The Journal of Nutrition
Nutritional Epidemiology

A Higher Adherence to a Mediterranean-Style Diet Is Inversely Associated with the Development of Frailty in Community-Dwelling Elderly Men and Women[1,2]

Sameera A. Talegawkar,[3]* Stefania Bandinelli,[5] Karen Bandeen-Roche,[4] Ping Chen,[3] Yuri Milaneschi,[6,7] Toshiko Tanaka,[6] Richard D. Semba,[8] Jack M. Guralnik,[9] and Luigi Ferrucci[6]

[3]Center for Human Nutrition, Department of International Health, and [4]Department of Biostatistics, Johns Hopkins Bloomberg School of Public Health, Baltimore, MD; [5]Azienda Sanitaria di Firenze, Florence, Italy; [6]National Institute on Aging, Baltimore, MD; [7]Department of Psychiatry, VU University Medical Center/GGZ Ingest, Amsterdam, The Netherlands; [8]Johns Hopkins University School of Medicine, Baltimore, MD; and [9]University of Maryland School of Medicine, Baltimore, MD

Abstract

Adherence to a Mediterranean-style diet is associated with a lower risk for mortality, cognitive decline, and dementia. Whether adherence to a Mediterranean-style diet protects against age-related frailty is unclear. Therefore, our objective was to examine the association between a Mediterranean-style diet with the risk of frailty in community-dwelling older persons. We conducted longitudinal analyses using data from 690 community-living persons (≥65 y) who were randomly selected from a population registry in Tuscany, Italy. Participants of the Invecchiare in Chianti study of aging completed the baseline examination in 1998–2000 and were re-examined at least once over 6 y. Adherence to a Mediterranean-style diet (scored 0–9, modeled categorically as ≤3, 4–5, and ≥6) was computed from the European Prospective Investigation into Cancer and nutrition FFQ previously validated in this cohort. Frailty was defined as having at least 2 of the following criteria: poor muscle strength, feeling of exhaustion, low walking speed, and low physical activity. After a 6-y follow-up, higher adherence (score ≥6) to a Mediterranean-style diet was associated with lower odds of developing frailty [OR = 0.30 (95% CI: 0.14, 0.66)] compared with those with lower adherence (score ≤3). A higher adherence to a Mediterranean-style diet at baseline was also associated with a lower risk of low physical activity (OR = 0.62; 95% CI: 0.40, 0.96) and low walking speed [OR = 0.48 (95% CI: 0.27, 0.86)] but not with feelings of exhaustion and poor muscle strength. In community-dwelling older adults, higher adherence to a Mediterranean-style diet was inversely associated with the development of frailty. J. Nutr. 142: 2161–2166, 2012.

Introduction

Frailty is a multidimensional clinical syndrome associated with a high risk, physical function decline and mobility loss as well as an increased risk of institutionalization and death (1–3). Primarily considered to be a loss of functional reserve and dynamic response to stressors in multiple physiological systems, frailty is thought to result from multifactorial etiology, including multiple morbidity, chronic inflammation, and perturbation of hormonal cascades (4–6).

Over the last few years, interest for interventions that can prevent frailty has grown steadily due to the fast aging of the population. Current forecasts suggest that the percentage of persons 65 y and older will increase 19% by 2030. Because the annual health care cost is almost 4-fold higher in people 65 y and older, the expansion of the older portion of the population will also lead to growing financial burden on individuals, families, and societies (7).

Although several conceptual definitions for frailty exist, the operational definition proposed by Fried et al. (5) is most commonly used in both research and clinical settings. Phenotypic manifestations used for the diagnosis of frailty include unintentional weight loss, low grip strength, low energy, low walking speed, and low physical activity. Data from US-based cohort studies and national surveillance indicate that prevalence rates of frailty in the elderly older than 65 y ranges from 7 to 12% and are as high as 25% in those older than 85 y (5,8–11).

Observational studies have suggested a putative role for several nutrients in frailty. Although there is evidence for single nutrients such as carotenoids, vitamins D, E, and C, folate, energy, protein, and whole grains (9,12–15), there is a paucity of data regarding the effects of food groups and patterns on the risk of frailty. A number of studies have shown that high adherence to a Mediterranean-style of dietary pattern is inversely associ-

[1] Supported by National Institute on Aging (NIA), Johns Hopkins University Claude D. Pepper Older Americans Independence Center, P30AG021334; NIA grant R01 AG027012; the Italian Ministry of Health (ICS110.1/RF97.71); and NIA contracts 263 MD 9164, 263 MD 821336, N.1-AG-1-1, N.1-AG-1-2111, and N01-AG-5-0002, the Intramural Research Program of the NIA, NIH, Baltimore, Maryland.
[2] Author disclosures: S. A. Talegawkar, S. Bandinelli, K. Bandeen-Roche, P. Chen, Y. Milaneschi, T. Tanaka, R. D. Semba, J. M. Guralnik, and L. Ferrucci, no conflicts of interest.
* To whom correspondence should be addressed. E-mail: sameera.talegawkar@alumni.tufts.edu.

Manuscript received June 13, 2012. Initial review completed July 18, 2012. Revision accepted September 5, 2012.
First published online October 24, 2012; doi:10.3945/jn.112.165498.

ated with the risk of mortality and chronic disease morbidity (16). Protective associations have also been reported for aging-associated health outcomes, including cognition, dementia, and mobility (17–19). We therefore examined the association between adherence to a Mediterranean-style dietary pattern and frailty using data from the Invecchiare in Chianti (InCHIANTI[10]; aging in the Chianti area) study of aging. We hypothesized that a higher adherence to a Mediterranean-style diet at baseline would be associated with a lower risk for frailty.

Participants and Methods

Participants and study design. These analyses are based on previously collected data for the InCHIANTI study. The InCHIANTI study is a Tuscany (Italy)-based, prospective population-based study designed to investigate factors contributing to decline of mobility in late life. A detailed description of the study rationale, design, and methods has been provided elsewhere (20). Briefly, in 1998–1999 a sample was randomly selected from 2 sites, Greve in Chianti and Bagno a Ripoli, using a multistage, stratified sampling method: 1270 persons ≥65 y were randomly selected from the population registry of the 2 sites and another 29 participants ≥90 y were oversampled. Thirty-nine participants were not eligible, because they had already died or emigrated. Among those who were eligible, 1155 (91.6%) were enrolled. The participation rate increased with age up to 85 y and was higher in each age group in women than in men. However, there was a drop in participation in the oldest old-age group (men, 77.1%; women, 78.4%). Data collection included: *1*) a home interview concerning demographics, health-related behaviors, functional status, cognitive function, and a FFQ; *2*) a medical examination including several performance-based tests of physical function conducted in the study clinic; and *3*) 24-h urine collection and blood drawing.

All participants were invited to follow-up visits conducted every 3 y starting from baseline assessment. The present study is based on data collected at baseline (1998–1999), exam 2 (2001–2003), and exam 3 (2004–2006). Of the participants aged ≥65 y enrolled in the study, we excluded 8 participants with implausible energy intakes (defined as <600 and >4000 kcal/d) as well as those participants with Mini Mental State Examination (MMSE) scores <24 (n = 364). Participants needing help in one or more Instrumental Activities of Daily Living (n = 11) and those with gastrointestinal disease (n = 34) and cancer (n = 48) were excluded from analysis. The final analytical sample was 690. All respondents signed informed consent and the Italian National Institute of Research and Care on Aging Ethical Committee approved the study protocol.

Dietary assessment and computation of the Mediterranean Diet Score. Adherence to a Mediterranean-style diet was computed using the Mediterranean Diet Score (MDS), previously developed by Trichopoulou et al. (21). This score was calculated using daily dietary intake data collected at baseline by the FFQ created for the European Prospective Investigation on Cancer and Nutrition study, which was previously validated in the InCHIANTI cohort (22). Briefly, the intakes of 9 food groups were dichotomized using sex-specific median values as cutoff. A score of 1 was assigned for consumption above the median level of presumed beneficial foods (vegetables, legumes, fruits, cereal, fish, and ratio of monounsaturated fats:saturated fats) and for consumption below the median level of presumed detrimental foods (meat and dairy products) and a score of 0 was assigned for all other. For alcohol, 1 point was assigned to men who consumed between 10 and 50 g/d and to women who consumed between 5 and 25 g/d versus a score of 0. Thus, the total MDS ranged from 0 (minimal adherence to the traditional Mediterranean diet) to 9 (maximal adherence).

Definition of frailty. We used the operational definition of frailty developed by Fried and colleagues (5). Since the objective of these analyses was to examine the associations between a dietary exposure and the risk of frailty, similarly to Bartali and colleagues, we did not include "weight loss" in our operational definition (12). Frailty was therefore defined as having two or more of the following criteria: *1*) exhaustion [self-reported feeling that "everything I did was an effort," at least three times a week in the last month. This information was obtained from the Center for Epidemiologic Studies Depression scale (23)]; *2*) poor muscle strength (grip strength in the lowest quintile, stratified by gender and body mass index [BMI] quartiles); *3*) low walking speed (time to walk 15 feet in the highest quintile, stratified by gender and standing height); and *4*) low physical activity (sedentary state or performing light intensity physical activity [i.e., walking less than 1 hour/week]). Level of physical activity in the previous 12 months was assessed using questionnaire (24). Briefly, data on current physical activity were collected by asking the following question: "Did you ever perform any sport or recreational physical activity, for at least three months, during the last year?" An affirmative answer led to the interviewer asking the participant to specify the type of each physical activity, the number of months of practice and the number of minutes at each practice. Using the responses and tables assessing the intensity of each activity, participants were classified as: *a*) inactive, including participants who were completely inactive and those who performed light intensity physical activity (i.e., walking, dancing; ≤4 Metabolic Equivalents) less than 1 hour per week; *b*) light physical activity, including participants who performed light intensity physical activity 2–4 hours per week; *c*) moderate–high physical activity, including participants who performed at least light physical activity 5 hours per week or more and those who performed moderate physical activity (i.e., gymnastics, swimming; >4 Metabolic Equivalents) 1–2 hours per week or more.

Covariates. Based on results from univariate analysis, we adjusted for several covariates that were assessed at baseline, including age, sex, energy intake, education, smoking status, BMI, MMSE score, and presence of chronic disease. Briefly, energy intake was collected by the European Prospective Investigation on Cancer and Nutrition Study FFQ and modeled on a continuous scale in kcal/d, level of education was assessed as years of education and modeled on a continuous scale, smoking status was assessed using standard study questionnaires and modeled categorically as current smoker (Y/N). Height and weight were measured at the study clinic and BMI was calculated as weight (in kilograms) divided by the square of height (in meters) and modeled on a continuous scale. Global cognitive performance was assessed with the MMSE (25), scores of which were modeled on a continuous scale. Major chronic diseases ascertained according to previously validated algorithms with information on self-reported history, pharmacological treatments, medical exam data, and hospital discharge records included: congestive heart failure, coronary heart disease including angina and myocardial infarction, stroke, chronic obstructive lung disease, hypertension, diabetes, and hip arthritis (26); the presence or absence of these conditions was modeled on a categorical basis.

Statistical analyses. We categorized the MDS into 3 categories as: low adherence (MDS ≤3), medium adherence (MDS 4–5), and high adherence (MDS ≥6) (19). Descriptive statistics (mean ± SD and percentage) were used to describe characteristics of the study populations at baseline and differences across the groups were assessed using generalized linear models (with Tukey-Kramer's adjustment for multiple comparisons) for continuous variables and χ^2 test for variables expressed as proportions. It was previously documented (27–29) that frailty in the elderly is a dynamic process and is characterized by frequent transitions between frailty states over time and the probability of transitioning between frailty states was highly dependent on one's preceding frailty state. We therefore used first-order transition models to determine the longitudinal association of baseline MDS with frailty and its components over the 6-y follow-up. By the first order, we assumed that the frailty (or its component) status at each follow-up was affected by its preceding status. Thus, the chance of developing frailty at every 3-y follow-up was a linear function of the influences of the previous frailty (or its component) status in addition to other covariates. We specified logit link function to fit the model given that the frailty (or its component) status at each follow-up was a binary variable. To determine whether the

[10] Abbreviations used: InCHIANTI, Invecchiare in Chianti; MDS, Mediterranean Diet Score; MMSE, Mini Mental State Examination; WHAS, Women's Health and Aging Studies.

influence varied among the spans of follow-up or varied among the categories of MDS, we included interaction terms of them. These terms were not significant ($P > 0.05$) and hence were dropped from the models. Initial models were adjusted for age (y) and sex and final multivariate models were adjusted for energy intake (kcal/d), status of frailty (or its components) at previous examinations, BMI (kg/m^2), education (y), current smoker (Y/N), MMSE score, and presence of chronic disease (Y/N). All models were fulfilled in the procedure of GENMOD. Analyses were performed using SAS (v. 9.2, SAS Institute) and all statistical tests were 2-sided with the significance level set at $P < 0.05$.

Results

The characteristics of the study population at enrollment are shown in **Table 1**. The mean age of the cohort at baseline was 73 y. Age and BMI differed across the MDS categories, wherein individuals with a higher adherence to a Mediterranean-style diet (MDS ≥6) were significantly younger and had a higher BMI than those with a lower adherence (MDS ≤3). Women made up 51.7% of the cohort; however, there were no significant differences across the MDS categories. Similarly, there were no significant differences across the MDS categories by smoking status, education, MMSE scores, chronic disease status, or medication use. We examined differences among foods and food group characteristic of a Mediterranean-style diet across the 3 MDS categories. Mean intakes of vegetables, fruit and nuts, fish and seafood, and the monounsaturated:saturated fat ratio differed significantly across all 3 MDS groups, with higher intakes and ratio associated with a higher MDS. For legumes, intakes did not differ between MDS 4–5 and ≥6 but were significantly higher than those with MDS ≤3. Intakes of cereal did not differ between MDS ≤3 and 4–5 but were significantly lower than those with MDS ≥6. Similar differences were observed for milk and dairy products, with lower intakes for MDS ≥6. Intakes of meat and alcohol did not differ across the

TABLE 1 Characteristics of the InCHIANTI study population (>65 y) at baseline according to MDS[1,2]

Characteristics	Total sample	MDS ≤3	MDS 4–5	MDS ≥6
n	690	202	299	189
Age, *y*	73.0 ± 6.24	74.1 ± 6.91[a]	73.2 ± 6.24[a]	71.5 ± 5.15
Female, *%*	51.7	50.5	56.5	45.5
Education, *y*	6.16 ± 3.54	6.37 ± 4.17[a]	5.88 ± 3.16[a]	6.38 ± 3.38[a]
Smoking status, *%*				
Nonsmoker	54.4	54.0	56.5	51.3
Former smoker	29.3	26.7	28.8	32.8
Current smoker	16.4	19.3	14.7	15.9
MMSE score	26.8 ± 1.77	26.6 ± 1.70[a]	26.8 ± 1.77[a]	26.9 ± 1.84[a]
BMI, *kg/m²*	27.5 ± 3.89	26.8 ± 4.29[a]	27.6 ± 3.92[b]	28.1 ± 3.30[b]
Chronic disease present, *%*	59.4	53.4	60.5	63.4
Medication use, *%*				
Type 2 diabetes	6.23	6.93	5.69	6.35
Hypertension	41.9	38.1	43.5	43.4
Vegetables, *g/d*	188 ± 96.1	138 ± 69.6[a]	180 ± 86.3[b]	252 ± 99.7[c]
Legumes, *g/d*	17.0 ± 10.6	12.3 ± 7.76	18.1 ± 11.6[a]	20.4 ± 9.83[a]
Fruit and nuts, *g/d*	310 ± 147	255 ± 120[a]	313 ± 149[b]	364 ± 151[c]
Cereals, *g/d*	248 ± 98.5	228 ± 89.9[a]	245 ± 100[a]	275 ± 99.3
Fish and seafood, *g/d*	24.1 ± 17.5	17.2 ± 12.6[a]	25.3 ± 18.6[b]	29.7 ± 17.9[c]
Milk and dairy products, *g/d*	176 ± 155	206 ± 141[a]	183 ± 191[a]	137 ± 82.7
Meat and meat products, *g/d*	105 ± 45.1	106 ± 43.0[a]	104 ± 45.5[a]	107 ± 46.9[a]
Monounsaturated:saturated lipids ratio	1.53 ± 0.36	1.31 ± 0.25[a]	1.54 ± 0.34[b]	1.75 ± 0.36[c]
Alcohol, *g/d*	16.4 ± 21.2	15.2 ± 22.3[a]	16.5 ± 22.8[a]	17.3 ± 16.8[a]
Energy, *kcal/d*	1970 ± 565	1850 ± 517[a]	1950 ± 581[a]	2140 ± 547
Carbohydrate, *g/d*	114 ± 50.1	235 ± 71.9[a]	252 ± 81.3[a]	281 ± 80.7
Protein, *g/d*	76.4 ± 21.1	74.0 ± 19.6[a]	75.8 ± 21.8[a]	79.7 ± 21.0
Fat, *g/d*	66.1 ± 20.5	62.2 ± 18.2[a]	65.1 ± 20.8[a]	71.9 ± 21.1
Monounsaturated lipids, *g/d*	33.2 ± 11.1	29.4 ± 8.96[a]	32.6 ± 10.7[b]	38.2 ± 12.0[c]
Saturated lipids, *g/d*	22.3 ± 7.66	22.9 ± 7.58[a]	22.0 ± 8.03[a]	22.3 ± 7.14[a]
Dietary fiber, *g/d*	20.0 ± 5.59	16.7 ± 4.38[a]	20.0 ± 5.16[a]	23.4 ± 5.31[a]
β-Carotene equivalents, *μg/d*	2230 ± 1190	1780 ± 917[a]	2150 ± 1060[b]	2830 ± 1380[c]
Vitamin E, *mg/d*	6.33 ± 1.93	5.40 ± 1.64[a]	6.26 ± 1.74[b]	7.43 ± 1.93[c]
Vitamin C, *mg/d*	114 ± 50.2	91.3 ± 39.9[a]	113 ± 47.5[b]	140 ± 52.2[c]
Vitamin D, *μg/d*	1.85 ± 0.79	1.74 ± 0.77[a]	1.87 ± 0.82[a]	1.92 ± 0.73[a]
Vitamin B-6, *mg/d*	1.68 ± 0.49	1.53 ± 0.43[a]	1.68 ± 0.50[b]	1.85 ± 0.46[c]
Folic acid, *μg/d*	263 ± 77.6	229 ± 63.2[a]	260 ± 76.1[b]	303 ± 76.4[c]

[1] Values are percentage or mean ± SD. Means that have no superscript in common are significantly different from each other, ($P < 0.05$, after Tukey-Kramer adjustment for multiple comparisons). MDS, Mediterranean Diet Score; MMSE, Mini Mental State Examination.
[2] For categorical variables, including smoking and chronic disease status and medication use, homogeneity across strata tested with χ^2 test showed $P > 0.05$.

MDS categories. Energy, carbohydrate, protein, and fat intakes did not differ between MDS ≤3 and 4–5 but were significantly lower than those with MDS ≥6. Intakes of monounsaturated fats differed across all 3 MDS categories, with higher intakes associated with higher MDS. No significant differences across MDS categories were observed for intakes of saturated fat and dietary fiber. Intakes of micronutrients, including β-carotene equivalents, vitamins E, C, and B-6, and folic acid differed significantly across all 3 MDS categories, with higher intakes associated with higher MDS. No differences were observed for vitamin D intakes.

Individuals with a higher score for adherence to a Mediterranean-style diet (MDS ≥6) had lower odds of developing frailty [OR = 0.30 (95% CI: 0.14, 0.66)] compared with those with low adherence (MDS ≤3). Protective associations for a higher adherence to a Mediterranean-style diet (compared with a low adherence) were also observed for components of frailty, including low physical activity [OR = 0.62 (95% CI: 0.40, 0.96)] and walking speed [OR = 0.48 (95% CI: 0.27, 0.86)]. No associations were observed for other frailty components such as feeling exhausted or having poor muscle strength.

Discussion

The purpose of this study was to evaluate whether a higher adherence to a Mediterranean-style diet was associated with frailty in an older population (**Table 2**). We found that after a follow-up of 6 y, individuals with a higher adherence to a Mediterranean-style diet at baseline (defined as a MDS ≥6 points) had lower odds of developing frailty compared with those with a lower adherence. When associations with components of frailty were examined, a higher adherence to a Mediterranean-style diet at baseline was associated with lower odds of low physical activity as well as low walking speed.

Frailty is a condition of multifactorial etiology, and nutrition is thought to influence both its etiology as well as its treatment. Several studies have examined the association between intake of nutrients as well as nutrient biomarkers with the frailty phenotype. Using baseline cross-sectional data from the InCHIANTI study, Bartali et al. (12) reported associations between low intakes of energy and protein and frailty. Inadequate intakes of micronutrients such as vitamins D, E, and C, and folate were also associated with higher odds of frailty. Protective associations between increased protein intake and incident frailty have also been reported by investigators of the Women's Health Initiative Observational Study (15). In the cohort of 24,417 women aged 65–79 y who were free of frailty at baseline, a 20% increase in protein intake (as a percentage of total energy) corrected for measurement error using biomarkers of energy and protein intake was associated with a 32% lower risk of incident frailty after a 3-y follow-up.

Studies have also been conducted examining the association between nutrient biomarkers and frailty. In the cross-sectional analysis of data for 754 women aged 70–80 y from the Women's Health and Aging Studies (WHAS) I and II, the age-adjusted odds of being frail were significantly higher in those women participants whose micronutrient concentrations were in the lowest quartile compared with the top 3 quartiles for total carotenoids, α-tocopherol, 25-hydroxyvitamin D, and vitamin B-6 (14). Similar results were reported by Semba et al. (13) using longitudinal data from WHASI. After a follow-up of 3 y, women in the lowest quartile of serum carotenoid and 25-hydroxyvitamin D concentrations had an increased risk of becoming frail compared with those in the upper 3 quartiles. Associations between serum 25-hydroxyvitamin D and frailty have also been reported cross-sectionally using nationally representative data from the third NHANES (9), where low 25-hydroxyvitamin D concentrations (defined as a serum concentration <37.4 nmol/L) were associated with a 3.7-fold increase in the odds of frailty among whites and a 4-fold increase in the odds of frailty among non-whites.

The development of frailty and other age-associated declines in physical function, mobility, and skeletal muscle strength have been attributed in part to oxidative stress and inflammation that invariably occur with aging (30–33). In the Cardiovascular Health Study, frail compared with non-frail participants had increased concentrations of C-reactive protein and other markers of blood clotting. These differences persisted even after individuals with chronic disease conditions such as cardiovascular disease and diabetes were excluded and after adjustment for age, sex, and race, supporting the hypothesis that frailty is characterized in part by increased inflammation (34). In general, a Mediterranean-style diet is associated with a high intake of fruit, vegetables, legumes, and low to moderate intake of alcohol and oils such as olive oil (35). A higher adherence to a Mediterranean-style diet among the InCHIANTI participants was associated with higher intakes of several antioxidant micronutrients, including β-carotene equivalents and vitamins C and E. These associations may partly explain the protective associations for adherence to a Mediterranean-style diet and frailty. Besides antioxidant nutrients, other food bioactives such as polyphenolic compounds present in plant foods may also be responsible for the beneficial effects of a Mediterranean-style diet.

TABLE 2 Association of adherence to a Mediterranean-style diet, assessed using the MDS at baseline and the odds of frailty and its components in InCHIANTI participants during a follow-up of 6 y[1,2]

Frailty and its components	Age, sex adjusted, OR (95% CI)	Multivariate, OR (95% CI)
MDS score		
Feeling of exhaustion		
Low	1.00	1.00
Medium	0.96 (0.66, 1.39)	0.94 (0.63, 1.41)
High	0. 69 (0.45, 1.07)	0.73 (0.45, 1.16)
Low physical activity		
Low	1.00	1.00
Medium	0.66 (0.46, 0.95)	0.69 (0.47, 1.01)
High	0.58 (0.39, 0.88)	0.62 (0.40, 0.96)
Poor muscle strength		
Low	1.00	1.00
Medium	1.14 (0.73, 1.79)	1.09 (0.69, 1.73)
High	0.85 (0.51, 1.43)	0.82 (0.48, 1.40)
Low walking speed		
Low	1.00	1.00
Medium	0.85 (0.54, 1.34)	0.85 (0.53, 1.37)
High	0.47 (0.27, 0.81)	0.48 (0.27, 0.86)
Frailty		
Low	1.00	1.00
Medium	0.60 (0.34, 1.06)	0.71 (0.42, 1.21)
High	0.26 (0.11, 0.59)	0.30 (0.14, 0.66)

[1] Multivariate model: adjusted for age (y), sex, energy intake (kcal/d), status of frailty (or its components) at previous examinations, BMI (kg/m^2), education (y), MMSE score, current smoker (Y/N), and presence of chronic diseases (Y/N). InCHIANTI, Invecchiare in Chianti; MDS, Mediterranean Diet Score; MMSE, Mini Mental State Examination.
[2] MDS scores for categories: low, ≤3; medium, 4–5; high, ≥6.

Although the role of single nutrients has been studied in relation to age-associated declines and frailty, no studies that we are aware of have examined the role of dietary patterns and frailty. In the present study, the associations between adherence to a Mediterranean-style diet at baseline and frailty over a follow-up of 6 y was examined. Though not as extensively studied with age-associated declines, observational studies have documented protective associations between a higher adherence to a Mediterranean-style diet and chronic disease morbidity and mortality. Recent investigations have demonstrated a protective role of a Mediterranean-style diet on age-associated cognitive decline and dementia (17,18). A higher adherence to a Mediterranean-style diet has also been shown to be associated with a slower decline of mobility in older persons (19).

The present investigation has several strengths. Dietary intake data in the cohort were collected using a FFQ that was validated in the cohort. Previous investigations on the role of nutrients on age-associated declines have been conducted in cohorts such as the WHAS, which consisted of only women; the current investigation was conducted in a cohort consisting of both women and men. Another important strength of the present study is its longitudinal design; we were able to adjust for the frailty status of an InCHIANTI participant at a previous visit. The study carefully collected information on several covariates and confounders and we were able to adjust for these in our analyses. The final model included adjustment for several variables, including chronic disease. Although it may be argued that this inclusion may be an overadjustment, excluding the variable from the final model did not significantly change our results. The study has some limitations. Although diet was assessed using a validated FFQ, measurement error due to the nature of the assessment tool cannot be ruled out (36). In the present study, the MDS was calculated using dietary intake data assessed when the participants were 65 y of age or older. It has been hypothesized that diet through one's life-course has a considerable impact on the health of older individuals (37). This is true more so for factors like muscle strength and mass, which attain their peak in early life (38). An important shortcoming of this research design is its observational design, which cannot rule out the possibility of residual confounding for those factors that were not measured or were imperfectly measured. The size of our cohort was relatively small; however, by a standard calculation for a 2-sample test of proportions assuming 2-sided testing at the 0.05 level, our design had at power of at least 80% to detect an OR of 0.30 (i.e., an absolute difference of ~0.06) to examine our proposed hypothesis. The sex-specific median cutoffs used in the derivation of the MDS may vary depending on the population under study and therefore our results may not be directly generalizable to other populations.

Diet is a significant predictor of chronic disease risk and the study of dietary patterns has recently emerged as a promising area in prevention. Examining combinations of foods allows accounting for interactions and high correlations between nutrients (39,40) and better reflects the true complexity of dietary exposures. This approach is especially critical when studying the effect of diet on complex health outcomes, such as frailty. Studies on the role of dietary patterns and disease outcomes can lead to clear recommendations more likely to be understood and accepted than recommendations about specific nutrients (41). The key finding of the current study was that a high adherence to a Mediterranean-style diet at baseline was associated with a lower risk of developing frailty over a follow-up of 6 y in a cohort of older, community-dwelling men and women. Although the health benefits of a Mediterranean-style diet have been well documented for chronic disease morbidity and mortality, its role in aging-related declines is only recently being studied. The protective association between a Mediterranean-style diet and frailty needs to be confirmed by other studies prior to being implemented as a nutritional intervention in clinical trials. Individuals older than 65 y represent an important and growing proportion of the population and pose a considerable healthcare expense. Dietary pattern-based interventions have the potential of being a cost-effective solution for preventing or potentially slowing age-associated declines.

Acknowledgments

L.F., S.B., and J.M.G. contributed to the original design and data collection for the InCHIANTI study of aging; S.A.T. was responsible for the design and analysis of this report and drafted the manuscript; P.C. conducted the statistical programming; L.F., K.B.-R., and R.D.S. consulted on the analysis; Y.M. and T.T. contributed to the analysis and design; all authors made critical comments during the preparation of the manuscript; and S.A.T. had primary responsibility for the final content. All authors read and approved the final manuscript.

Literature Cited

1. Buchman AS, Wilson RS, Bienias JL, Bennett DA. Change in frailty and risk of death in older persons. Exp Aging Res. 2009;35:61–82.
2. Boyd CM, Xue QL, Simpson CF, Guralnik JM, Fried LP. Frailty, hospitalization, and progression of disability in a cohort of disabled older women. Am J Med. 2005;118:1225–31.
3. Hastings SN, Purser JL, Johnson KS, Sloane RJ, Whitson HE. Frailty predicts some but not all adverse outcomes in older adults discharged from the emergency department. J Am Geriatr Soc. 2008;56:1651–7.
4. Whitson HE, Purser JL, Cohen HJ. Frailty thy name is ... Phrailty? J Gerontol A Biol Sci Med Sci. 2007;62:728–30.
5. Fried LP, Tangen CM, Walston J, Newman AB, Hirsch C, Gottdiener J, Seeman T, Tracy R, Kop WJ, Burke G, et al. Frailty in older adults: evidence for a phenotype. J Gerontol A Biol Sci Med Sci. 2001;56: M146–56.
6. Hubbard RE, Woodhouse KW. Frailty, inflammation and the elderly. Biogerontology. 2010;11:635–41.
7. U.S. Census Bureau. Projections of the Population by Selected Age Groups and Sex for the United States, 2010 to 2050 (NP2008–T2). August 14, 2008.
8. Newman AB, Gottdiener JS, McBurnie MA, Hirsch CH, Kop WJ, Tracy R, Walston JD, Fried LP. Associations of subclinical cardiovascular disease with frailty. J Gerontol A Biol Sci Med Sci. 2001;56: M158–66.
9. Wilhelm-Leen ER, Hall YN, Deboer IH, Chertow GM. Vitamin D deficiency and frailty in older Americans. J Intern Med. 2010;268:171–80.
10. Bandeen-Roche K, Xue QL, Ferrucci L, Walston J, Guralnik JM, Chaves P, Zeger SL, Fried LP. Phenotype of frailty: characterization in the women's health and aging studies. J Gerontol A Biol Sci Med Sci. 2006;61:262–6.
11. Graham JE, Snih SA, Berges IM, Ray LA, Markides KS, Ottenbacher KJ. Frailty and 10-year mortality in community-living Mexican American older adults. Gerontology. 2009;55:644–51.
12. Bartali B, Frongillo EA, Bandinelli S, Lauretani F, Semba RD, Fried LP, Ferrucci L. Low nutrient intake is an essential component of frailty in older persons. J Gerontol A Biol Sci Med Sci. 2006;61:589–93.
13. Semba RD, Bartali B, Zhou J, Blaum C, Ko CW, Fried LP. Low serum micronutrient concentrations predict frailty among older women living in the community. J Gerontol A Biol Sci Med Sci. 2006;61:594–9.
14. Michelon E, Blaum C, Semba RD, Xue QL, Ricks MO, Fried LP. Vitamin and carotenoid status in older women: associations with the frailty syndrome. J Gerontol A Biol Sci Med Sci. 2006;61:600–7.
15. Beasley JM, LaCroix AZ, Neuhouser ML, Huang Y, Tinker L, Woods N, Michael Y, Curb JD, Prentice RL. Protein intake and incident frailty

in the Women's Health Initiative observational study. J Am Geriatr Soc. 2010;58:1063–71.

16. Sofi F, Cesari F, Abbate R, Gensini GF, Casini A. Adherence to Mediterranean diet and health status: meta-analysis. BMJ. 2008;337:a1344.
17. Scarmeas N, Stern Y, Mayeux R, Manly JJ, Schupf N, Luchsinger JA. Mediterranean diet and mild cognitive impairment. Arch Neurol. 2009;66:216–25.
18. Féart C, Samieri C, Rondeau V, Amieva H, Portet F, Dartigues JF, Scarmeas N, Barberger-Gateau P. Adherence to a Mediterranean diet, cognitive decline, and risk of dementia. JAMA. 2009;302:638–48.
19. Milaneschi Y, Bandinelli S, Corsi AM, Lauretani F, Paolisso G, Dominguez LJ, Semba RD, Tanaka T, Abbatecola AM, Talegawkar SA, et al. Mediterranean diet and mobility decline in older persons. Exp Gerontol. 2011;46:303–8.
20. Ferrucci L, Bandinelli S, Benvenuti E, Di Iorio A, Macchi C, Harris TB, Guralnik JM. Subsystems contributing to the decline in ability to walk: bridging the gap between epidemiology and geriatric practice in the InCHIANTI study. J Am Geriatr Soc. 2000;48:1618–25.
21. Trichopoulou A, Costacou T, Bamia C, Trichopoulos D. Adherence to a Mediterranean diet and survival in a Greek population. N Engl J Med. 2003;348:2599–608.
22. Bartali B, Turrini A, Salvini S, Lauretani F, Russo CR, Corsi AM, Bandinelli S, D'Amicis A, Palli D, Guralnik JM, et al. Dietary intake estimated using different methods in two Italian older populations. Arch Gerontol Geriatr. 2004;38:51–60.
23. Radloff LS. The CES-D scale: a self-report depression scale for research in the general population. Appl Psychol Meas. 1977;1:385–401.
24. Ainsworth BE, Haskell WL, Leon AS, Jacobs DR Jr, Montoye HJ, Sallis JF, Paffenbarger RS Jr. Compendium of physical activities: classification of energy costs of human physical activities. Med Sci Sports Exerc. 1993;25:71–80.
25. Folstein MF, Folstein SE, McHugh PR. "Mini-mental state". A practical method for grading the cognitive state of patients for the clinician. J Psychiatr Res. 1975;12:189–98.
26. Guralnik JM, Fried LP, Simonsick EM, Kasper D, Lafferty ME. The Women's Health and Aging Study: Health and Social Characteristics of Older Women with Disability. Bethesda (MD): National Institute on Aging. NIH Publication No. 95–4009; 1995.
27. Xue QL. The frailty syndrome: definition and natural history. Clin Geriatr Med. 2011;27:1–15.
28. Gill TM, Gahbauer EA, Allore HG, Han L. Transitions between frailty states among community-living older persons. Arch Intern Med. 2006;166:418–23.
29. Shardell M, D'Adamo C, Alley DE, Miller RR, Hicks GE, Milaneschi Y, Semba RD, Cherubini A, Bandinelli S, Ferrucci L. Serum 25-hydroxyvitamin D, transitions between frailty states, and mortality in older adults: the Invecchiare in Chianti Study. J Am Geriatr Soc. 2012;60:256–64.
30. Howard C, Ferrucci L, Sun K, Fried LP, Walston J, Varadhan R, Guralnik JM, Semba RD. Oxidative protein damage is associated with poor grip strength among older women living in the community. J Appl Physiol. 2007;103:17–20.
31. Guttridge DC, Mayo MW, Madrid LV, Wang CY, Baldwin AS Jr. NF-kappaB-induced loss of MyoD messenger RNA: possible role in muscle decay and cachexia. Science. 2000;289:2363–6.
32. Ershler WB. A gripping reality: oxidative stress, inflammation, and the pathway to frailty. J Appl Physiol. 2007;103:3–5.
33. Kregel KC, Zhang HJ. An integrated view of oxidative stress in aging: basic mechanisms, functional effects, and pathological considerations. Am J Physiol Regul Integr Comp Physiol. 2007;292:R18–36.
34. Walston J, McBurnie MA, Newman A, Tracy RP, Kop WJ, Hirsch CH, Gottdiener J, Fried LP. Frailty and activation of the inflammation and coagulation systems with and without clinical comorbidities: results from the Cardiovascular Health Study. Arch Intern Med. 2002;162: 2333–41.
35. Sofi F, Abbate R, Gensini GF, Casini A. Accruing evidence on benefits of adherence to the Mediterranean diet on health: an updated systematic review and meta-analysis. Am J Clin Nutr. 2010;92:1189–96.
36. Kipnis V, Subar AF, Midthune D, Freedman LS, Ballard-Barbash R, Troiano RP, Bingham S, Schoeller DA, Schatzkin A, Carroll RJ. Structure of dietary measurement error: results of the OPEN biomarker study. Am J Epidemiol. 2003;158:14–21, discussion 2–6.
37. Robinson S, Cooper C, Aihie Sayer A. Nutrition and sarcopenia. A review of the evidence and implications for preventive strategies. J Aging Res. 2012;2012:510801.
38. Sayer AA, Syddall H, Martin H, Patel H, Baylis D, Cooper C. The developmental origins of sarcopenia. J Nutr Health Aging. 2008;12: 427–32.
39. Moeller SM, Reedy J, Millen AE, Dixon LB, Newby PK, Tucker KL, Krebs-Smith SM, Guenther PM. Dietary patterns: challenges and opportunities in dietary patterns research an Experimental Biology workshop, April 1, 2006. J Am Diet Assoc. 2007;107:1233–9.
40. Newby PK, Tucker KL. Empirically derived eating patterns using factor or cluster analysis: a review. Nutr Rev. 2004;62:177–203.
41. Tucker KL. Dietary patterns, approaches, and multicultural perspective. Appl Physiol Nutr Metab. 2010;35:211–8.