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**The association between dietary inflammatory index, muscle strength, muscle endurance, and body composition in Iranian adults**

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**Keywords:** Dietary inflammatory index; muscle endurance; muscle strength; body composition; Inflammation

**Running title:** Dietary inflammatory index and muscle endurance

## **Abstract**

**Objectives:** To investigate the association between dietary inflammatory index (DII) and muscle strength (MS), muscle endurance (ME), and body composition.

**Methods:** This cross-sectional study was conducted in 270 middle-aged subjects living in Tehran, Iran. The DII was calculated using a validated semi-quantified food frequency questionnaire. Body composition was measured using body composition analyzer; muscle strength was measured by a digital handgrip dynamometer; socio-economic status, anthropometric measures and blood pressure were also recorded.

**Results:** A significant decrease was found for MS ( $p<0.01$ ) and MSR ( $p<0.01$ ) across tertiles of DII. Participants who had greater scores of DII also had lower MER ( $p<0.01$ ), even after adjustment for confounding factors ( $p<0.02$ ). Higher DII was significantly related to MSL ( $p<0.01$ ), ME ( $p<0.01$ ), and MEL ( $p=0.02$ ) in the crude model, which disappeared after controlling for covariates. There were no significant differences for FFM, SMM, and WC ( $p<0.01$ ) among tertiles of DII after adjusting for confounding factors.

**Conclusions:** Higher DII scores were associated with less muscle strength and endurance among Iranian middle-aged adults. Further studies are needed to be conducted to confirm the veracity of our results.

## Introduction

Chronic inflammation is associated with several diseases, such as obesity, cardiovascular disease, and insulin resistance (1). Indeed, studies have shown that higher circulating levels of inflammatory markers, such as interleukin (IL)-6 and C-reactive protein (CRP), are correlated with lower muscle mass and strength (MS) (2-6). Moreover, accumulating evidence suggests that higher inflammatory markers are associated with lower muscle mass (7). Modifiable lifestyle factors, such as diet, affect the inflammatory response process; components of diet, such as saturated, trans fatty acid and refined grain, can modify inflammation status to pro-inflammatory, whilst fiber, omega 6 and antioxidant vitamin, can modify inflammation status to anti-inflammatory - inflammatory (8). There are several dietary indices to evaluate quality of diet (9, 10); indeed, the relationship between diet and inflammation can be examined with dietary patterns using the dietary inflammatory index (DII) (11). DII was developed by Cavicchia et al, and updated by Shivappa et al with thirty-six nutrients and nine food items, and can be used to predict inflammatory potential of the diet, including C-reactive protein (CRP), IL-6, and tumor necrosis factor (TNF)- $\alpha$  (9, 12), where higher DII scores indicate higher inflammatory potential (4, 13-15). In one study, it was suggested that DII score is inversely associated with skeletal muscle mass in boys (16). Results of a large study also showed that a pro-inflammatory diet was associated with higher body mass index (BMI) z-score, wrist circumference, waist circumference (WC), hip circumference (HC), and parental BM (17). Moreover, higher serum levels of anti-inflammatory markers are considered to play a protective role on fat free mass (FFM) (18, 19). Given that there is currently no study that has evaluated the association between DII and muscle and anthropometric indices, in an Iranian population, the aim of the present study was to analyze the relationship between DII and muscle endurance, strength, and body composition in middle aged adults in Iran.

## **Subjects and methods**

### *Study design*

This cross-sectional study was conducted on 270 adults (118 males and 152 females), aged between 18-60 years' old, who lived in Tehran, Iran between February 2018 and December 2019. Participants were recruited using local advertisement, distribution of flyers in common rooms, and information sessions held at residential facilities. The participants were selected based on the following inclusion criteria: 1) age range of 18-70 years, 2) no alcohol or drug abuse, 3) participants with special diets, such as weight loss or weight gain diets, adults with chronic diseases including diabetics, hormonal, and cardiovascular diseases, pregnant and lactating women, receiving any special medication or supplements (slimming medicine, hormone, sedative, supplements containing thermogenic substances such as caffeine and green tea, linoleic acid conjugate etc.), were excluded from the study. All necessary explanations about the project were given to the participants and all participants signed a written informed consent prior to the start of the study. All procedures were in accord with the ethical standards of the Tehran University of Medical Sciences TUMS.VCR.REC.1396.4085), who approved the protocol and informed consent form.

### *Dietary assessment*

A validated 147-item food frequency questionnaire was used to assess usual food intake (20). Nutritional information was collected by experienced and trained nutritionist through interviews; where participants reported their intake frequency for each food item during the past year on a daily, weekly, monthly or yearly basis. Portion sizes of consumed foods that were reported in household measures were converted to grams. The food items were analyzed for their energy content using the Nutritionist 4 software, modified for Iranian foods.

### *Anthropometric measures and body composition*

Weight, BMI, WC, skeletal muscle mass, waist-hip ratio, and body composition (including fat free mass (FFM), fat mass (FM), percent body fat (PBF), skeletal muscle mass (SMM), trunk fat (TF), visceral fat level (VFL)) were measured using a body composition analyzer (In Body 720, Biospace, Tokyo, Japan). MS was measured using a digital handgrip dynamometer (Saehan, model SH5003; Saehan Corporation, Masan, South Korea). In a standing position, with their arm hanging normally beside the body and an elbow angle of approximately 180°, participants were asked to squeeze the dynamometer as hard as possible to measure the maximal force for each hand. The procedure was repeated 3 times for each hand, totally, hand grip strength was measured 6 times and the average of three measurements in both hands, including muscle strength of right (MSR) hand and muscle strength of left (MSL) hand was used for data analyses(21). Subjects were then instructed to squeeze the digital handgrip dynamometer as hard as possible and to maintain maximal pressure during the test. Muscle endurance was recorded as the time (in seconds) for grip strength to reach 50% of maximum (22).

### *Blood pressure*

To assess blood pressure, first, we asked participants to sit for 10 min. Blood pressure was then measured using a standard mercury sphygmomanometer, twice with a 5 min interval, while participants were sitting. The mean of the two measurements was recorded as the participant's blood pressure.

### *Other measurements*

Information on lifestyle was collected via self-administered questionnaires included amongst others age, sex, educational level, physical activity, smoking, medical history and current use of medications. Smoking status was divided into current or never smoking. Education level was

indicated as the highest level of school achieved and participants were classified into either; under diploma, diploma, or educated.

### *Physical activity*

We used a valid and reliable short form of the International Physical Activity Questionnaire (IPAQ) to assess the level of physical activity. Vigorous physical activity, moderate physical activity, walking, and sitting in the past seven days was recorded using this questionnaire (24). Then, the Metabolic Equivalents (METs) was calculated to estimate total physical activity per week for each participant. Finally, METs were classified as weak ( $< 600$  MET-minutes/week), moderate ( $600 - 3000$  MET-minutes/week), and vigorous ( $> 3000$  MET-minutes/week).

### *Calculation of DII*

Dietary inflammatory weights (12) of 29 nutrients/food items were calculated, and subsequently, these values were summed to indicate DII. First, the daily intake of macro- and micronutrients (carbohydrate, protein, total fat, cholesterol, saturated fatty acids (SFA), monounsaturated fatty acids (MUFA), polyunsaturated fatty acids (PUFA), n-3 fatty acids, n-6 fatty acids,  $\beta$ -carotene, vitamin A, vitamin C, vitamin D, vitamin E, vitamin B6, vitamin B12, fiber, folic acid, niacin, riboflavin, thiamin, iron, zinc, selenium, magnesium, onion, caffeine) were calculated in order to reduce the between-person variation in dietary intake; some nutrients that were not available in our records (trans FAs, flavan-3-ol, flavones, flavonols, flavonones, anthocyanidins, isoflavones, pepper, thyme/oregano, rosemary, garlic, ginger, saffron, and turmeric and tea) were excluded. Adjusted intake of food parameters for each individual was standardized to its corresponding global mean and standard deviation. The derived Z score values were converted to percentile and centered by doubling the values and subtracting one to normalize the scoring system and to avoid skewness. The centered percentile value for each food parameter was then multiplied by its

respective overall food parameter score to obtain the food parameter-specific DII score. Finally, the DII score was determined by summing all of the food parameter-specific DII score. The greater the DII score, the more pro-inflammatory the diet, and more negative scores indicate a more anti-inflammatory diet.

### *Statistical analysis*

Participants were grouped based into tertiles of DII. To compare general characteristics among tertiles, we used one-way ANOVA and chi-square tests for quantitative and qualitative variables, respectively. An analysis of covariance (ANCOVA) test was performed to evaluate the association of DII score with muscle strength and muscle endurance after adjusting for potential confounders. All statistical analysis was performed with the SPSS (Statistical Package for Social Sciences) for Windows 25.0 software package (SPSS, Chicago, IL). The level of statistical significance was defined, *a priori*, at  $p < 0.05$ .

### **Results**

The demographic and anthropometric characteristics of the participants in the study are detailed in **Table 1**. A total of 270 participants (118 men and 152 women) were included in this study. Participants were, on average,  $36.77 \pm 13.19$  years old (152 women), and mean BMI was  $25.62 \pm 4.66$ . A significant decrease was found for blood pressure ( $p < 0.001$ ), weight ( $p < 0.001$ ), body mass index (BMI) ( $p < 0.001$ ), fat free mass (FFM) ( $p < 0.001$ ), waist circumference (WC) ( $p < 0.001$ ), and waist to hip ratio (WHR) ( $p < 0.001$ ) across tertiles of DII.

Dietary intake of participants by tertiles of DII are indicated in **Table 2**. Participants in the highest tertile of DII had less intake of vitamins, macronutrients, and minerals ( $p < 0.001$ ). A significant decrease was found for total cholesterol, energy, SFA, PUFA, MUFA, omega 3 and omega 6 across tertiles of DII ( $p\text{-value} < 0.001$ ).

**Table 3** shows multivariate-adjusted means for muscle strength and endurance (MS, MSL, MSR, ME, MEL and MER) across tertiles of DII. A significant decrease was found for both MS (p-value<0.01) and MSR (p-value<0.01) across tertiles of DII, after adjustment for confounding factors, including age, sex, education status, income, smoking, physical activity, BMI, and energy intake ( $P_{\text{ANCOVA}} < 0.01$ ). A significant decrease was also found for MSL (p-value<0.01) and MEL (p-value=0.02) across tertiles of DII, but after adjustment for confounding factors, this result was attenuated ( $P_{\text{ANCOVA}} = 0.08$  for MSL and  $P_{\text{ANCOVA}} = 0.4$  for MEL).

Multivariate adjusted means for FFM, FM, PBF, SMM, TF, VFL, and WC across tertiles of DII are detailed in **Table 4**. There was a significant decrease in mean of FFM (p<0.001), SMM (p<0.001), and WC (p<0.001) across tertiles of DII. However, after adjustment for confounding factors, no significant associations were observed in anthropometric measures and body composition.

## Discussion

To the best of our knowledge, this is the first study conducted to assess the relationship between DII and both muscle strength and endurance among an Iranian population. The present study highlighted that the DII scores, indicating inflammatory diet, were significantly and inversely associated muscle strength, even after all confounding variables were controlled for. When data was analysed by hand strata, the result was similar for right-hand muscle strength, but was not significant for the left-hand muscle strength. We also found that participants in the highest DII tertile had lower FFM, WC, and SMM compared to those in the lowest DII tertile; however, after adjusting for covariance, no significant difference was seen across tertiles.

Consistent with the results of the present study, previous studies among adults or elderly populations have reported positive associations between the DII and muscle strength; for instance,

it has reported that DII scores were positively associated with the risk of weight loss, low walking speed, and low grip strength particularly in older individuals with poor nutritional status (25). However, in a study by Amakye and colleagues (2018) among Chinese children aged 6-9 years, no associations were observed between DII and hand grip strength (16). Unlike the present study, the age, muscle mass, and physical activity level of the subjects in the study by Amakye, (2018) may contributing factors for the lack of significant association between the DII and muscle strength. Prior to this, no study, to the authors knowledge, has investigated the association of the DII and muscle endurance. In our study, we found a statistically significant inverse association between the pro-inflammatory capacity of the diet (as measured by the DII) and muscle endurance in the combined sample. However, after adjusting for confounding variables, the result became non-significant. When data were analysed by hand strata, the observed association was still significant for right-hand muscle endurance, even after adjusting for confounders. Changes in fiber composition brought about by consistent overuse associated with side dominance have been suggested as an explanation for differences in neuromuscular endurance features associated with dominant and non-dominant muscles of the hand (26-29). In a study by De Luca and colleges, they reported that the median frequency of the electromyography (EMG) signal decreased faster with sustained activity in the non-dominant first dorsal interosseous of right-handed subjects, whereas non-significant differences were found in left-handed individuals (26). Merletti et al. examined the longissimus dorsi muscle and found a statistically significant effect of hand dominance on fatigue indexes of longissimus dorsi in right hand dominant, but not left hand dominant, subjects. Indeed, these findings are all consistent with a greater type I muscle fiber content in muscles of the dominant compared with non-dominant side (27), and likely explains the discordance between hand strata observed in this study.

Previous studies have shown that muscle endurance, expressed as fatigue resistance or grip work, may be significantly related to circulating markers of inflammation in community-dwelling elderly persons (30), frail elderly nursing home residents (31), hospitalized geriatric patients (32, 33), and patients post abdominal surgery (34). In a cross-sectional study in 686 young healthy men, Vaara and colleagues (2014) found a weak inverse association of muscular endurance with CRP and IL-6 in individuals without abdominal obesity, and a moderate inverse association of muscular endurance with IL-6 in those with abdominal obesity (35). Additional muscle weakness caused by acute inflammatory conditions can lead to a disability at older ages very quickly (36); indeed, hospitalized geriatric patients with inflammation-induced acute infections and elevated circulation levels of IL-6 reported reduced muscle strength and endurance, relative to patients with no inflammation (32). Moreover, Mets et al reported evidence of a negative impact of inflammation on muscle endurance in hospitalized geriatric patients (33).

Higher DII scores, indicating pro-inflammatory diets, have been associated with increased levels of inflammatory cytokines such as interleukin-6 (IL-6) (37, 38), C-reactive protein (CRP) (9, 12, 39), and tumor necrosis factor-alpha (TNF- $\alpha$ ) (11). Chronic inflammation contributes to the loss of muscle mass, strength, and functionality, by affecting muscle protein degradation and synthesis through several signalling pathways (40). Indeed, numerous epidemiological studies have attributed poor muscular strength to high levels of inflammatory markers in middle-aged and older individuals (41). In a cross-sectional study, Visser and colleagues reported lower muscle mass and strength to be associated with higher plasma concentrations of IL-6 and TNF- $\alpha$  in 3075 healthy older population (6). Whilst in another cross sectional study by Volaklis *et al.* (2105), in elderly individuals with and without cardiac disease, lower levels of muscular strength were associated with higher concentrations of IL-6 and hs-CRP (41). Ruiz et al found that CRP, complement factor

C 3, and ceruloplasmin levels were negatively associated with muscle strength in Spanish adolescents (42); in addition, Steene-Johannessen et al also reported muscle strength to be independently associated with the CRP in 1306 Norwegian children (43).

The strengths of our study include the use of a validated dietary assessment method to generate the DII. The validated Iranian FFQ reflects the study subjects' usual intake over 12 months, which may accurately represent previous long-term dietary intake. The DII, derived after extensive literature reviewing, standardizes individuals' dietary intakes of inflammatory foods to world referent values. Furthermore, this is, to the authors knowledge, the first study conducted to assess the relationship between DII and both muscle strength and endurance among an Iranian population. However, despite numerous strengths, the present study has several limitations. First, the relatively small sample size might have attenuated the strength of, or underestimated, our results. Second, due to our sample size, we were not able to analyze based on gender; indeed, some studies have posited that pro-inflammatory diets may be more detrimental to musculoskeletal health in older men than in women (44). Finally, because of the cross-sectional study design, this study was not able to identify the causal relationship between DII with muscle strength and endurance in the study population.

## **Conclusion**

In conclusion, consumption of a pro-inflammatory diet, as indicated by higher DII scores, is associated with lower muscle strength and endurance among Iranian healthy men and women. These findings support the need for the development of dietary interventions targeting consumption of anti-inflammatory foods in the general population.

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