British Journal of Nutrition (2023), 130, 2174–2181 doi:10.1017/S0007114523001265

Associations of plasma retinol and α-tocopherol levels with skeletal muscle health in Chinese children

Jiapeng Huang#, Xuanrui Zhang#, Zhen Hong, Xiaoping Lin, Fengyan Chen, Jing Lan, Zheqing Zhang* and Hong Deng*

Department of Nutrition and Food Hygiene, Guangdong Provincial Key Laboratory of Tropical Disease Research, School of Public Health, Southern Medical University, Guangzhou 510400, People's Republic of China

(Submitted 6 December 2022 – Final revision received 8 May 2023 – Accepted 19 May 2023 – First published online 21 June 2023)

Abstract

Childhood is a critical period for muscle accumulation. Studies in elders have reported that antioxidant vitamins could improve muscle health. However, limited studies have assessed such associations in children. This study included 243 boys and 183 girls. A seventy-nine-item FFQ was used to investigate dietary nutrients intake. Plasma levels of retinol and α-tocopherol were measured using high-performance liquid chromatography with MS. Dual X-ray absorptiometry was used to assess appendicular skeletal muscle mass (ASM) and total body fat. The ASM index (ASMI) and ASMI Z-score were then calculated. Hand grip strength was measured using a Jamar® Plus+ Hand Dynamometer. Fully adjusted multiple linear regression models showed that for each unit increase in plasma retinol content, ASM, ASMI, left HGS and ASMI Z-score increased by $2{\cdot}43 \times 10^{-3}$ kg, $1{\cdot}33 \times 10^{-3}$ kg/m^2, $3{\cdot}72 \times 10^{-3}$ kg and $2{\cdot}45 \times 10^{-3}$ in girls, respectively ($P < 0{\cdot}001$–$0{\cdot}050$). ANCOVA revealed a dose–response relationship between tertiles of plasma retinol level and muscle indicators (P_{trend}: 0·001–0·007). The percentage differences between the top and bottom tertiles were 8·38 %, 6·26 %, 13·2 %, 12·1 % and 116 % for ASM, ASMI, left HGS, right HGS and ASMI Z-score in girls, respectively (P_{diff}: 0·005–0·020). No such associations were observed in boys. Plasma α-tocopherol levels were not correlated with muscle indicators in either sex. In conclusion, high circulating retinol levels are positively associated with muscle mass and strength in school-age girls.

Key words: Retinol: α-tocopherol: Skeletal muscle healthy: Children: Cross-sectional study

Skeletal muscle is the largest organ in the body and significantly affects locomotion and the maintenance of posture in both adults and children[1]. Skeletal muscle also plays a crucial role in whole-body protein metabolism and systemic glucose and energy homeostasis, thus modulating the risks of certain diseases like obesity, CVD, insulin resistance, diabetes, sarcopenia and osteoporosis[2]. Therefore, adequate skeletal muscle quantity and quality are essential for maintaining optimal health throughout life. Skeletal muscle mass increases throughout childhood and adolescence before it starts to decrease over time about mid-life[3]. Muscle mass and strength in later life are a reflection of both the rate of muscle loss and the peak muscle mass attained earlier in life[4]. Therefore, it is necessary to focus on the determinants of peak muscle mass and strength attained in early adulthood.

Skeletal muscle shows high plasticity in response to environmental cues such as exercise and nutrition[5–7]. There has been significant interest in the role of protein in muscle health[8]. However, evidence concerning several mechanistic pathways, including inflammation and oxidative stress[9], points to the importance of micronutrients. The high level of metabolic activity in skeletal muscle generates reactive oxygen species, and the accumulation of excess reactive oxygen species results in damage to biomolecules in muscle (DNA and proteins). Through their effects on signalling pathways, reactive oxygen species also play a role in inflammation[10,11]. Previous studies have shown that inflammatory markers such as plasma levels of IL-6 and tumour necrosis factor-α are negatively correlated with skeletal muscle mass and strength[12–14]. Reactive oxygen species production is normally balanced by the actions of endogenous antioxidant defense systems such as the enzymes superoxide dismutase and glutathione peroxidase and by exogenous anti-oxidants, which prevent excess accumulation[15]. This has focused attention on a range of dietary components with antioxidant effects, namely dietary antioxidants such as vitamin A and vitamin E[16]. Vitamin A is a fat-soluble vitamin that involves retinol and retinol

---

Abbreviations: ASM, appendicular skeletal muscle mass; ASMI, appendicular skeletal muscle index; HGS, hand grip strength.

* **Corresponding authors:** Zheqing Zhang, email zzqaa501@smu.edu.cn; Hong Deng, email hongd@smu.edu.cn

\# Co-first authors.

derivatives (retinoic acid, retinyl esters and retinaldehyde)(17). Vitamin E is also known as tocopherol which includes α, β, γ, δ-l tocopherol. α-Tocopherol is the most active form of vitamin E(18). Cross-sectional studies have shown that good antioxidant status is inversely associated with relevant lipid and oxidative stress markers(19), muscle strength(20,21) and the risk of frailty(22,23). Prospective cohort studies have shown that people with high serum retinol or α-tocopherol concentrations at baseline exhibit a lower rate of muscle decline and risk of frailty(24–28). However, the participants included in the above studies were middle-aged and elderly people. Few studies have focused on the associations of retinol and α-tocopherol levels with skeletal muscle health in children.

With the above in mind, we explored the associations of plasma retinol and α-tocopherol with skeletal muscle mass and strength in Chinese children aged 6–9 years.

Methods

Participants

This cross-sectional study was performed in Guangdong province in the south of China in 2015–2017(29). The investigators recruited healthy children aged 6–9 years from several kindergartens and primary schools. The recruitment strategy involved giving out leaflets to primary schools and contacting the mutual acquaintances of parents through public WeChat accounts. A total of 1600 children were invited to participate in the study, 521 of whom responded and agreed to participate in the study. We excluded ninety-five children based on the following criteria: The following exclusion criteria were applied: (1) twins and preterm births; (2) incomplete general data or skeletal muscle testing or hand grip strength testing data and (3) history of serious disease or disability. Finally, 426 participants (243 boys and 183 girls) were included. We obtained written informed consent from the parents of all enrolled children.

The study was conducted in accordance with the Declaration of Helsinki and approved by the Ethics Committee of the School of Public Health at Sun Yat-sen University (No. 201549).

Anthropometric measurements

Weight and height were measured with the participant's barefoot and wearing light clothing. BMI was then calculated. Whole-body dual X-ray absorptiometry scans were using a Hologic Discovery W System (Discovery W; Hologic Inc.) to determine the appendicular skeletal muscle mass (ASM). Thirty-three randomly selected subjects were replicating the measurements on the same day after repositioning to evaluate the reproducibility and the in vivo reproducibility of the ASM was 1·56 %. ASM index (ASMI) was calculated as follows:

$$\text{BMI} = \text{weight (kg))/height (m)}^2,$$
$$\text{ASM index (ASMI)} = \text{ASM (kg)/height (m)}^2,$$

ASMI Z-scores were calculated with respect to the ASMI value provided by Liu *et al.*(30). As such, children were classified as having high muscle mass (Z-score ≥ 1, n 234), medium muscle mass (Z-score 0–1, n 139) or low muscle mass (Z-score < 0, n 53).

Hand grip strength measurement

HGS was measured using a Jamar® Plus+ Hand Dynamometer (JAMAR® Hydraulic Hand Dynamometer, Sammons Preston) as previously described(3). All participants sat in a straight-backed chair with their feet flat on the floor. The participants were placed in a standardised position with their shoulders adducted and neutrally rotated, elbows flexed at 90°, forearms in neutral rotation and wrists between 0° and 30° of extension and between 0° and 15° of ulnar deviation. The handle of the device was set to the second knuckle. The children were instructed to squeeze the handle of the dynamometer as hard as possible during a 5-s period with both hands while exhaling. HGS was recorded in kilograms (kg). The mean of the three trials was calculated and used in subsequent analysis.

Laboratory examination

Venous blood samples were obtained from the children in the morning after 10 h of fasting. More than 90 % of blood samples are collected by investigators on the scene. The plasma was separated from blood within 2–4 h and setted up parallel samples to test the stability of the monitoring. Samples were stored at −80°C unexposed to light until assayed in 2022. Quantitative analysis of plasma retinol and α-tocopherol concentrations was performed using a Qlife Lab 9000 triple quadrupole mass spectrometer testing system under research protocols including quality assurance measures(31). A pooled serum sample was stored in separate EP tubes to prevent repeated freeze–thaw and analysed alongside batches of study samples to monitor analytic precision, with approximately coefficient of variation values of 7·7 %.

Covariates

The interviewers collected data concerning mode of delivery, household income and parental educational level through face-to-face interviews. Parental education level was classified into three categories: primary or lower, secondary and graduate or above. Household income per month was classified into four categories: ≤ 8000 yuan, 8000–15 000 yuan, $> 15\,000$ yuan and no response. The delivery mode was defined as a binary variable: cesarean or vaginal. Dietary intake over the prior year was assessed using a seventy-nine-item FFQ. During the interviews, the investigators checked the questionnaires for potentially incorrect responses and made clarifications when necessary. The reproducibility and validity of the FFQ were described previously(32). Energy and nutrient intakes were calculated based on the Chinese food composition tables (2018)(33). Each nutrient intake value was adjusted using the energy-residual method. Information on physical activity was obtained using a 3-day physical activity questionnaire. Physical activity was calculated by combining the metabolic equivalent score for each type of physical activity after multiplying it by its duration (hours) per day(34).

Statistical analysis

Normally distributed continuous variables are expressed as means ± standard deviations, while medians and interquartile ranges are used to describe non-normal distributions. Categorical variables are presented as percentages. Descriptive statistics of sex differences in subject characteristics were tested for significance using analysis of variance for continuous data, while the χ^2 test was used for categorical data. Multiple linear regression and ANCOVA were applied to examine the association of plasma retinol and *α*-tocopherol concentrations with muscle mass indicators. We constructed three models with minimum and maximum adjustments. In model 1, adjustments were made for age; in model 2, we added delivery mode, parental education, household income, physical activity, use of Ca and multivitamin supplements and energy-adjusted dietary intakes of total energy and protein. Whole-body fat was further adjusted for in model 3. All analyses were conducted using R version 4.1.2. The significance level was set at 0·05.

The sample size was estimated based on a similar study that the relationship between protein and skeletal muscle. We assumed that retinol and α-tocopherol have a similar or slightly lower magnitude of association with skeletal muscle than protein(35). Setting a two-tailed α of 0·05 and a power of 0·80, the current study initially required a sample size of 173 to detect the association between skeletal muscle status and the level of plasma retinol and α-tocopherol as low as $R^2 = 0{\cdot}05$ adjusting for eleven covariates in multiple linear regression models. Power analysis was performed using PASS software (version 15; Jerry Hintze, Kayville, UT).

Results

Participant characteristics

A total of 243 boys and 183 girls were included in this study. Table 1 shows the characteristics of caregivers and the differences between boys and girls. The mean age of the study population was 8·04 years (Q1–Q3:7·30–8·80). The boys tended to be older and had higher body weight, BMI, physical activity level, daily energy and protein intake, ASM, ASMI, left HGS and right HGS than the girls ($P < 0{\cdot}001$–0·016). However, there was no significant difference in ASMI Z-score between the boys and the girls ($P = 0{\cdot}210$). The boys had similar plasma retinol concentrations (312 ng/ml *v.* 326, ng/ml, $P = 0{\cdot}087$) but lower plasma *α*-tocopherol concentrations than the girls (5·42 µg/ml *v.* 5·75 µg/ml, $P = 0{\cdot}023$).

Relationship between plasma retinol and muscle mass

As shown in Table 2, after adjustment for potential confounders, multiple linear regression revealed that a per-unit increase in the plasma concentration of retinol led to a $2{\cdot}43 \times 10^{-3}$ kg, $1{\cdot}33 \times 10^{-3}$ kg/m^2, $3{\cdot}72 \times 10^{-3}$ kg and $2{\cdot}45 \times 10^{-3}$ increase in ASM, ASMI, left HGS and ASMI Z-score in the girls ($P < 0{\cdot}001$–0·050). In the boys, no significant association was detected between any of the muscle mass indicators and the plasma retinol concentration.

Figure 1 shows the results of ANCOVA. For the boys, none of the muscle mass indicators were associated with the plasma retinol concentration. In the girls, most of the muscle mass indices increased significantly with the tertile of the plasma retinol concentration, and the adjusted percentage mean differences for tertile 3 *v.* tertile 1 were 8·38 %, 6·26 %, 12·1 %, 13·2 %, and 116 % for ASM, ASMI, left HGS, right HGS and ASMI Z-score, respectively (P_{trend}: 0·001–0·007, P- diff: 0·005–0·020).

Relationship between plasma α-tocopherol and muscle mass

As shown in Table 2, no statistically significant associations between the plasma concentrations of *α*-tocopherol and muscle mass indicators were detected either in the boys or the girls using the three multiple linear regression models. Similar results were obtained using ANCOVA (Fig. 2).

Discussion

In this observational study, we demonstrated that girls with higher circulating levels of retinol had higher skeletal muscle mass and strength than girls with lower retinol levels, whereas no such relationship was present in boys. Furthermore, we detected no significant association between the circulating levels of *α*-tocopherol and skeletal muscle status in either sex.

Many studies in adults have evaluated the impacts of dietary antioxidants on skeletal muscle health. In the Invecchiare in Chianti study, which included 986 men and women aged 63–73 years, higher antioxidant concentrations (e.g. vitamin C, vitamin E, beta-carotene and retinol) were associated with greater knee extension strength and better physical performance metrics such as walking speed, ability to stand from a chair and ability to maintain balance in progressively more challenging positions(36). Another study in elderly people aged 60–85 years confirmed that the combined supplementation of whey protein, vitamin D and vitamin E can significantly improve relative skeletal muscle mass index (mean difference: 0·18 kg/m^2, 95 % CI: 0·01, 0·35, $P = 0{\cdot}040$) and muscle strength (mean difference: 2·68 kg, 95 % CI: 0·71, 4·65, $P = 0{\cdot}009$) in older adults when compared against a placebo group(37). Pilleron *et al.* reported that a greater prevalence of frailty was associated with lower concentrations of either carotenoids, retinol, or *α*-tocopherol(38). However, the findings obtained in the elderly have not always been confirmed in other populations. In young athletes, Teixeira *et al.* reported that antioxidant supplementation (e.g. *α*-tocopherol, vitamin C, lutein, Se, Zn and Mg) did not offer protection against exercise-induced lipid peroxidation and inflammation and might hinder recovery from muscle damage(39). Importantly, some studies have highlighted that prolonged antioxidant supplementation can lead to undesirable effects, such as the disruption of endogenous antioxidant levels leading to failure to counteract exercise-induced oxidative stress(40,41). To date, most studies have focused on adults and the elderly, and comparatively little research has investigated how antioxidant vitamin status correlates with skeletal muscle quality in children. In our study, we measured the concentrations of retinol and *α*-tocopherol in plasma and found that concentrations were significantly different between the sexes. This result was in line with other studies

Table 1. Baseline characteristics of participants

	Total *n* 426		Boys *n* 243		Girls *n* 183		
Variables	Mean	SD	Mean	SD	Mean	SD	*P*
Descriptives							
Age (years)							
Median	8·04		7·99		8·10		0·025
Q1–Q3	7·30–8·80		7·20–8·75		7·40–8·80		
Height (cm)	128	8·07	128	8·16	128	7·93	0·922
Weight (kg)	26·29	7·02	27·10	7·86	25·21	5·52	0·006
BMI (kg/m^2)	15·74	2·67	16·20	2·98	15·13	2·03	< 0·001
Physical activity (MET × h/d)	39·96	4·37	40·74	4·54	38·91	3·90	< 0·001
Daily energy intake (kcal/d)	1430	432	1501	444	1336	396	< 0·001
Daily protein intake (g/d)	64·71	22·8	67·01	23·7	61·65	21·3	0·016
	n	%	*n*	%	*n*	%	
Delivery mode							
Natural	211	49·6	111	45·9	100	54·6	0·074
Cesarean	215	50·4	132	54·1	83	45·4	
Household income							
< 8000 Yuan/month	77	18·1	45	18·6	32	17·5	0·990
8000–15 000 Yuan/month	130	30·6	75	31·0	55	30·1	
> 15 000 Yuan/month	144	33·9	81	33·5	63	34·4	
No response	74	17·4	41	16·9	33	18·0	
Maternal educational level							
Secondary or less	159	37·5	91	37·4	70	38·3	0·193
University	230	54·2	127	52·3	103	56·3	
Postgraduate or above	35	8·3	25	10·3	10	5·4	
Paternal educational level							
Secondary or less	177	41·0	102	42·0	75	41·0	0·450
University	196	46·4	107	44·0	89	48·6	
Postgraduate or above	53	12·6	34	14·0	19	10·4	
Use of Ca supplement							
No	143	33·4	72	29·6	71	38·8	0·060
Yes	283	66·6	171	70·4	112	61·2	
Use of multivitamin supplement							
No	246	57·4	137	56·4	109	59·6	0·576
Yes	180	42·4	106	43·6	74	40·4	
ASM (kg)							
Mean	7·43		7·79		6·95		< 0·001
SD	1·75		1·89		1·42		
ASMI (kg/m^2)							
Mean	4·44		4·65		4·17		< 0·001
SD	0·62		0·64		0·47		
ASMI-Z							
$Z > 1$	53	12·4	32	13·2	21	11·5	0·210
$0 < Z < 1$	139	32·6	85	35·0	54	29·5	
$Z < 0$	234	54·9	126	51·9	108	59·0	
	Mean	SD	Mean	SD	Mean	SD	
Left HGS (kg)	9·80	2·71	10·26	2·86	9·19	2·37	< 0·001
Right HGS (kg)	10·6	2·89	11·0	3·06	9·98	2·54	< 0·001
Blood biochemistry							
Plasma retinol (ng/ml)	318	3·88	312	4·90	326	6·22	0·087
Plasma α-tocopherol (ug/ml)	5·56	0·07	5·42	0·09	5·75	0·11	0·023

Continuous variables are presented as mean (SD) or median (Q1–Q3); ASM, appendicular skeletal muscle mass; ASMI, the ratio of appendicular skeletal mass to height^2; Left HGSm left handgrip strength, Right HGSm right handgrip strength; ASMI-Zm the Z score of ASMI.

in the literature[42–46]. In addition, the findings of the present study revealed that plasma retinol levels were positively correlated with skeletal muscle health in girls but not in boys. Furthermore, the plasma concentration of α-tocopherol was not correlated with skeletal muscle mass and strength in either sex.

Increasing evidence has shown that aging-mediated oxidative stress and inflammation are the main pathological characteristics of skeletal muscle[47]. Therefore, antioxidants derived from food may have beneficial effects on skeletal muscle health. The antioxidant and anti-inflammatory properties of vitamin A and vitamin E have been demonstrated in a multitude of studies in cells, animal models and humans[48,49]. However, increasing evidence suggests that the predominant effects of vitamin A within the body stem not directly from its antioxidant action but its metabolite all-*trans* retinoic acid, a potent transcriptional regulator that affects the expression levels of hundreds of distinct genes involved in responses to oxidative stress. In contrast, vitamin E supposedly acts as a direct antioxidant. Very little compelling evidence demonstrates that vitamin E has a direct effect on gene expression as vitamin A does[50]. Vitamin A also plays a vital role in helping cells and tissues to grow and develop[51]. These differences may collectively contribute to

Table 2. Multiplelinear regression between plasma retinol and α-tocopherol concentration and skeletal muscle indexes

	Plasma retinol						Plasma α-tocopherol					
	Boys (*n* 243)			Girls (*n* 183)			Boys (*n* 243)			Girls (*n* 183)		
Variables	*β*	SE	*P*	*β*	SE	*P*	*β*	SE	*P*	*β*	SE	*P*
ASM (10^{-3}kg)												
Model 1	2·50	1·27	0·050	3·10	1·01	0·002	–2·13	7·32	0·771	–6·05	5·70	0·290
Model 2	1·88	1·29	0·148	3·22	1·04	0·002	–5·07	7·23	0·484	–7·83	5·87	0·184
Model 3	–0·30	0·90	0·736	2·43	0·91	0·008	–1·49	4·95	0·763	–8·64	5·04	0·088
ASMI (10^{-3}kg/m^2)												
Model 1	0·83	0·50	0·097	1·34	0·39	0·001	–1·57	2·85	0·582	–2·24	2·22	0·314
Model 2	0·65	0·51	0·210	1·55	0·39	< 0·001	–2·36	2·86	0·410	–2·18	2·26	0·336
Model 3	–0·10	0·40	0·797	1·33	0·37	< 0·001	–1·14	2·22	0·610	–2·41	2·09	0·249
Left HGS (10^{-3}kg)												
Model 1	2·36	1·95	0·226	3·96	1·80	0·029	–6·36	11·1	0·568	–2·57	10·1	0·800
Model 2	1·85	2·02	0·360	4·41	1·94	0·024	–7·25	11·2	0·520	–6·77	10·8	0·532
Model 3	–0·13	1·85	0·943	3·72	1·90	0·050	–3·99	10·2	0·696	–7·50	10·5	0·475
Right HGS (10^{-3}kg)												
Model 1	2·65	2·04	0·195	4·65	1·90	0·015	–4·29	11·7	0·713	0·18	10·7	0·987
Model 2	2·12	2·12	0·319	4·70	2·08	0·025	–6·79	11·8	0·566	–5·12	11·6	0·659
Model 3	0·04	1·95	0·984	3·77	2·00	0·061	–3·37	10·7	0·754	–6·10	11·0	0·581
ASMI-Z (×10^{-3})												
Model 1	1·16	0·84	0·166	2·49	0·77	0·001	–3·26	4·78	0·496	–5·51	4·34	0·206
Model 2	0·75	0·86	0·383	2·85	0·77	< 0·001	–4·75	4·80	0·323	–5·14	4·37	0·241
Model 3	–0·42	0·71	0·549	2·45	0·73	0·001	–2·84	3·89	0·466	–5·57	4·08	0·173

ASM, appendicular skeletal mass; ASMI, the ratio of appendicular skeletal mass to height^2; AFM, appendicular fat mass; Left HGS, left handgrip strength, Right HGS, right handgrip strength; ASMI-Z, the Z score of ASMI.

Model 1: adjustment for age, model 2: adjustment for age, delivery mode, parental education, physical activity, use of Ca and multivitamin supplements, energy adjusted dietary intakes of total energy and protein and household income; model 3: adjustment for age, delivery mode, parental education, physical activity, use of Ca and multivitamin supplements, energy adjusted dietary intakes of total energy and protein, household income and whole-body fat.

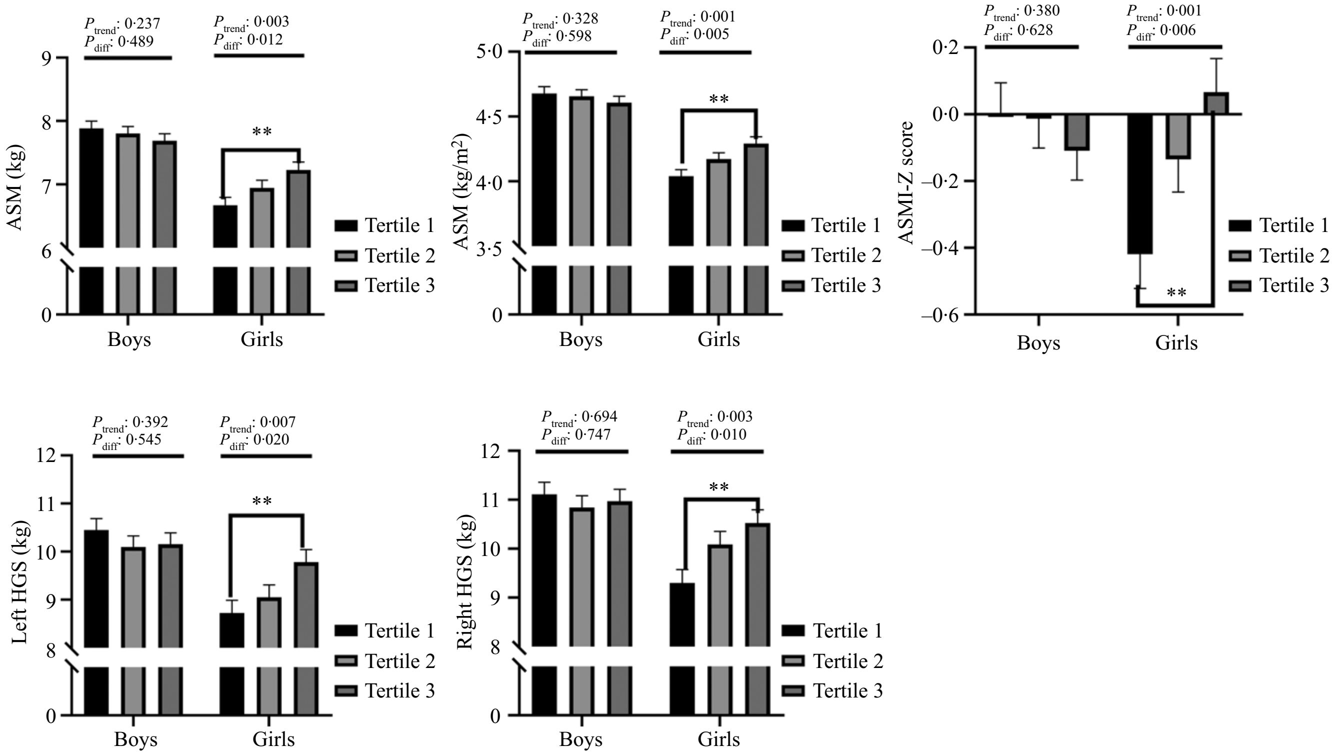

Fig. 1. Analysis of covariances for the association between plasma retinol concentration tertiles and muscle mass and muscle strength. Results were adjusted for age, delivery method, household income, parental education, physical activity, use of Ca and multivitamin supplements, energy adjusted dietary intakes of total energy and protein and whole-body fat. ASM, appendicular skeletal mass; ASMI, the ratio of appendicular skeletal mass to height^2; Left HGS, left handgrip strength, Right HGS, right handgrip strength; ASMI-Z score, the Z score of ASMI.

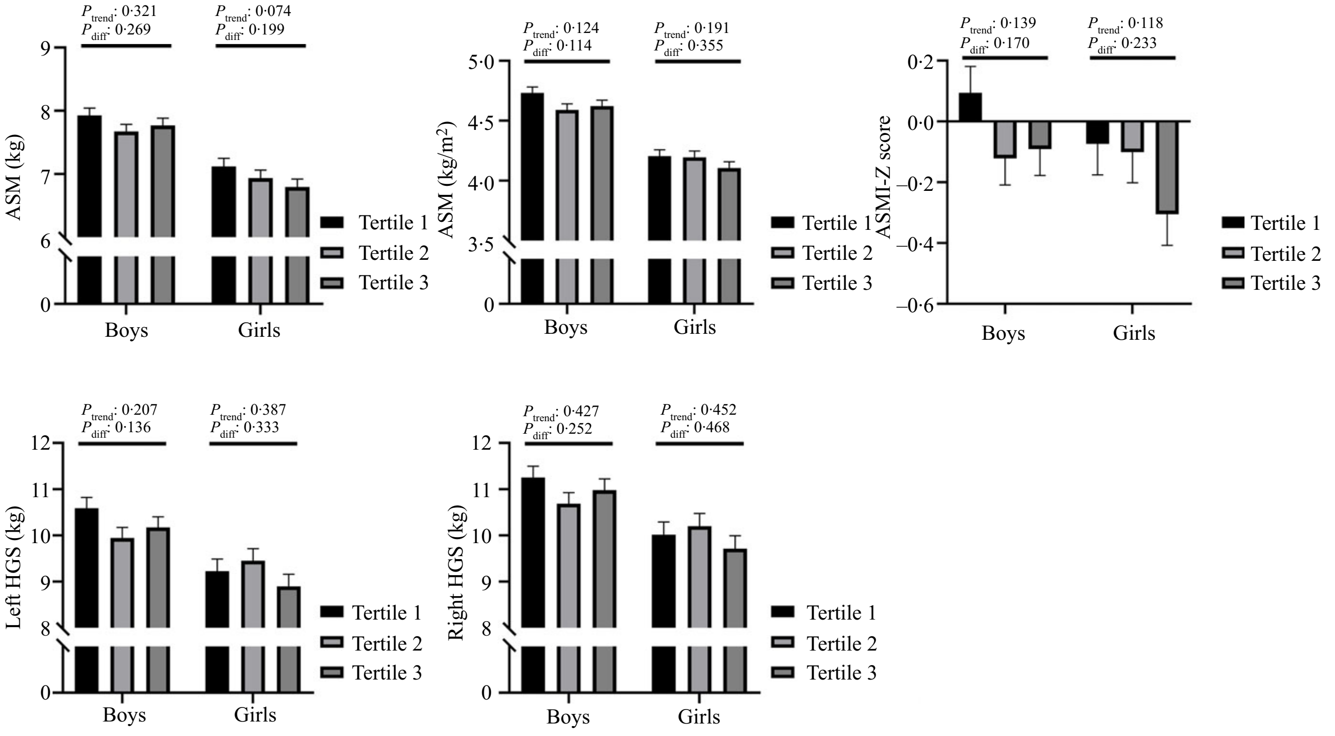

Fig. 2. Analysis of covariances for the association between plasma α-tocopherol concentration tertiles and muscle mass and muscle strength. Results were adjusted for age, delivery method, household income, parental education, physical activity, use of Ca and multivitamin supplements, energy adjusted dietary intakes of total energy and protein and whole-body fat. ASM, appendicular skeletal mass; ASMI, the ratio of appendicular skeletal mass to height^2; Left HGS, left handgrip strength, Right HGS, right handgrip strength; ASMI-Z score, the Z score of ASMI.

the different actions of vitamin A and vitamin E detected in the present study.

The mechanisms that mediate the sex-specific differences detected in the present study remain unclear. However, the considerable number of animal studies performed to date suggest a metabolic basis for the difference in response to changes in vitamin A status between the sexes. During experimental vitamin A depletion, male animals exhaust their liver stores more rapidly than females(52), which may predispose males to earlier developed severe manifestations of hypovitaminosis A(53,54). In breast cancer cells, estrogen receptor status was proven to sensitise the antiproliferative effects of retinoids(55). In males, on the other hand, androgens retard RA function by repressing RAR-α and RAR-γ(56). Previous researchers found that sex hormone concentrations are significantly higher in girls compared with boys in prepuberty, and the sex differences in terms of those hormones were more robust for 17β-estradiol(57). These studies suggest that a sex difference may exist in vitamin A storage, utilisation, or function mediated by sex hormones.

This research explored the association of retinol and α-tocopherol with skeletal muscle mass and strength in a relatively large sample of children, and all of the measurements were under strict quality control. However, there are some notable limitations. First, this study involved a cross-sectional design. As such, the longitudinal changes in the plasma concentrations of retinol and α-tocopherol were not evaluated. Conventional observational studies cannot completely rule out reverse causality and residual confounding, which makes it hard to infer causality. Future studies should collect data from the study population over time to evaluate longitudinal changes. Second, the plasma sample was assayed for retinol and α-tocopherol levels six years after collection. But at −70°C or colder, retinol and α-tocopherol are stable for 15 years(58). Third, this study focused on urban children from a narrow age range, which limits the generalisability of the findings. Finally, although the findings were adjusted for a range of dietary and lifestyle confounders, residual or unmeasured confounding factors inevitably remain unaccounted for.

In conclusion, the present study revealed that plasma retinol concentration is positively correlated with skeletal muscle mass and strength in girls. An improved understanding of the effects of increasing dietary intake of vitamin A may inform future strategies to improve muscle quality.

Acknowledgements

We thank the research team members from the Department of Nutrition and Food Hygiene and Food Safety and Health Research Center of Southern Medical University for their help in sample collection. We also thank the families who participated in this research. This work was supported by National Natural Science Foundation of China (No. 81973045) and Guangzhou Science and Technology Planning Project (No. 202102020967).

This work received support from the National Natural Science Foundation of China (No. 81973045) and Guangzhou Science and Technology Planning Project (No. 202102020967). The funders had no role in the study design, data collection, data analysis, writing of this article or in interpreting the results.

Conceptualization: Z. Z. and H. D.; Investigation: X. Z., J. H., F. C., Z. H., X. L. and J. L.; Writing – Original Draft: J. H. and X. Z.; Writing – Review & Editing: Z. Z. and D. H. . All authors have read and agreed to the published version of the manuscript.

The authors declare no conflict of interest.

References

1. Biolo G, Cederholm T & Muscaritoli M (2014) Muscle contractile and metabolic dysfunction is a common feature of sarcopenia of aging and chronic diseases: from sarcopenic obesity to cachexia - ScienceDirect. *Clin Nutr* **33**, 737–748.
2. Wolfe RR (2006) The underappreciated role of muscle in health and disease. *Am J Clin Nutr* **84**, 475–482.
3. Chen F, Li Q, Chen Y, *et al.* (2022) Association of the gut microbiota and fecal short-chain fatty acids with skeletal muscle mass and strength in children. *FASEB J* **36**, e22109.
4. Wilkinson DJ, Piasecki M & Atherton PJ (2018) The age-related loss of skeletal muscle mass and function: measurement and physiology of muscle fibre atrophy and muscle fibre loss in humans. *Ageing Res Rev* **47**, 123–132.
5. Carbone JW, Mcclung JP & Pasiakos SM (2012) Skeletal muscle responses to negative energy balance: effects of dietary protein. *Adv Nutr* **3**, 119–126.
6. Koletzko B, Demmelmair H, Grote V, *et al.* (2016) High protein intake in young children and increased weight gain and obesity risk. *Am J Clin Nutr* **103**, 303.
7. Landi F, Marzetti E, Martone AM, *et al.* (2014) Exercise as a remedy for sarcopenia. *Curr Opin Clin Nutr Metab Care* **17**, 25–31.
8. Gielen E, Beckwée D, Delaere A, *et al.* (2021) Nutritional interventions to improve muscle mass, muscle strength, and physical performance in older people: an umbrella review of systematic reviews and meta-analyses. *Nutr Rev* **79**, 121–147.
9. Cruz-Jentoft AJ & Sayer AA (2019) Sarcopenia. *Lancet* **393**, 2636–2646.
10. Damiano S, Muscariello E, La Rosa G, *et al.* (2019) Dual role of reactive oxygen species in muscle function: can antioxidant dietary supplements counteract age-related sarcopenia? *Int J Mol Sci* **20**, 3815.
11. Foreman NA, Hesse AS & Ji LL (2021) Redox signaling and sarcopenia: searching for the primary suspect. *Int J Mol Sci* **22**, 9045.
12. Fan Z, Yang J-Y, Guo Y, *et al.* (2022) Altered levels of circulating mitochondrial DNA in elderly people with sarcopenia: association with mitochondrial impairment. *Exp Gerontol* **163**, 111802.
13. Gholizade M, Farhadi A, Marzban M, *et al.* (2022) Association between platelet, white blood cell count, platelet to white blood cell ratio and sarcopenia in community-dwelling older adults: focus on Bushehr Elderly Health (BEH) program. *BMC Geriatr* **22**, 300.
14. Schaap LA, Pluijm SMF, Deeg DJH, *et al.* (2009) Higher inflammatory marker levels in older persons: associations with 5-year change in muscle mass and muscle strength. *J Gerontol A Biol Sci Med Sci* **64**, 1183–1189.
15. Mukund K & Subramaniam S (2020) Skeletal muscle: a review of molecular structure and function, in health and disease. *Wiley Interdiscip Rev Syst Biol Med* **12**, e1462.
16. Kim J-S, Wilson JM & Lee S-R (2010) Dietary implications on mechanisms of sarcopenia: roles of protein, amino acids and antioxidants. *J Nutr Biochem* **21**, 1–13.
17. Han X, Zhao R, Wang Y, *et al.* (2022) Dietary vitamin A intake and circulating vitamin A concentrations and the risk of three common cancers in women: a meta-analysis. *Oxid Med Cell Longev* **2022**, 7686405.
18. Meulmeester FL, Luo J, Martens LG, *et al.* (2022) Antioxidant supplementation in oxidative stress-related diseases: what have we learned from studies on alpha-tocopherol? *Antioxidants* **11**, 2322.
19. Cocate PG, Natali AJ, Alfenas RCG, *et al.* (2015) Carotenoid consumption is related to lower lipid oxidation and DNA damage in middle-aged men. *Br J Nutr* **114**, 257–264.
20. Welch AA, Jennings A, Kelaiditi E, *et al.* (2020) Cross-sectional associations between dietary antioxidant vitamins C, E and carotenoid intakes and sarcopenic indices in women aged 18–79 years. *Calcif Tissue Int* **106**, 331–342.
21. Semba RD, Blaum C, Guralnik JM, *et al.* (2003) Carotenoid and vitamin E status are associated with indicators of sarcopenia among older women living in the community. *Aging Clin Exp Res* **15**, 482–487.
22. Michelon E, Blaum C, Semba RD, *et al.* (2006) Vitamin and carotenoid status in older women: associations with the frailty syndrome. *J Gerontol A Biol Sci Med Sci* **61**, 600–607.
23. Kochlik B, Stuetz W, Pérès K, *et al.* (2019) Associations of fat-soluble micronutrients and redox biomarkers with frailty status in the FRAILOMIC initiative. *J Cachexia Sarcopenia Muscle* **10**, 1339–1346.
24. Alipanah N, Varadhan R, Sun K, *et al.* (2009) Low serum carotenoids are associated with a decline in walking speed in older women. *J Nutr Health Aging* **13**, 170–175.
25. Lauretani F, Semba RD, Bandinelli S, *et al.* (2008) Low plasma carotenoids and skeletal muscle strength decline over 6 years. *J Gerontol A Biol Sci Med Sci* **63**, 376–383.
26. Lauretani F, Semba RD, Bandinelli S, *et al.* (2008) Carotenoids as protection against disability in older persons. *Rejuvenation Res* **11**, 557–563.
27. Bartali B, Frongillo EA, Guralnik JM, *et al.* (2008) Serum micronutrient concentrations and decline in physical function among older persons. *JAMA* **299**, 308–315.
28. Sahni S, Dufour AB, Fielding RA, *et al.* (2021) Total carotenoid intake is associated with reduced loss of grip strength and gait speed over time in adults: the Framingham Offspring Study. *Am J Clin Nutr* **113**, 437–445.
29. Liang J, Chen F, Fang G, *et al.* (2020) Relationship between plasma copper concentration and body fat distribution in children in China: a cross-sectional study. *Biol Trace Elem Res* **198**, 430–439.
30. Liu J, Yan Y, Xi B, *et al.* (2019) Skeletal muscle reference for Chinese children and adolescents. *J Cachexia Sarcopenia Muscle* **10**, 155–164.
31. Lin X, Zhou Y, Li S, *et al.* (2022) Markers related to oxidative stress in peripheral blood in children with autism spectrum disorder. *Res Autism Spectr Disord* **99**, 102067.
32. Chen G, Li Y, Liang S, *et al.* (2021) Associations of dietary anthocyanidins intake with body composition in Chinese children: a cross-sectional study. *Food Nutr Res* **65**, 4428.
33. Yang Y, Wang G, Pang X, et al. (2019) *China Food Composition Table* (Standard Edition). Beijing : Peking University Medical Press.
34. Ainsworth BE, Haskell WL, Herrmann SD, *et al.* (2011) 2011 compendium of physical activities: a second update of codes and MET values. *Med Sci Sports Exerc* **43**, 1575–1581.
35. Asp ML, Richardson JR, Collene AL, *et al.* (2012) Dietary protein and beef consumption predict for markers of muscle

mass and nutrition status in older adults. *J Nutr Health Aging* **16**, 784–790.

36. Cesari M, Pahor M, Bartali B, *et al.* (2004) Antioxidants and physical performance in elderly persons: the Invecchiare in Chianti (InCHIANTI) study. *Am J Clin Nutr* **79**, 289–294.
37. Bo Y, Liu C, Ji Z, *et al.* (2019) A high whey protein, vitamin D and E supplement preserves muscle mass, strength, and quality of life in sarcopenic older adults: a double-blind randomized controlled trial. *Clin Nutr* **38**, 159–164.
38. Pilleron S, Weber D, Pérès K, *et al.* (2019) Patterns of circulating fat-soluble vitamins and carotenoids and risk of frailty in four European cohorts of older adults. *Eur J Nutr* **58**, 379–389.
39. Teixeira VH, Valente HF, Casal SI, *et al.* (2009) Antioxidants do not prevent postexercise peroxidation and may delay muscle recovery. *Med Sci Sports Exerc* **41**, 1752–1760.
40. Rowlands DS, Pearce E, Aboud A, *et al.* (2012) Oxidative stress, inflammation, and muscle soreness in an 894-km relay trail run. *Eur J Appl Physiol* **112**, 1839–1848.
41. Peternelj T-T & Coombes JS (2011) Antioxidant supplementation during exercise training: beneficial or detrimental? *Sports Med* **41**, 1043–1069.
42. de Dios O, Navarro P, Ortega-Senovilla H, *et al.* (2018) Plasma retinol levels and high-sensitivity C-reactive protein in prepubertal children. *Nutrients* **10**, 1257.
43. Teske M, Melges APB, de Souza FIS, *et al.* (2014) Plasma concentrations of retinol in obese children and adolescents: relationship to metabolic syndrome components. *Rev Paul Pediatr* **32**, 50–54.
44. Schweigert FJ, Klingner J, Hurtienne A, *et al.* (2003) Vitamin A, carotenoid and vitamin E plasma concentrations in children from Laos in relation to sex and growth failure. *Nutr J* **2**, 17.
45. Xiang J, Nagaya T, Huang X-E, *et al.* (2008) Sex and seasonal variations of plasma retinol, α-tocopherol, and carotenoid concentrations in Japanese dietitians. *Asian Pac J Cancer Prev* **9**, 413–416.
46. Borel P, Moussa M, Reboul E, *et al.* (2007) Human plasma levels of vitamin E and carotenoids are associated with genetic polymorphisms in genes involved in lipid metabolism. *J Nutr* **137**, 2653–2659.
47. Chen M, Wang Y, Deng S, *et al.* (2022) Skeletal muscle oxidative stress and inflammation in aging: focus on antioxidant and anti-inflammatory therapy. *Front Cell Dev Biol* **10**, 964130.
48. Liao S, Omage SO, Bormel L, *et al.* (2022) Vitamin E and metabolic health: relevance of interactions with other micronutrients. *Antioxidants* **11**, 1785.
49. Palace VP, Khaper N, Qin Q, *et al.* (1999) Antioxidant potentials of vitamin A and carotenoids and their relevance to heart disease. *Free Radic Biol Med* **26**, 746–761.
50. Blaner WS, Shmarakov IO & Traber MG (2021) Vitamin A and vitamin E: will the real antioxidant please stand up? *Annu Rev Nutr* **41**, 105–131.
51. Carazo A, Macakova K, Matousova K, *et al.* (2021) Vitamin A update: forms, sources, kinetics, detection, function, deficiency, therapeutic use and toxicity. *Nutrients* **13**, 1703.
52. Brenner S, Brookes MCH & Roberts LJ (1942) The relation of liver stores to the occurrence of early signs of vitamin A deficiency in the white rat: one figure. *J Nutr* **23**, 459–471.
53. Klein-Szanto AJ, Clark JN & Martin DH (1980) Sexual differences in the distribution of epithelial alterations in vitamin A-deficient rats. *Int J Vitam Nutr Res* **50**, 61–69.
54. McLaren DS (1959) Influence of protein deficiency and sex on the development of ocular lesions and survival time of the vitamin A deficient rat. *Br J Ophthalmol* **43**, 234–241.
55. Rousseau C, Nichol JN, Pettersson F, *et al.* (2004) ERbeta sensitizes breast cancer cells to retinoic acid: evidence of transcriptional crosstalk. *Mol Cancer Res* **2**, 523–531.
56. Huang HFS, Li M-T, Von Hagen S, *et al.* (1997) Androgen modulation of the messenger ribonucleic acid of retinoic acid receptors in the prostate, seminal vesicles, and kidney in the rat. *Endocrinology* **138**, 553–559.
57. Courant F, Aksglaede L, Antignac J-P, *et al.* (2010) Assessment of circulating sex steroid levels in prepubertal and pubertal boys and girls by a novel ultrasensitive gas chromatography-tandem mass spectrometry method. *J Clin Endocrinol Metab* **95**, 82–92.
58. Comstock GW, Alberg AJ & Helzlsouer KJ (1993) Reported effects of long-term freezer storage on concentrations of retinol, beta-carotene, and α-tocopherol in serum or plasma summarized. *Clin Chem* **39**, 1075–1078.