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Association between inflammatory potential of the diet and sarcopenia/its components in community-dwelling older Japanese men

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ABSTRACT

Purpose: Chronic inflammation is a pathophysiological cause of age-related diseases including sarcopenia. However, limited data are available on the association between the diet-derived inflammation and sarcopenia. Here, using the Dietary Inflammatory Index (DII), we examined the associations between inflammatory potentials of the diet, sarcopenia/its components, and serum inflammatory markers.

Materials and methods: This cross-sectional study was performed in 2014 among 1,254 community-dwelling older adults. Energy-adjusted DII score (E-adjusted DII) was calculated using a self-administered diet history questionnaire. Sarcopenia/its components was determined according to the Asian Working Group for Sarcopenia. Serum interleukin (IL)-1β, IL-4, IL-6, IL-10, tumor necrosis factor (TNF)α, and high-sensitivity C-reactive protein (hsCRP) were measured.

Results: The mean of E-adjusted DII was 0.13±2.1 (-4.92~5.29) in participants (74.6±5.5 y). After adjustment of confounders, men in the highest tertile of the E-adjusted DII showed a 2.89-times (95% CI: 1.04-8.04) higher risk of sarcopenia than those in the lowest tertile. Regarding its components (low muscle mass/strength/function), men in the highest tertile did not have significantly greater odds, respectively. Intriguingly, when the E-adjusted DII was calculated only based on anti-inflammatory food parameters, men who did not consume food with anti-inflammatory properties scored high E-adjusted DII and were significantly associated with sarcopenia in the highest tertile (OR: 2.96; 95% CI: 1.06-8.93). Higher serum hsCRP levels were seen in sarcopenic men with the highest E-adjusted DII (p=0.036).

Conclusions: These results suggest that a diet with pro-inflammatory potential is associated with the risk of sarcopenia. Further investigations whether anti-inflammatory diet could reduce its risk are needed.

1. Introduction

Chronic inflammation accompanies aging and is recognized as an underlying pathophysiological cause of age-related diseases (Chhetri et al., 2018; Chung et al., 2009; Lopez-Candales et al., 2017; Newcombe et al., 2018; Wellen & Hotamisligil, 2005), such as cardiovascular diseases (Lopez-Candales et al., 2017), chronic obstructive pulmonary disease (COPD) (Barnes et al., 2016), dementia (Newcombe et al., 2018), and sarcopenia (Chhetri et al., 2018).

Especially in sarcopenia, several inflammatory cytokines are responsible for decreasing muscle mass and strength (Schaap et al., 2006; Thoma & Lightfoot, 2018). For example, lower muscle mass and strength are associated with higher plasma concentrations of interleukin (IL)-6 and tumor necrosis factor (TNF)α in 3,075 well-functioning older adults (Visser et al., 2002). Furthermore, higher levels of C-reactive protein (CRP), IL-6, and IL-1 receptor antagonist (IL-1RA) are strongly associated with poorer physical performance in 1,020 older adults (Cesari et al., 2004). Regarding the molecular mechanisms underlying sarcopenia, it has been demonstrated that inflammatory cytokines disturb the balance of muscle protein synthesis and degradation by modulating critical regulators such as MyoD (Langen et al., 2004) or myostatin (Zhang et al., 2011), eventually leading to sarcopenia (Bian

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et al., 2017; Li et al., 2019; Rong et al., 2018).

Diet is one critical factor affecting immune responses. Higher intakes of fiber, omega-3-fatty acids, and vitamin C have been reported to contribute to the low levels of circulating inflammatory markers observed. Based on these findings, the majority of previous studies have focused on the inflammatory potential of specific nutrients rather than that of the diet as a whole. The Dietary Inflammatory Index (DII) was designed to assess the inflammatory potential of an individual's diet (Shivappa et al., 2014a), and is derived from an extensive literature review of diet and inflammatory markers (IL-1β, IL-4, IL-6, IL-10, TNFα, and CRP). This DII score is based on identifying 45 known nutrient/food intake parameters as having either a pro- or anti-inflammatory effect on a range of inflammatory biomarkers.

An increasing body of evidence has shown the association between a high DII score (indicating a pro-inflammatory diet), high levels of circulating inflammatory markers (Shivappa et al., 2017; Yang et al., 2020; Shin et al., 2019), and the prevalence of inflammation-mediated diseases, including cardiovascular disease (Park et al., 2018; Shivappa et al., 2018a; Ruiz-Canela et al., 2016), diabetes (Denova-Gutiérrez et al., 2018; Laouali et al., 2019; Mtintsilana et al., 2019), metabolic syndrome (Ren et al., 2018; Canto-Osorio et al., 2020; Kim et al., 2018), and COPD (Shivappa et al., 2016). Regarding sarcopenia and frailty, recent studies have shown that higher DII scores were associated with a higher incidence of frailty (Shivappa et al., 2018b), reduced appendicular lean mass and bone health (Cervo et al., 2020a), and further, increased hip fracture rate (Zhang et al., 2017). However, limited studies are available on the association of the inflammatory potential of the diet with sarcopenia.

In the present study, using energy-adjusted DII scores (E-adjusted DII), we aimed to examine the effects of the inflammatory potential of diets on sarcopenia/its components. Furthermore, we sought to clarify the association between this potential and circulating inflammatory biomarkers. Additionally, various parameters affecting diets, such as oral function, mental health, social interactions with friends or family, and dietary status (e.g., eating alone), were considered in this study.

2. Materials and methods

2.1. Design and participants

This Kashiwa-based study is a prospective cohort study designed to characterize the biological, psychosocial, and functional changes associated with aging in community- dwelling older adults in Kashiwa city, a commuter town of Tokyo in the Chiba prefecture, Japan. In 2012, a total of 2,044 older adults (1,013 men, 1,031 women) agreed to participate in the study, and these individuals comprised the inception cohort. Of the 1,308 older adults who participated in wave 3 of the Kashiwa-based study in 2014, the sample comprised 1,254 older adults, of which 650 (51.8%) were men. Participants with incomplete dietary data, extreme energy intake (over 3600 kcal/day), or lack of sociodemographic data were excluded. The experimental protocols were approved by the institutional review committee of the University of Tokyo (#12-8) and conformed to the guidelines of the appropriate Japanese governmental agency. All participants provided written informed consent.

2.2. Muscle mass, strength, and physical performance

Appendicular muscle mass was measured through bioelectrical impedance analysis (BIA) using the Inbody 430 (Biospace, Seoul, Korea). This method has been validated for the assessment of appendicular skeletal muscle mass, has a strong correlation with that of dual-energy X-ray absorptiometry, and has been used to investigate the prevalence of sarcopenia according to the Asian Working Group for Sarcopenia (AWGS) definition (Wang et al., 2016; Kim et al., 2015).

Muscle strength was assessed as handgrip strength, measured using a digital grip strength dynamometer (Takei Scientific Instruments, Niigata, Japan). The test was conducted twice, and the higher score was used in the analysis. Physical performance was measured based on usual gait speed. Participants were instructed to walk over an 11 m straight line, and the usual gait speed was derived from the speed over the middle 5 m distance (between 3 and 8 m from the start line).

2.3. Diagnosis of sarcopenia

Sarcopenia was defined according to the diagnostic criteria laid out by the AWGS 2019, including low muscle mass (< 7.0 kg/m^2 for men and < 5.7 kg/m^2 for women, as measured by BIA), low handgrip strength (< 28 kg for men and < 18 kg for women), and slow gait speed (< 1.0 m/s for both sexes). The presence of sarcopenia was defined as low muscle mass with low handgrip strength or slow gait speed (Chen et al., 2020).

2.4. Dietary assessment and calculation of energy-adjusted DII

Dietary intake was assessed with a brief self-administered diet history questionnaire (BDHQ), previously validated (Kobayashi et al., 2011). We used the method of Shivappa et al. (2014a) to compute the DII score. Briefly, the DII score was calculated across 25 food parameters (intake volume), data of which were obtained from the BDHQ. The parameters were alcohol, vitamin B12, vitamin B6, β-carotene, carbohydrate, cholesterol, total fat, fiber, folic acid, iron, magnesium, monounsaturated fatty acids, niacin, n-3 fatty acids, n-6 fatty acids, protein, polyunsaturated fatty acids, riboflavin, saturated fat, thiamine, vitamin A, vitamin C, vitamin E, zinc, and tea. The residual method was used to obtain the energy-adjusted amounts for all nutrients (Willett & Stampfer, 1986) and we used as the energy (E)-adjusted DII in this study. To normalize the scoring system and to avoid skewness, the derived Z score values were converted to percentiles and centered by doubling the values and subtracting one. Then, to obtain the food parameter-specific DII score, the centered percentile value for each food parameter was multiplied by its respective overall food parameter score. Finally, the DII score was determined by totaling the food parameter-specific DII scores. A more positive E-adjusted DII indicated a more pro-inflammatory diet, and a more negative score indicated a more anti-inflammatory diet.

2.5. Inflammatory biomarkers

Fasting blood samples were collected from each participant by well-trained nurses to determine the concentration of inflammatory biomarkers. Serum was stored at −80°C and was analyzed for five inflammatory cytokines (IL-1β, IL-4, IL-6, IL-10, and TNFα) using the Bio-Plex pro human cytokine assay kit (Bio-Rad). High-sensitivity C-reactive protein (hsCRP) was also analyzed in serum.

2.6. Dietary environment

Living status and eating status were assessed using a standardized self-reporting questionnaire, since it has recently been suggested that living with family yet eating alone is associated with frailty in community-dwelling older adults (Suthutvoravut et al., 2019). To examine the effects of oral frailty (Tanaka, et al., 2018), the number of remaining teeth were counted by dental hygienists. The Japanese version of the General Oral Health Assessment Index (GOHAI) was used to measure oral health-related life (Campos et al., 2017). Given that appetite has been suggested as one of the factors associated with sarcopenia (Tsutsumimoto et al., 2020), a question in this questionnaire was on self-reported appetite, namely, "Have you experienced a decreased appetite over the last month?" This was answered as "yes" or "no."

2.7. Other parameters

We obtained sociodemographic characteristics data (e.g., age, sex, and duration of education) using a standardized self-reporting questionnaire. Data on medical histories of hypertension, cardiovascular diseases, diabetes, and hyperlipidemia were obtained from patient interviews conducted by trained nurses. History of falling was ascertained through a short questionnaire. Physical activity was assessed using the Global Physical Activity Questionnaire (GPAQ) (Armstrong & Bull, 2016). The 15-item Geriatric Depression Scale (GDS) was also used. Scores ≥ 6 were defined as "depressive symptoms" (Montorio & Izal, 1996). The Mini-Mental State Examination was used, and a score < 27 was defined as "mild cognitive impairment". Social interactions with family and friends were also assessed based on the abbreviated Lubben Social Network Scale-6 (Gray et al., 2016).

2.8. Statistical analysis

Participants were classified based on the tertile of E-adjusted DII. Basic general characteristics of men and women across the tertiles of the E-adjusted DII score were compared using the Chi-square test for categorical variables and ANOVA for continuous variables. To examine the relationship between E-adjusted DII with overall score, and with only pro- or only anti-inflammatory score, and odds of sarcopenia or its components, binary logistic regression analysis was used to estimate the inter-tertile odds ratio (OR) and their 95% confidence interval (CI), using the lowest tertile as a reference. Regression models were built with two levels of adjustment: Model 1 was adjusted for age, and model 2 was additionally adjusted for education level, protein intake, physical activity, medical history (hypertension, diabetes, hyperlipidemia, or cardiovascular disease), eating alone, social interactions, GDS score ≥ 6, and oral health (GOHAI), which could be considered as a potential confounder, based on a p-value of < 0.100 by univariate analysis and the literature (Lopez-Candales et al., 2017; Guzik & Toyuz, 2017; Tietge 2014).

We examined six inflammatory markers using the serum samples of four groups, which were divided based on E-adjusted DII and presence of sarcopenia (the highest or lowest nine samples in each group; group 1: robust with the lowest E-adjusted DII (-4.19 ± 0.28); group 2: robust with the highest E-adjusted DII (3.62 ± 0.75); group 3: sarcopenia with the lowest E-adjusted DII (-1.73 ± 1.13); group 4: sarcopenia with the highest E-adjusted DII (4.68 ± 0.34)). When comparing the four groups, data were analyzed by Kruskal-Wallis non-parametric one-way ANOVA with Tukey's post hoc test. Statistical analyses were performed using IBM SPSS statistics version 26 for Windows (IBM Japan, Tokyo, Japan). The threshold of statistical significance was set at $p < 0.05$.

3. RESULTS

3.1. Characteristics of study participants

Of the 1,308 older adults who participated in wave 3 of the Kashiwa-based study, the 1,254 who completed dietary assessment and provided other relevant measurements were included in this analysis. Participants' mean age was 74.6±5.5 y (range: 67–96 y), and 51.8% were men. The mean E-adjusted DII for all study participants was 0.13±2.1 (range: −4.92 to 5.29).

Table 1 presents basic patient characteristics stratified by sex, along with the E-adjusted DII tertile. There was no difference in mean age (74.8±5.5 y *vs.* 74.4±5.4 y). The mean E-adjusted DII was 0.67±2.1 (range: −4.49 to 5.29) for men and −0.44±2.0 (range: −4.92 to 5.08) for women, indicating that women consumed a more anti-inflammatory diet than men. Men in the highest tertile who consumed a pro-inflammatory diet (tertile 3, higher E-adjusted DII) were more likely

Table 1
Basic characteristics of men and women by E-adjusted DII tertile.

	Men				Women			
Subject group by E-DII tertile	Tertile 1 n=217	Tertile 2 n=217	Tertile 3 n=216	p-value	Tertile 1 n=201	Tertile 2 n=201	Tertile 3 n=202	p-value
Basic attributes								
Age (yrs)	75.56±5.79	74.47±5.06	74.42±5.71	0.067	75.07±5.69	74.33±4.89	73.74±5.44	0.032*
DII score	-1.74±1.12	0.83±0.53	2.93±0.81	p<0.001*	-2.68±0.89	-0.45±0.57	1.79±1.03	p<0.001*
Education level (≤12 yrs)	93(42.9%)	93(42.9%)	94(43.5%)	0.987	142(70.6%)	146(72.6%)	155(76.7%)	0.370
Energy (Kcal)	2338.6±619.1	2120.0±608.9	2284.6±582.3	0.020*	1997.9±587.7	1851.6±488.1	1952.2±549.9	0.041*
Protein (g)	113.4±36.3	89.9±30.2	82.4±25.5	p<0.001*	103.3±34.8	84.5±25.5	76.3±23.7	p<0.001*
BMI (kg/m^2)	22.83±2.78	22.71±2.66	22.41±2.70	0.255	21.76±3.08	22.06±3.13	21.70±3.10	0.490
Body fat (%)	23.04±6.17	23.00±5.97	22.19±5.75	0.244	28.25±7.14	29.80±7.10	28.72±6.87	0.056
Comorbidity								
Hypertension (%)	100(50.5%)	101(48.6%)	98(48.0%)	0.873	81(41.8%)	80(43.0%)	74(39.6%)	0.792
Diabetes Mellitus (%)	34(17.1%)	32(15.4%)	20(9.6%)	0.088	24(12.4%)	21(11.3%)	17(9.1%)	0.592
Hyperlipidemia (%)	58(29.1%)	67(32.2%)	50(24.5%)	0.220	74(38.1%)	86(46.2%)	88(46.0%)	0.192
Cardiovascular disease (%)	53(26.9%)	52(25.0%)	61(30.0%)	0.511	37(19.1%)	40(21.5%)	23(12.4%)	0.057
Sarcopenia								
Sarcopenia (%)	11(5.1%)	17(7.8%)	22(10.2%)	0.135	15(7.5%)	9(4.5%)	16(7.9%)	0.321
Low Appendicular SMI (%)	57(26.4%)	67(30.6%)	70(32.6%)	0.359	73(36.3%)	70(34.8%)	76(38.2%)	0.782
Low hand grip strength (%)	21(9.7%)	21(9.6%)	28(13.0%)	0.427	14(7.0%)	15(7.5%)	20(10.1%)	0.481
Slow gait speed (%)	7(3.2%)	5(2.3%)	7(3.3%)	0.788	6(3.0%)	4(2.0%)	7(3.5%)	0.645
Physical function and activity								
Time up and go (sec)	5.49±1.24	5.44±1.20	5.57±1.28	0.410	5.96±1.18	5.96±1.42	5.94±1.46	0.779
GPAQ (METs/day)	410.2± 456.7	432.4±895.6	349.6±426.0	0.394	479.3± 793.2	456.7±673.2	293.7±379.9	0.026*
Fall (1≥ fall in last 1 yr, %)	27(12.5%)	24(11.1%)	34(15.8%)	0.332	41(20.5%)	32(15.9%)	42(20.8%)	0.378
Oral function								
Remaining teeth (<20, %)	71(32.7%)	69(31.9%)	80(37.0%)	0.484	62(31.0%)	46(23.0%)	74(36.8%)	0.010*
GOHAI	56.11±6.03	55.57±5.79	55.09±5.60	0.012*	55.39±6.51	55.26±5.93	53.40±6.99	0.005*
Cognitive and mental function								
MMSE (<27, %)	22(10.1%)	21(9.7%)	22(10.2%)	0.981	18(9.0%)	18(9.0%)	21(10.4%)	0.849
GDS (≥6, %)	24(11.4%)	33(15.6%)	47(22.2%)	0.010*	31(16.0%)	32(16.6%)	34(17.2%)	0.951
Environment of food								
LSNS friends	7.08±3.76	6.61±3.83	6.21±3.97	0.099	7.93±3.37	7.90±3.02	7.05±3.15	0.005*
LSNS family	6.84±3.43	6.42±3.39	6.44±3.43	0.217	7.21±3.45	7.93±2.99	7.10±2.91	0.014*
Living alone (%)	19(8.8%)	14(6.5%)	21(9.7%)	0.448	46(22.9%)	25(12.4%)	35(17.3%)	0.022*
Eating alone (%)	21(9.7%)	27(12.2%)	37(16.7%)	0.092	51(25.4%)	31(15.4%)	36(17.8%)	0.032*
Loss of appetite (%)	5(2.3%)	6(2.8%)	5(2.3%)	0.939	4(2.0%)	3(1.5%)	7(3.5%)	0.392

to have lower protein intake, higher carbohydrate intake, poorer oral health, and greater depressive symptoms, compared with those who consumed an anti-inflammatory diet (tertile 1, lower E-adjusted DII score). Women who consumed a pro-inflammatory diet were younger and, like men, had lower protein intake, higher carbohydrate intake, and poorer oral health than those who consumed an anti-inflammatory diet. However, unlike men, women in the highest tertile (tertile 3) had lower physical activity, a higher proportion of remaining teeth (< 20), and lower scores for their social network of friends and family than those in the lowest tertile of E-adjusted DII.

3.2. E-adjusted DII and sarcopenia

In this cross-sectional analysis, 7.2% of all participants were diagnosed with sarcopenia according to the AWGS criteria. No differences were found in the prevalence of this phenotype between men (7.7%) and women (6.6%). Table 2 shows the association between E-adjusted DII and sarcopenia or its diagnostic parameters (low appendicular skeletal mass index (SMI), low handgrip strength, and low gait speed) stratified by men and women.

In men, a significant association between E-adjusted DII tertile 3 and sarcopenia was observed in crude (OR: 2.12, 95% CI: 1.00–4.50), age-adjusted (OR: 2.82, 95% CI: 1.27–6.23), and fully-adjusted models (OR: 2.89, 95% CI: 1.04–8.04), compared with the association between E-adjusted DII tertile 1 and sarcopenia. Of the three diagnostic parameters of sarcopenia, a significant association between E-adjusted DII tertile 3 and low appendicular SMI was detected only in the age-adjusted model (OR: 1.59, 95% CI: 1.02–2.48) and not in the fully-adjusted model. No significant associations between E-adjusted DII tertile and low handgrip strength or slow gait speed were observed. However, for women, no significant associations were observed between E-adjusted DII and sarcopenia or any of its three diagnostic parameters in the crude, age-adjusted, and fully-adjusted models.

To further clarify the characteristics of an inflammatory diet associated with sarcopenia in men, we examined whether a different association exists between a high DII score and high intake of pro-inflammatory nutrients (seven food parameters), such as total fat or cholesterol, or whether a high DII score is the result of low intake of anti-inflammatory nutrients (18 food parameters), such as fiber or β-carotene. Further examination of the association between pro- and anti-inflammatory food parameter-derived E-adjusted DII and sarcopenia were performed. As shown in Table 3, we found that a lower anti-inflammatory E-adjusted DII (eventually leading to a high E-adjusted DII) was strongly associated with sarcopenia (OR: 2.96, 95% CI: 1.06–8.93), whereas a higher pro-inflammatory E-adjusted DII alone was not associated with sarcopenia (OR: 1.01, 95% CI: 0.40–2.55), suggesting that the pro-inflammatory diet contributing to sarcopenia was a result of the low intake of anti-inflammatory nutrients and not the high intake of pro-inflammatory nutrients in this population.

3.3. Serum inflammatory markers and E-adjusted DII in men with sarcopenia

To obtain a more in-depth insight into the relationship between E-adjusted DII and sarcopenia, we measured six inflammatory markers using the serum samples of men with or without sarcopenia and available E-adjusted DII (4 groups: robust or sarcopenia having the lowest or the highest E-adjusted DII). Table 4 shows the serum levels of hsCRP, IL-1β, IL-6, TNFα, IL-4, and IL-10 in the four groups. We found that serum levels of hsCRP were significantly associated with a high E-adjusted DII in sarcopenia (p=0.036). Levels of the other inflammatory cytokines (IL-1β, IL-4, IL-6, IL-10, TNFα) were not significantly different between the groups.

4. Discussion

In the present study, men in the highest tertile (with a more pro-inflammatory diet) of the E-adjusted DII, showed a higher risk of sarcopenia, even after adjusting for potential confounders. Notably, the E-adjusted DII derived from anti-inflammatory food parameters was

Table 2
Associations among E-adjusted DII and sarcopenia and its diagnostic parameters stratified by sex.

	Men						Women					
	Crude		Age-adjusted		Fully-adjusted		Crude		Age-adjusted		Fully-adjusted	
	OR	(95% CI)	OR	(95%CI)	OR	(95%CI)	OR	(95%CI)	OR	(95%CI)	OR	(95%CI)
Sarcopenia												
Tertile 1 low (reference)	1		1		1		1		1		1	
Tertile 2 middle	1.59	(0.73-3.48)	2.20	(0.96-5.04)	2.68	(0.95-7.58)	0.97	(0.45-2.09)	0.67	(0.28-1.61)	0.57	(0.22-1.50)
Tertile 3 high (more inflammatory)	2.12*	(1.00-4.50)	2.82*	(1.27-6.23)	2.89*	(1.04-8.04)	1.60	(0.69-3.71)	1.29	(0.60-2.75)	1.54	(0.69-3.44)
Low appendicular SMI												
Tertile 1 low (reference)	1		1		1		1		1		1	
Tertile 2 middle	1.20	(0.79-1.82)	1.44	(0.93-2.25)	1.40	(0.84-2.32)	1.00	(0.74-1.34)	0.99	(0.65-1.50)	0.99	(0.62-1.56)
Tertile 3 high (more inflammatory)	1.31	(0.87-1.99)	1.59*	(1.02-2.48)	1.45	(0.85-2.46)	1.04	(0.77-1.41)	1.20	(0.79-1.81)	1.08	(0.68-1.71)
Low handgrip strength												
Tertile 1 low (reference)	1		1		1		1		1		1	
Tertile 2 middle	1.00	(0.53-1.89)	1.28	(0.66-2.51)	1.35	(0.61-3.00)	1.38	(0.63-3.06)	1.37	(0.62-3.04)	1.35	(0.57-3.18)
Tertile 3 high (more inflammatory)	1.39	(0.76-2.53)	1.74	(0.92-3.31)	1.56	(0.71-3.44)	1.99	(0.93-4.28)	1.96	(0.92-4.21)	2.15	(0.94-4.90)
Slow gait speed												
Tertile 1 low (reference)	1		1		1		1		1		1	
Tertile 2 middle	0.71	(0.22-2.27)	1.00	(0.30-3.37)	1.03	(0.22-4.88)	0.78	(0.21-2.88)	0.79	(0.22-2.90)	0.68	(0.18-2.60)
Tertile 3 high (more inflammatory)	1.01	(0.35-2.92)	1.28	(0.42-3.88)	1.29	(0.31-5.33)	1.40	(0.45-4.34)	1.40	(0.45-4.34)	1.62	(0.49-5.36)

The fully-adjusted model was adjusted by age, education level, protein intake, physical activity, medical history (hypertension, diabetes, hyperlipidemia, cardiovascular disease), eating alone, Lubben Social Network Scale (LSNS) social ties (<12), Geriatric Depression Scale (GDS) ≥6, and Geriatric Oral Health Assessment Index (GOHAI) score.
*p < 0.05. OR: odds ratio CI: confidence interval Binary logistic regression.

Table 3
Association among anti- and pro-inflammatory E-adjusted DII, and sarcopenia and its diagnostic parameters in men.

	Anti-inflammatory E-adjusted DII						Pro-inflammatory E-adjusted DII					
	Crude		Age-adjusted		Fully-adjusted		Crude		Age-adjusted		Fully-adjusted	
	OR	(95%CI)	OR	(95% CI)	OR	(95%CI)	OR	(95%CI)			OR	(95%CI)
Sarcopenia												
Tertile 1 low (reference)	1		1		1		1		1		1	
Tertile 2 middle	2.22*	(1.02-4.83)	3.14*	(1.37-7.19)	4.46*	(1.53-12.98)	0.88	(0.43-1.81)	0.77	(0.36-1.63)	0.92	(0.39-2.17)
Tertile 3 high (more inflammatory)	2.00	(0.91-4.40)	2.82*	(1.22-6.51)	2.96*	(1.06-8.93)	1.06	(0.53-2.12)	0.83	(0.40-1.72)	1.01	(0.40-2.55)
Low appendicular SMI												
Tertile 1 low (reference)	1		1		1		1		1		1	
Tertile 2 middle	1.22	(0.81-1.86)	1.47	(0.94-2.29)	1.56	(0.93-2.60)	1.01	(0.67-1.51)	0.92	(0.60-1.41)	1.08	(0.68-1.73)
Tertile 3 high (more inflammatory)	1.29	(0.85-1.95)	1.61*	(1.03-2.51)	1.42	(0.83-2.42)	0.86	(0.57-1.29)	0.70	(0.45-1.10)	0.76	(0.45-1.27)
Low handgrip strength												
Tertile 1 low (reference)	1		1		1		1		1		1	
Tertile 2 middle	1.42	(0.76-2.65)	1.87	(0.96-3.64)	1.84	(0.82-4.11)	0.96	(0.51-1.79)	0.85	(0.44-1.64)	0.88	(0.43-1.83)
Tertile 3 high (more inflammatory)	1.36	(0.73-2.56)	1.82	(0.93-3.55)	1.60	(0.70-3.65)	1.26	(0.69-2.29)	1.02	(0.54-1.92)	1.06	(0.49-2.30)
Slow gait speed												
Tertile 1 low (reference)	1		1		1		1		1		1	
Tertile 2 middle	1.00	(0.35-2.90)	1.40	(0.46-4.28)	1.31	(0.31-5.51)	0.57	(0.16-1.96)	0.46	(0.13-1.69)	0.46	(0.10-2.15)
Tertile 3 high (more inflammatory)	0.71	(0.22-2.28)	0.97	(0.29-3.25)	1.10	(0.24-5.02)	1.15	(0.41-3.22)	0.83	(0.28-2.46)	0.91	(0.23-3.55)

The model was fully adjusted by age, education level, protein intake, physical activity, medical history (hypertension, diabetes, hyperlipidemia, or cardiovascular disease), eating alone, Lubben Social Network Scale (LSNS) social ties (< 12), Geriatric Depression Scale (GDS) score ≥ 6, and Geriatric Oral Health Assessment Index (GOHAI) score.
*p < 0.05; OR: odds ratio; CI: confidence interval Binary logistic regression.

Table 4
Serum concentrations of inflammatory cytokines and high-sensitivity CRP (hsCRP) in the lowest and the highest E-adjusted DII with and without sarcopenia.

	Robust	Sarcopenia			
	The Lowest E-adjusted DII	The Highest			
E-adjusted DII	The Lowest				
E-adjusted DII	The Highest				
E-adjusted DII	p				
hsCRP (pg/mL)	0.06 ± 0.02	0.07 ± 0.02	0.06 ± 0.01	0.27 ± 0.11	0.036*
IL-1β (pg/mL)	0.04 ± 0.01	0.17 ± 0.09	0.18 ± 0.08	0.07 ± 0.02	0.280
IL-6 (pg/mL)	0.45 ± 0.05	0.57 ± 0.08	0.96 ± 0.25	0.99 ± 0.21	0.066
TNFα (pg/mL)	1.95 ± 0.10	2.24 ± 0.21	2.60 ± 0.30	2.29 ± 0.26	0.278
IL-4 (pg/mL)	0.01 ± 0.002	0.01 ± 0.002	0.01 ± 0.004	0.01 ± 0.002	0.212
IL-10 (pg/mL)	0.13 ± 0.015	0.23 ± 0.06	0.33 ± 0.08	0.21 ± 0.04	0.095

Note: All values are presented as mean ± standard error (n=9). *p <0.05, one-way ANOVA with Tukey's post hoc test. hsCRP: high-sensitivity C-reactive protein.

significantly associated with sarcopenia. To the best of our knowledge, this is the first report showing an association between the E-adjusted DII and AWGS-defined sarcopenia. Furthermore, sarcopenic men with the highest E-adjusted DII, showed significantly higher levels of serum hsCRP than men in the other three groups.

Consistent with the results of the present study, a positive association between higher E-adjusted DII and greater odds of sarcopenia has been suggested among 300 elderly people, using the definition of the European Working Group on Sarcopenia (EWGSOP) (Bagheri, et al., 2020). Also consistent with our results, no significant association was seen between DII and components of sarcopenia, including low muscle mass, low handgrip strength, and slow gait speed.

Recently, several studies have suggested the association between the DII score and muscle mass, strength, and function both with negative and positive findings. For example, a prospective population-based study with 1,099 Austrian subjects aged 50-79 years revealed that unit increase in DII score was not associated with lower appendicular lean mass and hand grip strength after adjustment for potential confounders (Cervo et al., 2020a). With respect to muscle strength, a cross-sectional study with 270 adults living in Iran, showed that a significant decrease was found in grip strength across the tertiles of the DII score. However, compared with those in the lowest tertile of DII score, no significant difference in skeletal muscle mass was seen in subjects in the highest tertile of DII score. Furthermore, DII score was significantly related to muscle endurance in the crude model, an association that disappeared after adjustment of confounders (Shahinfar et al., 2021).

On the other hand, in contrast to our results, those of another study showed that a higher energy-adjusted DII (E-DII) was associated with a lower appendicular lean mass (ALM/BMI), as measured by dual-energy X-ray absorptiometry (Cervo et al., 2020b). Furthermore, a recent study demonstrated that the DII score is associated with slow gait speed in older adults (Laclaustra et al., 2020). This inconsistency observed in the association between our E-adjusted DII or E-DII, DII score and muscle mass, strength, and function might require additional examination with sufficient sample sizes and diagnosis of sarcopenia to clarify.

Regarding the characteristics of diets, inadequate protein intake is recognized as an etiological factor contributing to sarcopenia (Baum et al., 2016; Tessier & Chevalier, 2018). In the present study, we found that men in the highest tertile of E-adjusted DII were more likely to have lower protein intake than those in the lowest tertile. However, the highest tertile protein intake was 1.4±0.5 g/kg/day, which is sufficient as per recent recommendations (1.0–1.2 g/kg/day) for healthy individuals. Thus, in this population, protein intake was considered to be

adequate and not an etiologic factor of sarcopenia. Interestingly, when we examined the highest tertile group of E-adjusted DII only calculated using anti-inflammatory food parameters, the association between anti-inflammatory E-adjusted DII and sarcopenia was significant, implying that the association between total E-adjusted DII and sarcopenia was mainly due to a low intake of anti-inflammatory food parameters, and not due to the high intake of pro-inflammatory food parameters.

Supporting our findings, a recent study has demonstrated that older adults in the highest tertile of sarcopenia had significantly lower intakes of the anti-inflammatory components of DII. This finding indicates that individuals with greater adherence to a pro-inflammatory diet have lower intakes of fruits, vegetables, and protein (Bagheri et al., 2020). Given that the strong anti-inflammatory potential of a Mediterranean diet is comparable to a DII score of -3.96 (Steck, et al., 2014), which has been associated with lower odds for the development of EWGSOP-defined sarcopenia among community-dwelling men and women with an average age of 66 years (Hashemi et al., 2015), these results are consistent with our study findings.

Furthermore, the Japanese dietary pattern, which is characterized by the high consumption of rice, fish, soybean products, and vegetables, might be relevant to the inflammatory potential caused by high intake of carbohydrates or low intake of fish, soybean products, and vegetables in Japanese older adults. Further investigation is needed to elucidate the balance between protein intake (a pro-inflammatory food parameter) and consumption of anti-inflammatory food parameters to prevent sarcopenia.

Among the mechanisms addressing sarcopenia pathogenesis, we found that higher E-adjusted DII was associated with higher serum levels of hsCRP in the sarcopenic men. Congruently, Cavicchia et al. (2009) and Shivappa et al. (2014b) have suggested that the DII score predicts changes in serum hsCRP levels, showing an inverse association between the inflammatory index score and hsCRP levels in 494 adult men and women in the seasonal variation of blood cholesterol study (SEASON). Furthermore, supporting our notion that CRP could be a potential parameter for sarcopenia, a recent meta-analysis of cross-sectional studies demonstrated the proportional relationship between serum CRP levels and sarcopenia (Bano et al., 2017; Hamer & Molloy, 2009). Namely, in the analysis of 17 studies with a total of 11,249 participants, sarcopenic participants were found to have significantly higher levels of CRP than those without sarcopenia, whereas serum levels of IL-6 or TNFα were not significantly different between participants with and without sarcopenia.

Consistent with a previous study (Shivappa et al., 2018b), a significant association between E-adjusted DII and sarcopenia was identified only in men. For example, compared with men in the lowest tertile, men in the highest tertile seemed to be more depressive. In contrast, women in the highest tertile seemed to be less physically active, and had poor oral health and weak social interactions with friends. This might have caused sex-related differences in the association between DII score and sarcopenia. To clarify why men might be more susceptible to the negative effects of an inflammatory diet than women, future research comparing these effects across genders is needed.

There are strengths and limitations to the present study. Our study's strengths include the well-defined cohort of older adults with a large sample size (1,254 participants contributing to a total of 1,308 participants). Furthermore, since these cohort study participants were randomly selected from the resident register, they are representative of older adults in the study area and have similar health characteristics. A wealth of information, including information relating to eating status and the attributes of the diet (e.g., appetite, food enjoyment, and food preparation), was collected, which allowed for the appropriate control of several other variables, thus decreasing the possibility of residual confounding effects. Notably, we assessed all six inflammatory mediators in the context of the DII score and sarcopenia to better understand this relationship, although we used the serum of nine representative participants across the four groups (DII: low or high × sarcopenia: with or without).

Several limitations of this work should also be addressed. We used cross-sectional data, therefore, we could not draw causal inferences. It is possible that, with the occurrence of sarcopenia, cooking healthy food becomes harder to do and, in turn, diets turn more towards easier to prepare meals, which may not be as healthy. Further, E-adjusted DII was calculated using 25 nutrients only; however, in a validation study, the predictive ability of DII scores was found to remain the same when the number of food variables decreased from 45 to 28 (Shivappa et al., 2014b), suggesting that this measurement is valid with a lower number of nutrients being included. Although the diet history questionnaire used in this study has been validated, it only accounted for dietary intake in the previous month. Thus, it is impossible to determine whether seasonal variations in dietary intake influence the association between the DII score and sarcopenia and its diagnostic parameters. Comparing the levels of serum inflammatory markers using only nine samples in each group is not sufficient to validate the effects of an inflammatory diet.

Taken together, our findings, obtained using E-adjusted DII, indicate the significant positive association between a pro-inflammatory diet and sarcopenia in men, which might be further attributable to a low intake of anti-inflammatory food parameters and, partly, to an increase in serum hsCRP levels. This suggests a significant potential of dietary intervention to modulate systemic inflammation through the intake of anti-inflammatory foods in older adults. Future randomized controlled trials on the effects of anti-inflammatory diets on sarcopenia in men are warranted. Furthermore, a sex-stratified methodology should be considered.

CRediT authorship contribution statement

Bo-Kyung Son: Conceptualization, Data curation, Writing – original draft. **Masahiro Akishita:** Writing – review & editing. **Takashi Yamanaka:** Investigation. **Koichi Toyoshima:** Methodology. **Tomoki Tanaka:** Formal analysis, Investigation. **Unyaporn Suthutvoravut:** Formal analysis. **Katsuya Iijima:** Writing – review & editing, Supervision, Project administration.

Declaration of Competing Interest

All authors declare that they have no conflicts of interest.

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BK.S. analysed data and wrote the manuscript. BK.S and M.A designed the study. T.Y consulted on the project. K.T., T.T., and S.U. analysed and interpreted the data. Katsuya Iijima supervised the project. All authors discussed results and approved the final manuscript. The authors acknowledge the all staff of Kashiwa study for their contribution to data collection.

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References

Armstrong, T., & Bull, F. (2016). Development of the world health organization global physical activity questionnaire (GPAQ). *J. Public Health, 14*(2), 66–70. https://doi.org/10.1007/s10389-006-0024-x

Bagheri, A., Soltani, S., Hashemi, R., Heshmat, R., Motlagh, A. D., & Esmaillzadeh, A. (2020). Inflammatory potential of the diet and risk of sarcopenia and its components. *Nutrit. J., 19*(1), 129. https://doi.org/10.1186/s12937-020-00649-2

Bano, G., Trevisan, C., Carraro, S., Solmi, M., Luchini, C., Stubbs, B., Manzato, E., Sergi, G., & Veronese, N. (2017). Inflammation and sarcopenia: A systematic review and meta-analysis. *Maturitas, 96*, 10–15. https://doi.org/10.1016/j.maturitas.2016.11.006

Barnes, P. J. (2016). Inflammatory mechanisms in patients with chronic obstructive pulmonary disease. *J. Allergy Clin. Immunol., 138*(1), 16–27. https://doi.org/10.1016/j.jaci.2016.05.011

Baum, J. I., Kim, I. Y., & Wolfe, R. R. (2016). Protein consumption and the elderly: what is the optimal level of intake? *Nutrients, 8*(6). https://doi.org/10.3390/nu8060359, 359-357.

Bian, A. L., Hu, H. Y., Rong, Y. D., Wang, J., Wang, J. X., & Zhou, X. Z. (2017). A study on relationship between elderly sarcopenia and inflammatory factors IL-6 and TNF-α. *Eur. J. Med. Res., 22*(1), 25. https://doi.org/10.1186/s40001-017-0266-9

Campos, J. A. D. B., Zucoloto, M. L., Bonafé, F. S. S., & Maroco, J. (2017). General oral health assessment index: a new evaluation proposal. *Gerodontology, 34*(3), 334–342. https://doi.org/10.1111/ger.12270

Canto-Osorio, F., Denova-Gutierrez, E., Sánchez-Romero, L. M., Salmerón, J., & Barrientos-Gutierrez, T. (2020). Dietary inflammatory index and metabolic syndrome in Mexican adult population. *Am. J. Clin. Nutr., 112*(2), 373–380. https://doi.org/10.1093/ajcn/nqaa135

Cavicchia, P. P., Steck, S. E., Hurley, T. G., Hussey, J. R., Ma, Y., Ockene, I. S., & Hébert, J. R. (2009). A new dietary inflammatory index predicts interval changes in serum high-sensitivity C-reactive protein. *J. Nutr., 139*(12), 2365–2372. https://doi.org/10.3945/jn.109.114025

Cervo, M. M., Shivappa, N., Hebert, J. R., Oddy, W. H., Winzenberg, T., Balogun, S., Wu, F., Ebeling, P., Aitken, D., Jones, G., & Scott, D. (2020a). Longitudinal associations between dietary inflammatory index and musculoskeletal health in community-dwelling older adults. *Clin. Nutr., 39*(2), 516–523. https://doi.org/10.1016/j.clnu.2019.02.031

Cervo, M. M. C., Scott, D., Seibel, M. J., Cumming, R. G., Naganathan, V., Blyth, F. M., Le Couteur, D. G., Handelsman, D. J., Riberio, R. V., Waite, L. M., Shivappa, N., Hebert, J. R., & Hirani, V. (2020b). Proinflammatory diet increases circulating inflammatory biomarkers and falls risk in community-dwelling older men. *J. Nutr., 150*(2), 373–381. https://doi.org/10.1093/jn/nxz256

Cesari, M., Penninx, B. W., Pahor, M., Lauretani, F., Corsi, A. M., Williams, G. R., Guralnik, J. M., & Ferrucci, L. (2004). Inflammatory markers and physical performance in older persons: the InCHIANTI study. *J. Gerontol. Series A, 59*(3), M242–M248. https://doi.org/10.1093/gerona/59.3.m242

Chen, L. K., Woo, J., Assantachai, P., Auyeung, T. W., Chou, M. Y., Iijima, K., Jang, H. C., Kang, L., Kim, M., Kim, S., & Kojima, T. (2020). Asian Working Group for Sarcopenia: 2019 consensus update on sarcopenia diagnosis and treatment. *J. Am. Med. Dir. Assoc., 21*(3), 300–307. https://doi.org/10.1016/j.jamda.2019.12.012

Chhetri, J. K., de Souto Barreto, P., Fougère, B., Rolland, Y., Vellas, B., & Cesari, M. (2018). Chronic inflammation and sarcopenia: a regenerative cell therapy perspective. *Exp. Gerontol., 103*, 115–123. https://doi.org/10.1016/j.exger.2017.12.023

Chung, H. Y., Cesari, M., Anton, S., Marzetti, E., Giovannini, S., Seo, A. Y., Carter, C., Yu, B. P., & Leeuwenburgh, C. (2009). Molecular inflammation: underpinnings of aging and age-related diseases. *Ageing Res. Rev., 8*(1), 18–30. https://doi.org/10.1016/j.arr.2008.07.002

Denova-Gutiérrez, E., Muñoz-Aguirre, P., Shivappa, N., Hébert, J. R., Tolentino-Mayo, L., Batis, C., & Barquera, S. (2018). Dietary inflammatory index and type 2 diabetes mellitus in adults: the diabetes mellitus survey of Mexico City. *Nutrients, 10*(4), 385. https://doi.org/10.3390/nu10040385

Gray, J., Kim, J., Ciesla, J. R., & Yao, P. (2016). Rasch analysis of the Lubben social network scale–6 (LSNS-6). *J. Appl. Gerontol., 35*(5), 508–528. https://doi.org/10.1177/0733464814560468

Guzik, T. J., & Touyz, R. M. (2017). Oxidative stress, inflammation, and vascular aging in hypertension. *Hypertension, 70*(4), 660–667. https://doi.org/10.1161/HYPERTENSIONAHA.117.07802

Hamer, M., & Molloy, G. J. (2009). Association of C-reactive protein and muscle strength in the English longitudinal study of ageing. *Age, 31*(3), 171–177. https://doi.org/10.1007/s11357-009-9097-0

Hashemi, R., Motlagh, A. D., Heshmat, R., Esmaillzadeh, A., Payab, M., Yousefinia, M., Siassi, F., Pasalar, P., & Baygi, F. (2015). Diet and its relationship to sarcopenia in community dwelling Iranian elderly: a cross sectional study. *Nutrition, 31*, 97–104. https://doi.org/10.1016/j.nut.2014.05.003

Kim, H. Y., Lee, J., & Kim, J. (2018). Association between dietary inflammatory index and metabolic syndrome in the general Korean population. *Nutrients, 10*(5), 648. https://doi.org/10.3390/nu10050648

Kobayashi, S., Murakami, K., Sasaki, S., Okubo, H., Hirota, N., Notsu, A., Fukui, M., & Date, C. (2011). Comparison of relative validity of food group intakes estimated by comprehensive and brief-type self-administered diet history questionnaires against 16 d dietary records in Japanese adults. *Public Health Nutr., 14*(7), 1200–1211. https://doi.org/10.1017/S1368980011000504

Laclaustra, M., Rodriguez-Artalejo, F., Guallar-Castillon, P., Banegas, J. R., Graciani, A., Garcia-Esquinas, E., & Lopez-Garcia, E. (2020). The inflammatory potential of diet is related to incident frailty and slow walking in older adults. *Clin. Nutr., 39*(1), 185–191. https://doi.org/10.1016/j.clnu.2019.01.013

Langen, R. C., Van Der Velden, J. L., Schols, A. M., Kelders, M. C., Wouters, E. F., & Janssen-Heininger, Y. M. (2004). Tumor necrosis factor-alpha inhibits myogenic differentiation through MyoD protein destabilization. *FASEB J., 18*(2), 227–237. https://doi.org/10.1096/fj.03-0251com

Laouali, N., Mancini, F. R., Hajji-Louati, M., El Fatouhi, D., Balkau, B., Boutron-Ruault, M. C., Bonnet, F., & Fagherazzi, G. (2019). Dietary inflammatory index and type 2 diabetes risk in a prospective cohort of 70,991 women followed for 20 years: the mediating role of BMI. *Diabetologia, 62*(12), 2222–2232. https://doi.org/10.1007/s00125-019-04972-0

Li, C. W., Yu, K., Shyh-Chang, N., Li, G. X., Jiang, L. J., Yu, S. L., Xu, L. Y., Liu, R. J., Guo, Z. J., Xie, H. Y., Li, R. R., Ying, J., Li, K., & Li, D. J. (2019). Circulating factors associated with sarcopenia during ageing and after intensive lifestyle intervention. *J. Cachexia, Sarcopenia Muscle, 10*(3), 586–600. https://doi.org/10.1002/jcsm.12417

Lopez-Candales, A., Burgos, P. M. H., Hernandez-Suarez, D. F., & Harris, D. (2017). Linking chronic inflammation with cardiovascular disease: from normal aging to the metabolic syndrome. *J. Nature Sci., 3*(4), e341.

Montorio, I., & Izal, M. (1996). The Geriatric Depression Scale: a review of its development and utility. *Int. Psychogeriatr., 8*(1), 103–112. https://doi.org/10.1017/s1041610296002505

Mtintsilana, A., Micklesfield, L. K., Chorell, E., Olsson, T., Shivappa, N., Hebert, J. R., Kengne, A. P., & Goedecke, J. H. (2019). Adiposity mediates the association between the dietary inflammatory index and markers of type 2 diabetes risk in middle-aged black South African women. *Nutrients, 11*(6), 1246. https://doi.org/10.3390/nu11061246

Kim, M., Shinkai, S., Murayama, H., & Mori, S. (2015). Comparison of segmental multifrequency bioelectrical impedance analysis with dual-energy X-ray absorptiometry for the assessment of body composition in a community-dwelling older population. *Geriatr. Gerontol. Int., 15*, 1013–1022. https://doi.org/10.1111/ggi.12384

Newcombe, E. A., Camats-Perna, J., Silva, M. L., Valmas, N., Huat, T. J., & Medeiros, R. (2018). Inflammation: the link between comorbidities, genetics, and Alzheimer's disease. *J. Neuroinflammation, 15*(1), 276. https://doi.org/10.1186/s12974-018-1313-3

Park, S. Y., Kang, M., Wilkens, L. R., Shvetsov, Y. B., Harmon, B. E., Shivappa, N., Wirth, M. D., Hebert, J. R., Haiman, C. A., Le Marchand, L., & Boushey, C. J (2018). The Dietary inflammatory index and all-cause, cardiovascular disease, and cancer mortality in the multiethnic cohort study. *Nutrients, 10*(12), 1844. https://doi.org/10.3390/nu10121844

Ren, Z., Zhao, A., Wang, Y., Meng, L., Szeto, I. M. Y., Li, T., Gong, H., Tian, Z., Zhang, Y., & Wang, P. (2018). Association between dietary inflammatory index, C-reactive protein and metabolic syndrome: a cross-sectional study. *Nutrients, 10*(7), 831. https://doi.org/10.3390/nu10070831

Rong, Y. D., Bian, A. L., Hu, H. Y., Ma, Y., & Zhou, X. Z. (2018). Study on relationship between elderly sarcopenia and inflammatory cytokine IL-6, anti-inflammatory cytokine IL-10. *BMC Geriatrics, 18*(1), 308. https://doi.org/10.1186/s12877-018-1007-9

Ruiz-Canela, M., Bes-Rastrollo, M., & Martínez-González, M. A. (2016). The role of dietary inflammatory index in cardiovascular disease, metabolic syndrome and mortality. *Int. J. Mol. Sci., 17*(8), 1265. https://doi.org/10.3390/ijms17081265

Schaap, L. A., Pluijm, S. M., Deeg, D. J., & Visser, M. (2006). Inflammatory markers and loss of muscle mass (sarcopenia) and strength. *Am. J. Med., 119*(6), 526-e9-17. https://doi.org/10.1016/j.amjmed.2005.10.049

Shin, D., Lee, K. W., Brann, L., Shivappa, N., & Hébert, J. R. (2019). Dietary inflammatory index is positively associated with serum high-sensitivity C-reactive protein in a Korean adult population. *Nutrition, 63*, 155–161. https://doi.org/10.1016/j.nut.2018.11.016

Shahinfar, H., Shahavandi, M., Tijani, A. J., Jafari, A., Davarzani, S., Djafarian, K., Clark, C., & Shab-Bidar, S. (2021). The association between dietary inflammatory index, muscle strength, muscle endurance, and body composition in Iranian adults. *Eat. Weight Disord.*. https://doi.org/10.1007/s40519-020-01096-y

Shivappa, N., Godos, J., Hébert, J. R., Wirth, M. D., Piuri, G., Speciani, A. F., & Grosso, G. (2018a). Dietary inflammatory index and cardiovascular risk and mortality—a meta-analysis. *Nutrients, 10*(2), 200. https://doi.org/10.3390/nu10020200

Shivappa, N., Hebert, J. R., Marcos, A., Diaz, L. E., Gomez, S., Nova, E., Michels, N., Arouca, A., González-Gil, E., Frederic, G., González-Gross, M. Castillo, M., J., Manios, Y., Kersting, M., Gunter, M. J., De Henauw, S., Antonios, K., Widhalm, K., Molnar, D., Moreno, L., & Huybrechts, I (2017). Association between dietary inflammatory index and inflammatory markers in the HELENA study. *Mol. Nutr. Food Res., 61*(6), 10. https://doi.org/10.1002/mnfr.201600707

Shivappa, N., Steck, S. E., Hurley, T. G., Hussey, J. R., & Hébert, J. R. (2014a). Designing and developing a literature-derived, population-based dietary inflammatory index. *Public Health Nutr., 17*(8), 1689–1696. https://doi.org/10.1017/S1368980013002115

Shivappa, N., Steck, S. E., Hurley, T. G., Hussey, J. R., Ma, Y., Ockene, I. S., Tabung, F., & Hébert, J. R. (2014b). A population-based dietary inflammatory index predicts levels of C-reactive protein in the Seasonal Variation of Blood Cholesterol Study (SEASONS). *Public Health Nutr., 17*(8), 1825–1833. https://doi.org/10.1017/S1368980013002565

Shivappa, N., Stubbs, B., Hébert, J. R., Cesari, M., Schofield, P., Soysal, P., Maggi, S., & Veronese, N. (2018b). The relationship between the dietary inflammatory index and incident frailty: a longitudinal cohort study. *J. Am. Med. Dir. Assoc., 19*(1), 77–82. https://doi.org/10.1016/j.jamda.2017.08.006

Steck, S., Shivappa, N., Tabung, F., Harmon, B., Wirth, M., Hurley, T., & Hebert, J. (2014). The dietary inflammatory index: a new tool for assessing diet quality based on inflammatory potential. *Digest, 49*, 1–9.

Suthutvoravut, U., Tanaka, T., Takahashi, K., Akishita, M., & Iijima, K. (2019). Living with family yet eating alone is associated with frailty in community- dwelling older adults: the Kashiwa Study. *J. Frailty Aging, 8*(4), 198–204. https://doi.org/10.14283/jfa.2019.22. PMID: 31637406.

Tanaka, T., Takahashi, K., Hirano, H., Kikutani, T., Watanabe, Y., Ohara, Y., Furuya, H., Tetsuo, T., Akishita, M., & Iijima, K. (2018). Oral frailty as a risk factor for physical

frailty and mortality in community- dwelling elderly. *J. Gerontol. A Biol. Sci. Med. Sci., 73*(12), 1661–1667. https://doi.org/10.1093/gerona/glx225. PMID: 29161342.

Tessier, A. J., & Chevalier, S. (2018). An update on protein, leucine, omega-3 fatty acids, and vitamin D in the prevention and treatment of sarcopenia and functional decline. *Nutrients, 10*(8), 1099–1115. https://doi.org/10.3390/nu10081099

Thoma, A., & Lightfoot, A. P. (2018). NF-kB and inflammatory cytokine signalling: role in skeletal muscle atrophy. *Adv. Exp. Med. Biol., 1088*, 267–279. https://doi.org/10.1007/978-981-13-1435-3_12

Tietge, U. J. (2014). Hyperlipidemia and cardiovascular disease: inflammation, dyslipidemia, and atherosclerosis. *Curr. Opin. Lipidol., 25*(1), 94–95. https://doi.org/10.1097/MOL.0000000000000051

Tsutsumimoto, K., Doi, T., Nakakubo, S., Kim, M., Kurita, S., Ishii, H., & Shimada, H. (2020). Association between anorexia of ageing and sarcopenia among Japanese older adults. *J. Cachexia, Sarcopenia Muscle, 11*, 1250–1257. https://doi.org/10.1002/jcsm.12571

Visser, M., Pahor, M., Taaffe, D. R., Goodpaster, B. H., Simonsick, E. M., Newman, A. B., Nevitt, M., & Harris, T. B. (2002). Relationship of interleukin-6 and tumor necrosis factor-α with muscle mass and muscle strength in elderly men and women: the Health ABC Study. *J. Gerontol. Ser. A, 57*(5), M326–M332. https://doi.org/10.1093/gerona/57.5.m326

Wang, H., Hai, S., Cao, L., Zhou, J., Liu, P., & Dong, B. R. (2016). Estimation of prevalence of sarcopenia by using a new bioelectrical impedance analysis in Chinese community-dwelling elderly people. *BMC Geriatrics, 16*, 216. https://doi.org/10.1186/s12877-016-0386-z

Wellen, K. E., & Hotamisligil, G. S. (2005). Inflammation, stress, and diabetes. *J. Clin. Invest., 115*(5), 1111–1119. https://doi.org/10.1172/JCI25102

Willett, W., & Stampfer, M. J. (1986). Total energy intake: implications for epidemiologic analyses. *Am. J. Epidemiol., 124*(1), 17–27. https://doi.org/10.1093/oxfordjournals.aje.a114366

Yang, Y., Hozawa, A., Kogure, M., Narita, A., Hirata, T., Nakamura, T., Tsuchiya, N., Nakaya, N., Ninomiya, T., Okuda, N., Kadota, A., Ohkubo, T., Okamura, T., Ueshima, H., Okayama, A., & Miura, K. (2020). Dietary inflammatory index positively associated with high-sensitivity c-reactive protein level in Japanese from NIPPON DATA2010. *J. Epidemiol., 30*(2), 98–107. https://doi.org/10.2188/jea.JE20180156

Zhang, L., Rajan, V., Lin, E., Hu, Z., Han, H. Q., Zhou, X., Song, Y., Min, H., Wang, X., Du, J., & Mitch, W. E. (2011). Pharmacological inhibition of myostatin suppresses systemic inflammation and muscle atrophy in mice with chronic kidney disease. *FASEB J., 25*(5), 1653–1663. https://doi.org/10.1096/fj.10-176917

Zhang, Z., Cao, W., Shivappa, N., Hebert, J. R., Li, B., He, J., , … Chen, Y., & Chen, Y. (2017). Association between diet inflammatory index and osteoporotic hip fracture in elderly Chinese population. *J. Am. Med. Dir. Assoc., 18*, 671–677. https://doi.org/10.1016/j.jamda.2017.02.011