	27.7	2.8	<0.001
ALMI (kg)	9.5	2.4	11.5	0.9	6.9	0.7	<0.001
Total Skeletal Mass (kg)	18.1	3.7	18.9	4.0	17.0	3.0	<0.001
TSM/Height^2 (kg/m^2)	10.8	1.2	11.3	1.3	10.2	0.9	<0.001
TSM/Weight (%)	69.0	5.9	70.0	5.9	67.6	5.6	<0.001

BMI: body mass index; DII: Dietary Inflammatory Index; ASM: appendicular skeletal mass; ALMI: appendicular lean mass index; TSM: total skeletal mass.
†Physical activity, evaluated by metabolic equivalent (MET) hours per day.

of physical activity after multiplying it by its duration per day (h/d).[39]

Statistical analysis
Basic data were presented as means and standard deviations for continuous variables and percentages for categorical variables. The analyses were firstly conducted separately for boys and girls. DII were adjusted for the total energy intake using the residual method.[40] Two multiple linear regression models were applied to detect the association between DII and muscle mass by the entered method. In model 1, adjustments were made for child's age, and in model 2, we further adjusted for height (except for ASM/Height^2 and TSM/Height^2), birth weight, physical activity, maternal educational level, paternal educational level, maternal BMI, paternal BMI and total body fat. Differences in means of the skeletal mass and strength were compared across the quartiles of DII using analysis of covariance (ANCOVA) after controlling for similar potential covariates as used in Model 2 of linear regression analysis and pairwise comparison was analyzed by the Bonferroni method (three pairwise combinations within each outcome). The interactions between DII and sex were estimated by adding interaction terms in all models. Because no significant interactions were found between DII and sex (p-interactions: 0.405–0.935), the analyses were further performed for boys and girls combined. In the whole sample, sex was also added as a confounder. Potential confounders were identified by drawing a directed acyclic graph (DAG) using DAGitty version 2.3.[41] All statistical procedures were done with SPSS® for windows software (version 21.0, SPSS Inc., Chicago, IL) and a p-value of less than 0.05 was considered significant in all cases.

RESULTS
Detailed characteristics of the study participants are presented in Table 1. There were a total of 466 children (266 boys and 200 girls) with mean ages of 8.0±1.0 years for boys and 8.1±1.0 years for girls who completed the study. BMI was higher in boys than girls (16.3 vs 15.2 kg/m^2, p<0.001). There were significant gender differences in ASM, ASMI, TSM, ALMI and hand grip strength with boys having higher values for all these indices (p<0.05). However, there were no statistical differences in DII between girls and boys (1.93 vs 1.91, p=0.863).

Table 2 shows the detailed nutrient intake of participants which was used to calculate the DII.

Table 3 shows the multiple linear regression analysis of the association between DII and muscle fitness measures. After controlling for age, a negative association was observed between DII and ASM, ASM/Height^2, ALMI, TSM, and TSM/Height^2 in boys but not in girls. Further adjustment for other con-founders attenuated all of the associations but remained significant. When boys and girls were combined, a unit increase in DII resulted in a

Table 2. Total diary energy and nutrient intake of participants

Variables	Total (N=466)		Boys (N=266)		Girls (N=200)		p
	Mean	SD	Mean	SD	Mean	SD	
Energy (kcal)	1437	435	1513	448	1336	395	<0.001
Carbohydrate (g)	200	58	211	61	185	51	<0.001
Protein (g)	64.9	22.8	67.4	23.7	61.7	21.3	0.008
Total fat (g)	43.8	19.5	46.2	20.0	40.7	18.4	0.003
Saturated fats (g)	14.2	6.5	14.9	6.7	13.2	6.0	0.005
Monounsaturated fatty acids (g)	15.1	7.5	15.9	7.7	14.1	7.1	0.010
Polyunsaturated fatty acids (g)	9.3	5.3	9.7	5.3	8.7	5.3	0.043
n-3 polyunsaturated fatty acids (g)	0.6	0.3	0.6	0.3	0.6	0.4	0.139
n-6 polyunsaturated fatty acids (g)	5.7	3.1	5.8	2.7	5.6	3.7	0.679
Flavan-3-ols (mg)	8.7	7.9	8.7	6.6	8.6	9.5	0.879
Flavones (mg)	2.4	2.4	2.4	2.6	2.4	2.1	0.975
Flavonols (mg)	15.9	11.9	15.8	13.1	16.0	10.0	0.910
Flavanones (mg)	15.2	19.8	14.5	15.9	16.2	24.1	0.338
Anthocyanidins (mg)	28.3	23.7	27.2	22.7	29.9	24.9	0.228
Isoflavones (mg)	12.2	12.7	12.3	10.3	12.0	15.3	0.771
Cholesterol (mg)	362	167	377	180	342	146	0.023
Fiber (g)	7.7	4.0	7.7	3.5	7.6	4.6	0.760
Beta-carotene (μg)	4238	2973	4217	3126	4366	2766	0.861
Selenium (μg)	46.5	20.5	47.5	20.9	45.2	20.0	0.248
Iron (mg)	15.6	5.1	16.1	5.2	14.9	4.8	0.012
Magnesium (mg)	263	92	268	91	255	93	0.123
Folic Acid (mg)	190	74	195	74	185	75	0.171
Zinc (mg)	10.6	3.4	11.1	3.5	10.0	3.2	<0.001
Niacin (mg)	18.1	6.2	19.1	6.6	16.9	5.4	<0.001
Riboflavin (mg)	1.1	0.3	1.1	0.4	1.0	0.3	0.028
Thiamin (mg)	0.8	0.3	0.8	0.3	0.7	0.3	0.052
Vitamin A (RE)	684	355	685	372	682	336	0.943
Vitamin C (mg)	80.4	43.6	79.5	45.1	81.5	41.7	0.612
Vitamin D (μg)	2.4	1.4	2.5	1.5	2.3	1.2	0.042
Vitamin E (mg)	11.4	5.7	11.5	5.2	11.3	6.3	0.789
Vitamin B-12 (μg)	1.5	0.9	1.5	0.9	1.5	0.9	0.386
Vitamin B-6 (mg)	0.8	0.4	0.7	0.4	0.8	0.4	0.047

60.6 g, 118 g and 60.1 g decrease in ASM, TSM and ALMI after adjustment for all the potential covariates, respectively ($p<0.05$). In terms of ASM/Height^2, TSM/Height^2 ASM/Weight, TSM/Weight, there were 0.034 kg/m^2, 0.066 kg/m^2, 0.197% and 0.285% decrease per unit increase in DII, respectively ($p<0.05$). No significant relationship between grip strength of either hand and DII was detected.

A graded association of muscle mass across quartiles of DII was observed in ANCOVA analysis for boys and the whole sample (Table 4). Total sample analysis suggested that the mean percentage differences between quartiles 4 and 1 were -4.03%, -4.15%, -1.74%, -3.24%, -2.73%, -1.15%, and -3.08% for ASM, ASM/Height^2, ASM/Weight, TSM, TSM/Height^2, TSM/Weight and ALMI, respectively (*p*-trend: <0.001–0.013). No group differences were observed for hand grip strength.

Figure 2 presents the conceptual diagram showing hypotheses and findings of the present study.

DISCUSSION

To the best of our knowledge, this is the first study conducted to investigate the association between DII and muscle mass and strength in healthy children aged 6-9 years old. We found that boys but not girls with higher DII scores exhibited lower total body and limb muscle mass. However, no significant correlation between DII and hand grip strength were observed in both genders.

Inflammation has been proven to trigger protein catabolism and impair the anabolic response in the skeletal muscle.[42] Pro-inflammatory cytokines such as TNF-α, IL-1, IL-6, and IFN-γ, are well known to impinge on muscle protein metabolism. In experimental models, administration of IL-6 or TNF-α in rats increased skeletal muscle protein breakdown, decreased the rate of protein synthesis, reduced the total skeletal muscle amino acid concentration, and caused muscle wasting.[13,14] In a cross-sectional study of 3075 Black and White men and women aged 70–79 years, Visser et al suggested that elderly persons having high levels of IL-6 (>1.80 pg/mL) as well as high levels of TNF-α (>3.2 pg/mL) had less appendicular muscle mass and a lower grip strength compared with those with low levels of both cytokines.[15] The results from the National Health and Nutrition Examination Surveys 1999-2004 also revealed a significant inverse associations between ALM:BMI and ln CRP (β=-2.58; $p=0.001$) and fibrinogen (β=-124.2; $p<0.001$).[16] Such an association has also been shown in longitudinal studies. In a 5-year prospective study including 115 non-sarcopenic older men and women aged 60–84 years, Alemán et al found that the risk of ASM loss was 1.29 times higher (95% confidence interval [CI], 1.01–1.64) per unit increase in IL-6 (pg/mL) and 1.28 times higher (95% CI, 1.04–1.58) per unit increase in CRP (mg/L).[43] In accordance with the findings in older adults, Ruiz et al found that CRP (β=-0.208, $p=0.007$), complement factor C3 (β=-0.115, $p=0.047$),

Table 3. Linear regression analysis of the associations between DII and muscle mass and strength

Variables	Model 1				Model 2			
	β (×10^-2^)	95% CI	*p*	R^2	β (×10^-2^)	95% CI	*p*	R^2
ASM (kg)								
Boys	-16.7	-27.3, -6.20	0.002	0.374	-6.34	-11.9, -0.74	0.027	0.841
Girls	-1.65	-12.0, 8.72	0.754	0.318	-4.33	-10.5, 1.81	0.166	0.781
Overall	-11.0	-18.6, -3.41	0.005	0.386	-6.06	-10.2, -1.87	0.006	0.827
ASM/Height^2 (kg/m^2)								
Boys	-7.20	-11.3, 3.11	0.001	0.185	-3.57	-6.78, -0.36	0.029	0.549
Girls	-1.98	-6.10, 2.15	0.346	0.065	-2.49	-6.18, 1.20	0.184	0.304
Overall	-5.21	-8.17, -2.24	0.001	0.260	-3.36	-5.78, -0.95	0.006	0.547
ASM/Weight (%)								
Boys	7.66	-11.4, 26.7	0.430	0.020	-10.8	-22.3, 0.73	0.066	0.682
Girls	-9.27	-33.8, 15.3	0.457	0.030	-7.92	-21.8, 6.01	0.263	0.700
Overall	1.21	-13.8, 16.2	0.875	0.070	-10.9	-19.7, -1.98	0.017	0.692
ALMI (kg)								
Boys	-7.05	-13.0, -1.10	0.020	0.033	-5.97	-12.1, 0.17	0.057	0.078
Girls	-4.52	-11.1, 20.3	0.175	0.037	-4.76	-11.1, 1.61	0.206	0.127
Overall	-6.08	-10.5, -1.64	0.007	0.888	-6.01	-10.5, -1.51	0.009	0.893
TSM (kg)								
Boys	-36.1	-58.7, -13.6	0.002	0.342	-12.5	-23.1, -1.85	0.022	0.869
Girls	-1.84	-24.0, 20.3	0.870	0.301	-8.01	-20.0, 3.95	0.188	0.815
Overall	-23.0	-39.2, -6.85	0.005	0.363	-11.8	-19.8, -3.73	0.004	0.856
TSM/Height^2 (kg/m^2)								
Boys	-14.8	-23.2, -6.43	0.001	0.100	-7.07	-13.1, -1.02	0.022	0.581
Girls	-3.53	-11.5, 4.47	0.385	0.015	-4.84	-11.8, 2.09	0.170	0.315
Overall	-10.5	-16.5, -4.56	0.001	0.228	-6.64	-11.2, -2.10	0.004	0.587
TSM/Weight (%)								
Boys	32.8	-7.5, 73.1	0.110	0.035	-14.4	-31.6, 2.72	0.099	0.844
Girls	-14.9	-64.4, 34.7	0.554	0.003	-11.0	-29.1, 7.15	0.234	0.872
Overall	14.6	-16.6, 45.8	0.358	0.054	-15.6	-28.5, -2.58	0.019	0.847
Right handgrip strength (kg)								
Boys	-16.7	-33.6, 0.26	0.054	0.373	-6.27	-20.9, 8.33	0.399	0.578
Girls	0.37	-18.7, 19.4	0.969	0.263	-2.55	-19.3, 14.2	0.765	0.464
Overall	-10.2	-22.9, 2.53	0.117	0.351	-5.13	-16.1, 5.81	0.357	0.549
Left handgrip strength (kg)								
Boys	-16.0	-32.1, 0.15	0.052	0.344	-6.28	-20.7, 8.18	0.393	0.527
Girls	-3.03	-21.4, 15.3	0.745	0.236	-6.02	-22.6, 10.5	0.474	0.428
Overall	-11.0	-23.2, 1.10	0.075	0.328	-6.73	-17.6, 4.11	0.223	0.502

DII: dietary inflammation index; ASM: appendicular skeletal mass; ALMI: appendicular lean mass index; TSM: total skeletal mass.
Model 1: adjusted for age and sex (for the overall analysis).
Model 2: additionally adjusted for height (except for ASM/Height2 and TSM/Height2), birth weight, physical activity, maternal educational level, paternal educational level, maternal BMI, paternal BMI, and total body fat.

and ceruloplasmin (β=-0.142, *p*=0.003) levels were negatively associated with muscle strength in a cross-sectional study of Spanish adolescents.[17] Steene-Johannessen et al also reported that muscle strength was independently associated with the CRP (β=-0.122, *p*<0.002) in 1306 nine-years old Norwegian children.[18] Although limited epidemiological evidence exists to rule out a link between inflammatory markers and muscle mass content in children, muscle wasting observed in pediatric patients with high pro-inflammatory state such as chronic kidney disease, burns, inflammatory bowel disease, and immune disorders also evidenced such an association.[11,12]

Diet is a strong moderator of chronic, systemic inflammation.[19] The DII is a relatively new dietary index that is based on peer-reviewed research used to determine the overall inflammatory potential of diet, characterizing both pro- and anti-inflammatory potential. In previous research, the DII was validated against inflammatory biomarkers such as blood IL-6[21,23] and CRP[44] concentrations. The effects of specific components of DII on muscle fitness have been detected in some studies among older adults. In a 5-year follow-up study of 836 participants aged 66–96 y at baseline, a positive association between concentrations of total PUFAs and muscle size was detected in cross-sectional but not longitudinal analyses, and no relationship between PUFAs and grip strength was observe.[45] A population-based study in Italy enrolling 628 older subjects suggested that adults with lower plasma carotenoids levels were at a higher risk of decline in skeletal muscle strength over a 6-year follow-up.[46] Lauretani et al reported that older participants in the bottom versus the top quartile of plasma selenium were at higher risk of poor hip strength [odds ratio (OR): 1.69; 95% CI: 1.02, 2.83], knee strength (OR: 1.94; 95% CI: 1.18, 3.19), and grip strength (OR: 1.94; 95% CI: 1.19, 3.16).[47] In 986 Italians aged ≥65 years, plasma level of α-tocopherol, γ-tocopherol, vitamin C and β-carotene were found to correlate positively with muscle strength.[48] In contrast, from 2689 women aged 18-79 years, Welch et al reported that extreme quintile differences of fat-free mass index for daily SFAs, and total fatty acids intake were -0.29 and -0.24 kg/m^2, respectively.[49] In the pediatric group, only the relation between vitamin D (an anti-inflammatory food parameter of DII) status and muscle mass and function

Table 4. Analysis of covariance of the associations between quartiles of DII and muscle fitness measures

Variables	Quartiles of DII								% Diff	ANCOVA	
	Q1		Q2		Q3		Q4				
	Mean	95% CI	Mean	95% CI	Mean	95% CI	Mean	95% CI		*p*-diff	*p*-trend
ASM (kg)											
Boys	8.10	7.91, 8.29	7.92	7.73, 8.11	7.74	7.55, 7.93	7.75	7.56, 7.95	-4.32	0.033	0.006
Girls	7.11	6.91, 7.31	7.00	6.81, 7.19	6.87	6.67, 7.06	6.89	6.70, 7.09	-3.09	0.248	0.077
Overall	7.69	7.55, 7.83	7.53	7.39, 7.66	7.36**	7.22, 7.50	7.38*	7.24, 7.51	-4.03	0.004	0.001
ASM/Height^2 (kg/m^2)											
Boys	4.81	4.70, 4.92	4.68	4.57, 4.79	4.58*	4.47, 4.69	4.60*	4.49, 4.71	-4.37	0.019	0.004
Girls	4.27	4.15, 4.39	4.18	4.07, 4.30	4.13	4.01, 4.24	4.13	4.01, 4.24	-3.28	0.249	0.059
Overall	4.58	4.50, 4.66	4.47	4.39, 4.55	4.38**	4.30, 4.46	4.39**	4.31, 4.47	-4.15	0.002	<0.001
ASM/Weight (%)											
Boys	29.3	28.9, 29.7	29.0	28.6, 29.4	28.9	28.5, 29.3	28.7	28.3, 29.1	-2.05	0.189	0.032
Girls	27.9	27.4, 28.3	27.8	27.4, 28.3	27.5	27.0, 27.9	27.5	27.1, 28.0	-1.43	0.458	0.163
Overall	28.7	28.4, 29.0	28.5	28.2, 28.8	28.3	28.0, 28.6	28.2	27.9, 28.5	-1.74	0.051	0.006
ALMI (kg)											
Boys	11.7	11.5, 12.0	11.6	11.4, 11.8	11.4	11.2, 11.3	11.4	11.2, 11.6	-2.56	0.132	0.025
Girls	7.07	6.86, 7.27	6.95	6.75, 7.15	6.80	6.60, 7.00	6.84	6.64, 7.04	-3.25	0.247	0.071
Overall	9.73	9.58, 9.88	9.59	9.45, 9.74	9.43*	9.28, 9.57	9.43*	9.28, 9.58	-3.08	0.015	0.002
TSM (kg)											
Boys	19.4	19.0, 19.7	19.0	18.6, 19.4	18.7	18.3, 19.0	18.7	18.3, 19.1	-3.61	0.033	0.006
Girls	17.2	16.8, 17.6	17.1	16.7, 17.4	16.8	16.4, 17.2	16.8	16.4, 17.2	-2.33	0.374	0.094
Overall	18.5	18.2, 18.7	18.2	17.9, 18.4	17.9*	17.6, 18.1	17.9*	17.6, 18.1	-3.24	0.001	0.005
TSM/Height^2 (kg/m^2)											
Boys	11.5	11.3, 11.7	11.3	11.1, 11.5	11.1*	10.9, 11.3	11.1	10.9, 11.3	-3.48	0.022	0.004
Girls	10.4	10.2, 10.6	10.2	10.0, 10.4	10.1	9.9, 10.3	10.1	9.9, 10.3	-2.88	0.284	0.060
Overall	11.0	10.9, 11.2	10.8	10.7, 11.0	10.7**	10.5, 10.8	10.7**	10.5, 10.8	-2.73	0.002	<0.001
TSM/Weight (%)											
Boys	70.4	69.8, 71.0	70.0	69.4, 70.6	70.1	69.5, 70.7	69.6	67.0, 70.2	-1.14	0.276	0.081
Girls	67.6	67.1, 68.2	68.2	67.6, 68.7	67.5	67.0, 68.0	67.3	66.7, 67.9	-0.44	0.175	0.190
Overall	69.3	68.8, 69.7	69.2	68.8, 69.6	69.0**	68.5, 69.4	68.5**	68.1, 69.0	-1.15	0.076	0.013
Right handgrip strength (kg)											
Boys	11.2	10.7, 11.7	11.2	10.7, 11.7	11.0	10.5, 11.5	11.0	10.5, 11.5	-1.79	0.853	0.427
Girls	10.0	9.50, 10.6	10.1	9.53, 10.6	9.55	9.02, 10.1	10.1	9.61, 10.7	1.00	0.404	0.864
Overall	10.7	10.3, 10.1	10.7	10.3, 11.1	10.4	10.0, 10.7	10.6	10.2, 11.0	-0.93	0.551	0.427
Left handgrip strength (kg)											
Boys	10.5	10.0, 11.0	10.6	10.1, 11.1	10.3	9.83, 10.8	10.2	9.70, 10.7	-2.86	0.675	0.292
Girls	9.43	8.91, 9.93	9.40	8.89, 9.92	8.89	8.37, 9.40	9.49	8.97, 10.0	0.64	0.346	0.758
Overall	10.0	9.68, 10.4	10.1	9.75, 10.5	9.73	9.37, 10.1	9.87	9.51, 10.2	-1.30	0.452	0.274

ASM: appendicular skeletal mass; ALMI: appendicular lean mass index; TSM: total skeletal mass.
All analysis were adjusted for age, sex (for overall models only), height (except for ASM/Height^2 and TSM/Height^2), birth weight, physical activity, maternal educational level, paternal educational level, maternal BMI, paternal BMI, and total body fat.
%Diff=(Q4-Q1/Q1)*100; P-diff: *p* value of the differences among groups; *p* -trend: *p* value of the linear trend among groups.
$^*p<0.05$; $^{**}p<0.01$; compared with Q1 in Bonferroni pairwise comparison model.

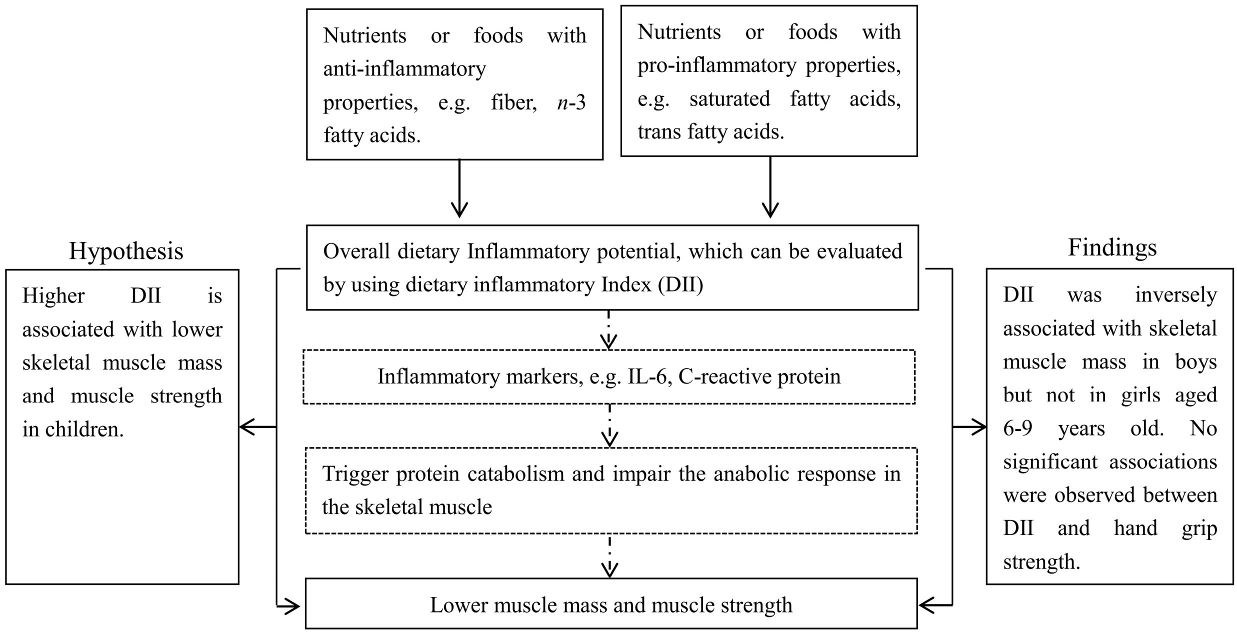

Figure 2. Conceptual diagram showing hypotheses and findings of the study.

has been studied and the results are conflicting.[50]

Single nutrients or foods may be highly correlated, and it may not be possible to separate individual effects, and the effect of any single nutrient may be too small to observe; and examining numerous individual food constituents may lead to chance findings. Instead of examining individual nutrients or foods in relation to disease, the DII score takes into account interaction and intercorrelations among foods and nutrients. As such, it can provide more promising strategies for preventing and controlling diseases.

Prior to this, no study has tested the association of the DII and muscle fitness. We found a statistically significant inverse association between the proinflammatory capacity of the diet (as measured by the DII) and muscle mass in the combined sample. When data was analyzed in sex strata, the observed associations were not significant in girls. It is worth noting that some studies have shown the existence of a significant difference in inflammation markers between boys and girls less than 10 years[51] and also differences in inflammatory response.[52] Such gender dimorphism may provide potential explanations for the differences between boys and girls observed in our study. No significant relationship between DII and muscle strength was observed. Other factors, such as muscle mass and physical activity level, may play more important and direct roles in the muscle strength of children. Further studies in pediatric populations, with larger sample size and multiple ethnic groupings, are needed to confirm these findings.

The strength of our study includes the use of DXA for the estimation of skeletal muscle mass, and assessments of both muscle mass and muscle strength. There are also study limitations to consider. First, because of the cross-sectional design of the study, the analyses of the relation between micronutrient concentrations and muscle fitness cannot presume causality, only association. Therefore, we cannot establish the directionality of the reported associations. Second, 13 food parameters were not included for complete calculation of DII scores. However, some of these food parameters such as thyme, eugenol, saffron, and rosemary are usually consumed in small amounts, infrequently or not consumed at all in the Chinese pediatric population; so non-availability of these parameters may not have played a major impact. In previous validation studies, Shivappa et al reported that the DII's predictive ability remained the same when the number of food variables was decreased from 45 to 28.[21] Third, the USDA databases were used to calculate the dietary flavonoid, vitamin D and β-carotene intake. Different climatic, soil composition, growing, and harvesting conditions of plants, and their storage and preparation conditions may bring about wide variability in the nutrient contents of foods. In addition, the US food supply is supplemented with vitamin D. The measurement error caused by these factors may have led to attenuated estimates of effect. However, sensitivity analyses conducted in this study (e.g., excluding the subclass of flavonoids) revealed very consistent and stable results. Fourth, the observational design of the present study cannot rule out the possibility of residual confounding by unknown risk factors including genetic predispositions. Finally, our study population was drawn from the same ethnicity, race and social class with a relatively smaller age range. The results therefore cannot be readily generalized to other populations.

Conclusion

DII scores were inversely associated with skeletal muscle mass in boys but not in girls aged 6-9 years old. There was no significant association between DII scores and muscle strength.

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AUTHOR DISCLOSURES

Dr James R. Hébert owns a controlling interest in Connecting

Health Innovations LLC (CHI), a company planning to license the right to his invention of the dietary inflammatory index (DII) from the University of South Carolina in order to develop computer and smart phone applications for patient counseling and dietary intervention in clinical settings. Dr Nitin Shivappa is an employee of CHI. The funding sponsors had no role in the design of the study; in the collection, analyses, or interpretation of data; in the writing of the manuscript, and in the decision to publish the results.

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