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Original Study

The Relationship Between the Dietary Inflammatory Index and Incident Frailty: A Longitudinal Cohort Study

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A B S T R A C T

Objective: Inflammation is key risk factor for several conditions in the elderly. However, the relationship between inflammation and frailty is still unclear. We investigated whether higher dietary inflammatory index (DII) scores were associated with higher incidence of frailty in a cohort of North Americans.
Design: Longitudinal, with a follow-up of 8 years.
Setting: Osteoarthritis Initiative.
Participants: A total of 4421 participants with, or at high risk of, knee osteoarthritis.
Measurements: DII scores were calculated using the validated Block Brief 2000 Food-Frequency Questionnaire and categorized into sex-specific quartiles. Frailty was defined as 2 out of 3 of the criteria of the Study of Osteoporotic Fracture study (ie, weight loss, inability to rise from a chair 5 times, and poor energy). The strength of the association between baseline DII score and incident frailty was assessed through a Cox's regression analysis, adjusted for potential baseline confounders, and reported as hazard ratios.
Results: A total of 4421 community-dwelling participants (2564 female participants; mean age: 61.3 years) without frailty at baseline were identified from the Osteoarthritis Initiative. During 8 years of follow-up, 356 individuals developed frailty (8.2%). Using Cox's regression analysis, adjusting for 11 potential confounders, participants with the highest DII score (quartile 4) had a significantly higher risk of experiencing frailty (hazard ratio 1.37; 95% confidence interval 1.01−1.89; $P = .04$) compared with participants with the lowest DII score (quartile 1). The association between DII score and frailty was significant only in men.
Conclusions: Higher DII scores, indicating a more proinflammatory diet, are associated with higher incidence of frailty, particularly in men.

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Dr Hébert owns controlling interest in Connecting Health Innovations LLC (CHI), a company planning to license the right to his invention of the dietary inflammatory index (DII) from the University of South Carolina to develop computer and smart phone applications for patient counseling and dietary intervention in clinical settings. Dr Shivappa is an employee of CHI.

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Frailty is typically defined as an age-associated decline in reserve and function that result in a reduced ability to cope with acute or external stressors faced every day.[1] Frailty is a common condition in the elderly, with a prevalence of 10% for those older than 65 years and 30% for those older than 80 years.[2,3] Frailty is significantly associated with several deleterious outcomes in the elderly, including depression,[4,5] cardiovascular disease,[6] hospitalization,[7] and in some instances, mortality.[8] Consequently, understanding, preventing, and managing frailty in older adults is of high importance.

Despite this increasing interest in frailty, the pathophysiological changes underlying and preceding frailty are still largely unknown. Serum markers of inflammation linearly increase with age[9] probably because of a combination of factors, such as decline in immune function[10] and increase in medical conditions (eg, osteoarthritis, dementia, cardiovascular disease) associated with inflammation.[11] Inflammation is also associated with low muscular performance,[12] and it has been proposed that this condition may be closely linked with frailty.[13] From a molecular point of view, proinflammatory cytokines may influence frailty either directly by promoting protein degradation, or indirectly, by affecting important metabolic pathways.[14] However, the evidence regarding inflammation and frailty in human beings is still conflicting. In a recent systematic review and meta-analysis, we found that in 32 cross-sectional studies, both frail and prefrail participants had significantly higher levels of inflammatory markers.[15] However, in 4 longitudinal studies,[16–19] higher inflammatory markers were not associated with any increased risk of frailty at follow-up, suggesting that additional findings from longitudinal studies are needed.

Diet is a key source of inflammation and the Dietary Inflammatory Index (DII) is a literature-derived dietary tool, useful for assessing the overall inflammatory potential of individual's diet.[20] Higher DII values are strongly correlated with serum inflammatory markers, suggesting a close relationship between this index and bio-humoral inflammatory parameters.[21] The DII also has been used to assess the relationship between diet quality related to inflammation and numerous chronic inflammation-related outcomes, such as metabolic and respiratory diseases, cancer, and fractures.[22–25] However, no study has yet explored the association between DII and frailty. Therefore, the purpose of this study was to investigate whether increasing DII scores are associated with increased incidence of frailty, using a large cohort of North American adults.

Methods

Data Source and Participants

Data were included from the Osteoarthritis Initiative (OAI) database. The OAI is freely available (http://www.oai.ucsf.edu/). Within the OAI, potential participants were recruited across 4 clinical sites in the United States of America (Baltimore, MD; Pittsburgh, PA; Pawtucket, RI; and Columbus, OH) between February 2004 and May 2006. In this database, we identified people who either (1) had knee osteoarthritis (OA) with knee pain for a 30-day period in the past 12 months or (2) were at high risk of developing knee OA[26] with data collected during baseline and screening evaluations in November 2008. All participants provided informed written consent.

The OAI study was given full ethical approval by the institutional review board of the OAI Coordinating Center, at University of California in San Francisco.

Dietary Data and Dietary Inflammatory Index (Exposure)

Dietary intake was assessed using a validated tool, the Block Brief 2000 Food Frequency Questionnaire (FFQ) during the baseline visit.[27] Seventy items were assessed to determine an individual's typical food and beverage consumption over the past year. The frequency of consumption was reported at 9 levels of intake from "never" to "every day." In addition, 7 dietary behavior questions were asked regarding food preparation methods and fat intake, 1 question on fiber intake, and 13 questions on vitamin and mineral intakes.

The details of development of DII is described by Shivappa et al[20] elsewhere. High sensitivity C-reactive protein (CRP) measurements were used to examine construct validity of the DII in a longitudinal cohort using multiple (up to 15) 24-hour dietary recall interviews and up to five 7-day dietary recalls. The DII was subsequently validated in 4 studies among different populations with a variety of inflammatory biomarkers [ie, interleukin (IL), IL-6, hs-CRP, fibrinogen, homocysteine, and tumor necrosis factor-α].[21,25,28–31] In this updated version of the DII, 1943 articles were reviewed and scored. Forty-five food parameters, including foods, nutrients, and other bioactive compounds, were identified based on their inflammatory effect on 6 specific inflammatory markers, including CRP, IL-1β, IL-4, IL-6, IL-10, and tumor necrosis factor -α. A regionally representative world database representing diet surveys from 11 countries was used as a comparative standard for each of the 45 parameters (ie, foods, nutrients, and other food components). Intake values from this database were used to calculate the DII scores. This is explained in more detail in the DII Methods paper.[20] Briefly, a standard mean for each parameter from the representative world database was subtracted from the actual individual exposure and divided by its standard deviation to generate Z scores. These Z scores were converted to proportions (thus minimizing effects of outliers/right-skewing). These values were then doubled, and 1 was subtracted to achieve symmetrical distribution with values centered on 0. The resulting value was then multiplied by the corresponding inflammatory score for each food parameter and summed across all food parameters, to obtain the overall DII score. Using the FFQ, we calculated the DII based on energy-adjusted intake of the 24 single food parameters of the 45 possible food parameters that were available from the FFQ using the energy density approach, which calculated the DII per 4184 kJ (1000 kcal) of energy.[32] The 24 food parameters available for DII calculation in this study were vitamin B_{12}, vitamin B_6, β-carotene, carbohydrate, cholesterol, fat, fiber, folic acid, iron, magnesium, monounsaturated fat acids, niacin, protein, polyunsaturated fatty acids, riboflavin, saturated fat acids, selenium, thiamin, vitamin A, vitamin C, vitamin E, vitamin D, zinc, niacin, and caffeine.

Outcome

The study's outcome of interest was incident frailty. In accordance with the Study of Osteoporotic Fracture index,[33,34] frailty was defined as the presence of ≥2 out of 3 of the following criteria: (1) weight loss ≥5% taking place between baseline and the follow-up examinations [at the baseline examination a body mass index (BMI) of less than 20 kg/m^2, a common cut-off for identifying underweight people the elderly,[35] was used, because no information regarding weight changes were recorded]; (2) the inability to rise from a chair 5 times without arm support (hereafter referred to as inability to carry out chair stands); and (3) poor energy based on the SF12 questionnaire response of "little at a time" or "none at a time" to the question "in the past 4 weeks, did you have a lot of energy?" The assessment of the outcome was made at the baseline and during the V01 (12 months), V03 (24 months), V05 (36 months), V06 (48 months), V08 (72 months), and V10 (96 months).

Covariates

Ten covariates (other than the number of frailty indexes at baseline) were identified a *priori* as potential confounding factors. These