

# Protein Intake and Risk of Falls: A Prospective Analysis in Older Adults

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**BACKGROUND:** The prospective association between protein intake and falls has been little studied. We assessed this association in a Spanish community-dwelling cohort.

**METHODS:** We performed a prospective cohort study of 2464 men and women 60 years or older who were recruited in 2008-2010 and followed up through 2012. At baseline, the habitual protein intake was determined with a validated dietary history. At the end of follow-up, participants reported the number of falls experienced in the preceding year. Participants were stratified by an unintentional weight loss of 4.5 kg or more. Logistic regression was used after adjustment for the main confounders.

**RESULTS:** A total of 522 participants (21.2%) experienced at least one fall. The odds ratios (ORs) and 95% confidence intervals (CIs) of falling for the three increasing tertiles of total protein intake were 1.00, 0.86 (0.66-1.11), and 0.93 (0.70-1.24) ( $p$  for trend = 0.14). However, a statistically significant interaction with unintentional weight loss was observed for the association between protein intake and fall risk ( $p$  for interaction = 0.004). Among 163 participants (6.6%) who experienced unintentional weight loss, the ORs (95% CI) of falling for the three increasing tertiles of total protein intake were 1.00, 0.68 (0.21-2.23), and 0.23 (0.05-1.08) ( $p$  for trend = 0.01).

**CONCLUSION:** No protective association between protein intake and fall risk in older adults was found. However,

high total protein intake tended to confer substantial benefits to participants who experienced an unintentional weight loss of 4.5 kg or more in the preceding year. *J Am Geriatr Soc* 67:329-335, 2019.

**Key words:** falls; protein intake; animal protein intake; vegetable protein intake; unintentional weight loss; older adults

## INTRODUCTION

Falls are a major public health concern for the older adult population.<sup>1-3</sup> Several epidemiological studies have identified medical risk factors for falling among older adults, such as age, depression, polypharmacy, sleeping medications, and hypotension.<sup>4,5</sup> However, the prevention of falls among the elderly is complex,<sup>5</sup> and potential dietary determinants are only poorly identified.<sup>6</sup>

Previous results from the Framingham Study<sup>7</sup> showed no association between protein intake and falls. However, the Framingham Study showed a protective association among those who had lost weight. Moreover, in the Study of Osteoporotic Fractures,<sup>8</sup> neither dietary protein intake nor vitamin D was associated with a decreased risk of falls. In addition, there is no conclusive information about the role of protein intake and the risk of hip fracture in older adults.<sup>9,10</sup>

The main objective of this study was to assess the prospective association between total protein intake and the risk of falling in a community-dwelling population of older adults from Spain. Secondary objectives were to assess the association of animal protein and vegetable protein intake with the risk of falling in the same population and to summarize the findings from the literature. Furthermore, the analysis was stratified according to participants who experienced unintentional weight loss.

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## METHODS

### Study Design and Population

The data were collected for the Seniors-ENRICA study that focused on a cohort of noninstitutionalized individuals 60 years and older in Spain. The cohort was derived from the ENRICA study, a survey conducted in 2008-2010 that was representative of the noninstitutionalized adult population in Spain.<sup>11,12</sup> ENRICA study participants 60 years or older comprised the Seniors-ENRICA cohort ( $n = 3289$ ). At baseline, data were collected in three stages. First, a computer-assisted telephone interview was performed to obtain information on sociodemographic factors, health behaviors, and morbidity. Second, a home visit was made to collect blood and urine samples. Third, a second home visit was made to obtain a dietary history and prescribed medications; a physical examination was also performed during this visit. Participants were followed up until 2012 (mean follow-up time of 3.5 y) when a second wave of data collection was performed. Of the initial sample, 675 participants were lost to follow-up, 95 died, 18 were excluded for a lack of data related to falls, 36 were excluded for a lack of data on potential confounders, and 1 was excluded for a lack of reliable dietary information data. The final analyses were performed with 2464 subjects. The baseline sociodemographic, lifestyle, and clinical characteristics of the participants included in the analyses were similar to those of the participants lost to follow-up (data not shown).<sup>11</sup>

The study participants gave written informed consent. The Clinical Research Ethics Committee of La Paz University Hospital in Madrid approved the study.

### Diet

Information on diet was collected using a computerized dietary history (HD-ENRICA) that collects habitual dietary consumption practices during the previous year with questions related to all possible meals throughout the day. The history first asks about the food eaten upon arising in the morning and ends with asking about the food consumed before going to bed. Questions were asked about the food consumed in a typical week, and all foods consumed at least once every 15 days were recorded. In addition, information on seasonal and weekend food consumption was obtained. The data were collected by certified interviewers. The protein consumption collected with this instrument was validated against seven 24-hour recalls in the preceding year, and high correlation coefficients were obtained (total protein  $\rho = 0.59$ ; animal protein  $\rho = 0.62$ ; vegetable protein  $\rho = 0.62$ ).<sup>13</sup> The intake of total energy, total protein, animal protein, and vegetable protein, as well as the intake of caffeine, calcium, vitamin D, and alcohol, was estimated using standard food composition tables from Spain.<sup>14,15</sup>

### Falls

A fall was defined as “an event which resulted in a person coming to rest inadvertently on the ground or floor or other lower level.”<sup>16</sup> At the end of follow-up, participants reported the number of falls experienced in the preceding year by answering this question: “How many times did you

fall during the past year?” The responses were recorded on a continuum from zero (no falls) to nine or more. Participants who had fallen were asked this question: “As a consequence of the fall, did you need to go to the doctor, go to the emergency room, or be hospitalized, or did you not need medical attention?” A participant was deemed to have required medical attention when the answer to any of the first three options was “yes.”

### Other Variables

At baseline, information on sex, age, educational level, smoking status, and alcohol consumption was obtained. Weight and height were measured under standardized conditions,<sup>17,18</sup> and the body mass index (weight in kilograms divided by height in meters squared [ $\text{kg}/\text{m}^2$ ]) was calculated. In addition, participants reported their physical activity during leisure activities and at home with the European Prospective Investigation into Cancer and Nutrition cohort questionnaire.<sup>17</sup> The time devoted to each activity was transformed into metabolic equivalent (MET)-hours/week, and the MET-hours/week from the different activities were summed. Participants also self-reported the time spent sleeping during the night or during the day, as well as the time devoted to watching TV. Participants were also asked whether they had different chronic conditions such as cardiovascular diseases, hypertension, diabetes, chronic pulmonary disease, arthritis or osteoarthritis, hip fracture, cancer, and/or depression requiring medication. The number of daily medications was checked against medication containers, and participants reported whether they usually took medications for sleeping or hypertension. The quality of the diet was estimated by the Mediterranean Diet Adherence Screener without considering wine consumption.<sup>19</sup> Finally, participants reported whether they lived alone, and we inquired about their dependence in performing instrumental activities of daily living (IADLs) using the Lawton and Brody questionnaire.<sup>20</sup>

In 2012, unintentional weight loss was self-reported. Every participant was asked if he or she had experienced an involuntary weight loss of 4.5 kg (10 lb) or more in the preceding year, in accordance with the standardized definition developed by Fried et al.<sup>21</sup>

### Statistical Analysis

Logistic models were used to assess the risk of falls. Protein intake was classified into sex-specific tertiles, and the lowest tertile was used as the reference. The models were adjusted not only for socioeconomic variables, lifestyle, diseases, and nonprotein dietary components but also for other variables associated with falls in the literature.<sup>22</sup>

Logistic models were established to adjust for sex; age (continuous); educational level (primary or less, secondary, or university); smoking status (never-smoker, ex-smoker, or smoker); alcohol intake status (never-drinker, occasional drinker, usual drinker, or ex-drinker); body mass index in  $\text{kg}/\text{m}^2$  ( $\leq 25$ ,  $>25$  to  $<30$ , or  $\geq 30$ ); physical activity in MET-hours/week (continuous); time spent sleeping (continuous); time spent watching TV (continuous); presence of cardiovascular disease, hypertension, diabetes, chronic pulmonary disease, arthritis or osteoarthritis, history of hip fracture,

cancer, and/or depression requiring medication; number of medications (continuous); use of sleeping or hypertension medications; intake of energy, caffeine, calcium, and vitamin D; adherence to a Mediterranean diet (continuous); living alone; dependence in performing IADLs, and intake of animal protein (quartiles) or vegetable protein (quartiles) as appropriate. The *p* for trend was calculated by treating the tertiles as a continuous variable. Interactions between the association of interest with both unintentional weight loss and age were assessed using the likelihood ratio test, and models were compared with and without the interaction terms.

The adjusted predictive risk of falls according to unintentional weight loss status (no weight loss or weight loss) was plotted against the total protein intake considered as a continuous variable. Statistical significance was set at a two-sided *p* < 0.05. The analyses were conducted with Stata/SE, v.14.1 (StataCorp, College Station, TX).

## RESULTS

The final sample comprised 2464 participants (53.0% female) with a mean age of 69 years at baseline. After a mean follow-up of 3.5 years, a total of 522 participants (21.2%) had fallen at least once in the preceding year. The means for protein consumption were as follows: 92 g/d (standard deviation [SD] = 26 g/d) for total protein, 61 g/d (SD = 22 g/d) for animal protein, and 31 g/d (SD = 10 g/d) for vegetable protein.

Participants consuming more total protein and animal protein were younger, less frequently ex-drinkers, heavier, taller, and more frequently obese; suffered from cancer more frequently; had higher consumption of energy, calcium, and vitamin D; followed a Mediterranean diet more frequently, lived alone less frequently; and had less dependence in performing IADLs than those consuming less total protein and animal protein. However, those who consumed more vegetable protein had similar ages, weighed less, were more physically active, had cancer less frequently, and did not consume a greater amount of vitamin D than those who consumed less vegetable protein (Table 1).

Supplementary Table S1 presents the crude results for the risk of falling. The adjusted odd ratios (ORs) and 95% confidence intervals (CIs) of falling for the three increasing tertiles of total protein intake were 1.00, 0.86 (0.66–1.11), and 0.93 (0.70–1.24) (*p* for trend = 0.14). Thus when the association between total protein intake and having experienced at least one fall was assessed, the estimates were less than 1 in the fully adjusted model, but none of the associations were statistically significant. Similar results were obtained for animal and vegetable protein intake.

However, a statistically significant interaction was observed with unintentional weight loss when the association between protein intake and risk of falls was assessed (*p* for interaction = 0.004). For participants who lost 4.5 kg or more in the preceding year, the adjusted ORs and 95% CIs of falling for the three increasing tertiles of total protein intake were 1.00, 0.68 (0.21–2.23), and 0.23 (0.05–1.08) (*p* for trend = 0.01) (Table 2). In all cases, the estimators decreased linearly, but the interactions were statistically significant only for vegetable protein intake when those in the highest consumption tertile were compared with those in

the lowest consumption tertile (OR = 0.20; 95% CI = 0.05–0.84). The interaction was statistically significant in all analyses (Table 2 and Figure 1).

We performed sensitivity analyses to assess the robustness of the main results. We obtained similar results when excluding participants with a history of hip fracture, when reestimating the study association using different methodologies to adjust for energy consumption, when adjusting for ethanol (g/d), and when excluding Mediterranean diet as a confounder. When falls requiring medical attention were used as an end point, the results exhibited a trend similar to those of the other analyses, but the associations were not statistically significant due to a lack of events. Finally, we did not find a statistically significant interaction between protein intake and age.

## DISCUSSION

No protective association was found between protein intake and the risk of falling in older adults in this community-dwelling cohort of older adults. However, when the association between protein intake and fall risk was assessed, a statistically significant interaction was observed with unintentional weight loss. An inverse trend was observed between protein intake and the risk of falls in participants who had a weight loss of 4.5 kg or more in the preceding year.

The association between protein intake and falls has been little studied. However, a cross-sectional study conducted with 100 healthy volunteers found that the protein intake of fallers and nonfallers was similar.<sup>23</sup>

Concerning longitudinal studies, our results are in line with those from the Framingham Study<sup>7</sup> that included 807 participants with a mean age of 75 years, in showing no association between protein intake and falls. However, in the Framingham Study, the results for the participants who had lost weight were statistically significant and more extreme than the results in our study. Compared with our sample, the sample in the Framingham Study was slightly older and had a lower protein intake.

In the Study of Osteoporotic Fractures,<sup>8</sup> neither dietary protein intake nor vitamin D intake was associated with falls. This study comprised more than 4000 very old postmenopausal women with a relatively low protein intake. Furthermore, neither dietary protein intake nor vitamin D was associated with falls after adjusting for potential confounders.

Hip fracture was used as the outcome in two cohort studies.<sup>9,10</sup> In both studies, the number of events was small, and the estimates were less than 1 but not statistically significant. However, these results are not totally comparable with those in our study. Higher protein intake was related to an increase in urinary calcium that may lead to osteoporosis.<sup>24</sup> Additionally, other studies found that higher protein intake is associated with an increased intestinal absorption of calcium,<sup>25</sup> suggesting the higher urinary calcium observed indicates calcium absorption and not bone resorption. Associations of protein intake with falls could have determinants different from those for associations of protein intake with fractures, thus requiring further studies with a larger sample size.

Table 1. Baseline characteristics of the study participants<sup>a</sup>

|                                          | Total protein intake |             |             |             | Animal protein intake |             |             |             | Vegetable protein intake |             |             |             |
|------------------------------------------|----------------------|-------------|-------------|-------------|-----------------------|-------------|-------------|-------------|--------------------------|-------------|-------------|-------------|
|                                          | T1                   | T2          | T3          | P for trend | T1                    | T2          | T3          | P for trend | T1                       | T2          | T3          | P for trend |
| Age, y, mean (SD)                        | 69.5 (6.7)           | 68.5 (6.4)  | 67.9 (5.9)  | <.001       | 69.3 (6.6)            | 68.6 (6.5)  | 68.0 (5.9)  | <.001       | 68.7 (6.5)               | 68.6 (6.2)  | 68.6 (6.4)  | .71         |
| Educational level, %                     |                      |             |             |             |                       |             |             |             |                          |             |             |             |
| Primary or less                          | 56.3                 | 53.9        | 53.7        | .48         | 55.7                  | 55.6        | 52.6        | 0.57        | 52.1                     | 54.0        | 57.8        | .19         |
| Secondary                                | 22.1                 | 25.8        | 24.6        |             | 22.9                  | 24.5        | 25.2        |             | 25.4                     | 24.0        | 23.2        |             |
| University                               | 21.5                 | 20.3        | 21.7        |             | 21.4                  | 20.0        | 22.2        |             | 22.5                     | 22.0        | 19.0        |             |
| Smoking status, %                        |                      |             |             |             |                       |             |             |             |                          |             |             |             |
| Never-smoker                             | 59.5                 | 59.5        | 57.4        | .69         | 60.6                  | 57.8        | 58.1        | .79         | 57.7                     | 58.8        | 60.0        | .48         |
| Ex-smoker                                | 28.8                 | 30.3        | 30.5        |             | 28.5                  | 30.5        | 30.6        |             | 29.6                     | 29.9        | 30.1        |             |
| Smoker                                   | 11.7                 | 10.2        | 12.1        |             | 10.9                  | 11.7        | 11.3        |             | 12.8                     | 11.3        | 9.9         |             |
| Alcohol consumption, %                   |                      |             |             |             |                       |             |             |             |                          |             |             |             |
| Never-drinker                            | 33.7                 | 34.6        | 38.2        | .05         | 34.4                  | 34.1        | 37.9        | .13         | 36.7                     | 33.6        | 36.1        | <.001       |
| Occasional drinker                       | 9.3                  | 7.9         | 7.4         |             | 9.5                   | 8.5         | 6.6         |             | 5.6                      | 9.9         | 9.6         |             |
| Usual drinker                            | 46.6                 | 49.3        | 47.9        |             | 47.2                  | 48.1        | 48.5        |             | 46.0                     | 48.1        | 49.7        |             |
| Ex-drinker                               | 10.5                 | 8.3         | 6.5         |             | 8.9                   | 9.4         | 7.0         |             | 11.7                     | 8.5         | 5.0         |             |
| Weight, kg, mean (SD)                    | 73.0 (12.4)          | 73.5 (13.1) | 76.1 (13.4) | <.001       | 72.5 (12.4)           | 74.0 (12.8) | 76.1 (13.6) | <.001       | 74.9 (13.4)              | 74.3 (12.8) | 73.3 (12.8) | .009        |
| Height, cm, mean (SD)                    | 160.3 (8.8)          | 161.3 (9.2) | 162.0 (8.9) | <.001       | 160.6 (8.8)           | 161.1 (8.8) | 161.8 (9.3) | .005        | 160.8 (9.4)              | 161.5 (8.8) | 161.3 (8.7) | .22         |
| Body mass index                          |                      |             |             |             |                       |             |             |             |                          |             |             |             |
| ≤25 kg/m <sup>2</sup>                    | 18.0                 | 22.6        | 17.4        | .005        | 21.4                  | 18.5        | 18.2        | .003        | 15.8                     | 20.2        | 22.1        | .003        |
| >25 to <30 kg/m <sup>2</sup>             | 52.0                 | 47.9        | 47.1        |             | 51.7                  | 49.4        | 45.9        |             | 48.4                     | 49.3        | 49.3        |             |
| ≥30 kg/m <sup>2</sup>                    | 30.1                 | 29.4        | 35.5        |             | 26.9                  | 32.1        | 36.0        |             | 35.8                     | 30.5        | 28.7        |             |
| Physical activity, MET-h/week, mean (SD) | 57.5 (34.0)          | 61.0 (34.3) | 60.2 (34.4) | .11         | 59.2 (34.2)           | 60.2 (35.0) | 59.2 (34.6) | .94         | 55.6 (33.1)              | 61.2 (35.4) | 61.9 (34.9) | <.001       |
| Time sleeping, h, mean (SD)              | 7.2 (1.6)            | 7.1 (1.6)   | 7.2 (1.5)   | .53         | 7.1 (1.5)             | 7.2 (1.5)   | 7.1 (1.5)   | .99         | 7.1 (1.5)                | 7.2 (1.4)   | 7.1 (1.5)   | .81         |
| Time watching TV, h, mean (SD)           | 2.6 (1.7)            | 17.8 (10.9) | 2.6 (1.4)   | .89         | 2.6 (1.7)             | 17.8 (10.6) | 2.6 (1.6)   | .69         | 2.6 (1.7)                | 17.9 (10.9) | 2.6 (1.4)   | .99         |
| Cardiovascular disease, %                | 5.2                  | 5.5         | 5.7         | .91         | 5.7                   | 5.7         | 5.0         | .76         | 5.0                      | 6.3         | 5.1         | .42         |
| Hypertension, %                          | 65.2                 | 63.9        | 65.5        | .76         | 65.3                  | 63.8        | 65.5        | .71         | 66.8                     | 64.5        | 63.3        | .32         |
| Diabetes, %                              | 16.4                 | 13.9        | 16.5        | .98         | 14.7                  | 16.6        | 15.5        | .59         | 15.9                     | 16.3        | 14.5        | .57         |
| Chronic pulmonary disease, %             | 7.5                  | 6.8         | 7.3         | .84         | 8.0                   | 6.3         | 7.3         | .41         | 7.5                      | 6.2         | 7.9         | .37         |
| Arthritis or osteoarthritis, %           | 46.2                 | 49.8        | 50.0        | .23         | 47.0                  | 49.8        | 49.2        | .48         | 47.6                     | 48.1        | 50.4        | .48         |
| History of hip fracture, %               | 1.7                  | 1.0         | 1.5         | .67         | 1.7                   | 1.5         | 1.0         | .21         | 1.8                      | 0.6         | 1.7         | .83         |
| Cancer, %                                | 1.2                  | 1.7         | 2.9         | .01         | 1.1                   | 2.1         | 2.7         | .02         | 2.0                      | 2.0         | 2.0         | .99         |
| Depression requiring medication, %       | 8.6                  | 8.3         | 7.9         | .87         | 8.9                   | 7.9         | 8.1         | .74         | 8.5                      | 8.3         | 8.1         | .94         |
| No. of medications, mean (SD)            | 2.1 (1.9)            | 1.9 (1.9)   | 2.0 (2.0)   | .36         | 2.0 (1.9)             | 2.0 (1.9)   | 2.0 (2.0)   | .55         | 2.0 (1.9)                | 1.9 (1.9)   | 2.0 (2.0)   | .60         |
| Sleeping treatment, %                    | 20.1                 | 20.9        | 19.5        | .77         | 21.6                  | 19.2        | 19.6        | .42         | 21.4                     | 19.2        | 19.8        | .52         |
| Hypertension treatment, %                | 38.6                 | 38.8        | 37.2        | .77         | 39.1                  | 37.8        | 37.7        | .82         | 40.1                     | 37.7        | 36.7        | .34         |
| Energy, kcal/d, mean (SD)                | 1843 (1036)          | 2053 (514)  | 2,262 (560) | <.001       | 1963 (1039)           | 2033 (549)  | 2,162 (582) | <.001       | 1861 (1060)              | 2045 (519)  | 2,252 (521) | <.001       |
| Caffeine intake, mg/d, mean (SD)         | 69.0 (119)           | 74.7 (110)  | 70.1 (103)  | .84         | 70.1 (123)            | 73.2 (123)  | 70.5 (101)  | .96         | 69.5 (114)               | 74.5 (110)  | 69.8 (110)  | .96         |
| Calcium intake, mg/d, mean (SD)          | 714 (244)            | 891.4 (254) | 1,058 (428) | <.001       | 729 (237)             | 884.6 (261) | 1,049 (439) | <.001       | 872 (441)                | 884.4 (307) | 907 (279)   | .04         |
| Vitamin D, μ/d, mean (SD)                | 2.4 (2.2)            | 3.4 (2.5)   | 4.6 (3.9)   | <.001       | 2.5 (2.0)             | 3.4 (2.6)   | 4.5 (4.1)   | <.001       | 3.4 (3.7)                | 3.4 (2.8)   | 3.5 (2.7)   | .53         |
| Mediterranean diet, MEDAS, mean (SD)     | 6.6 (1.7)            | 7.0 (1.8)   | 7.2 (1.7)   | <.001       | 6.7 (1.9)             | 6.9 (1.7)   | 7.1 (1.6)   | <.001       | 6.7 (1.5)                | 6.9 (1.7)   | 7.3 (1.9)   | <.001       |
| Living alone, %                          | 20.2                 | 15.1        | 14.8        | .004        | 19.8                  | 13.3        | 17.0        | .002        | 19.2                     | 17.5        | 13.3        | .004        |
| Dependence in performing IADLs, %        | 13.1                 | 8.5         | 10.0        | .008        | 12.4                  | 9.7         | 9.5         | .10         | 11.9                     | 10.0        | 9.8         | .29         |

<sup>a</sup>According to tertiles of total protein, animal protein, and vegetable protein intake in the Seniors-ENRICA cohort study (N = 2464).

Note: Cutoff points for protein intake tertiles (in g/d): for men, total protein: T1, 18.4–87.9; T2, 88.0–108.5; T3, 108.6–284.7; animal protein: T1, 10.3–55.7; T2, 55.8–74.5; T3, 74.6–260.2; vegetable protein: T1, 8.1–28.5; T2, 28.6–37.1; T3, 37.2–79; for women, total protein: T1, 26.8–72.8; T2, 72.9–90.7; T3, 90.8–207.1; animal protein: T1, 11.3–45.7; T2, 45.8–61.2; T3, 61.3–374.5; vegetable protein: T1, 1.6–23.4; T2, 23.5–31.1; T3, 31.2–88.4.

Abbreviations: IADLs = instrumental activities of daily living; MEDAS = Mediterranean Diet Adherence Screener without alcohol intake; MET = Metabolic equivalent; SD = standard deviation; T1 = tertile 1 (lowest); T3 = tertile 3 (highest).

The association of protein intake with falls among individuals with unintentional weight loss could be related to frailty. Frailty is an age-associated syndrome that includes sarcopenia as its pathophysiologic basis,<sup>26</sup> and unintentional weight loss, evaluated as the involuntary loss of 4.5 kg or more in the preceding year, is one of the frailty criteria in the definition developed by Fried et al.<sup>21</sup> Another

frailty criterion is muscle weakness, defined as classification in the lowest quintile of grip strength within groups based on sex and body mass index in our cohort. In addition, the daily consumption of at least 1 g/kg/d protein is associated with a decreased loss of knee strength that might be an additional mechanism by which protein intake protects against falls.<sup>27</sup> Evidence suggests that interventions to

Table 2. Odds ratios and incidence rate ratios (95% confidence intervals) for the risk of falls<sup>a</sup>

|                          | All participants  |                  | Participants without weight loss |                  | Participants with weight loss (≥4.5 kg) |                  | <i>P</i> for interaction |
|--------------------------|-------------------|------------------|----------------------------------|------------------|-----------------------------------------|------------------|--------------------------|
|                          | Events/n 522/2464 | OR (95% CI)      | Events/n 477/2301                | OR (95% CI)      | Events/n 45/163                         | OR (95% CI)      |                          |
| <b>Total protein</b>     |                   |                  |                                  |                  |                                         |                  | .004                     |
| Tertile 1, lowest        | 184/822           | 1 (ref.)         | 164/767                          | 1 (ref.)         | 20/55                                   | 1 (ref.)         |                          |
| Tertile 2                | 164/822           | 0.86 (0.66-1.11) | 147/762                          | 0.86 (0.66-1.23) | 17/60                                   | 0.68 (0.21-2.23) |                          |
| Tertile 3, highest       | 174/820           | 0.93 (0.70-1.24) | 166/772                          | 0.98 (0.73-1.31) | 8/48                                    | 0.23 (0.05-1.08) |                          |
| <i>P</i> for trend       |                   | 0.14             |                                  | 0.35             |                                         | 0.01             |                          |
| <b>Animal protein</b>    |                   |                  |                                  |                  |                                         |                  | .017                     |
| Tertile 1, lowest        | 189/822           | 1 (ref.)         | 169/765                          | 1 (ref.)         | 20/57                                   | 1 (ref.)         |                          |
| Tertile 2                | 156/822           | 0.81 (0.62-1.06) | 140/760                          | 0.81 (0.62-1.06) | 16/62                                   | 0.65 (0.19-2.24) |                          |
| Tertile 3, highest       | 177/820           | 0.96 (0.71-1.28) | 168/776                          | 0.96 (0.72-1.28) | 9/44                                    | 0.29 (0.07-1.28) |                          |
| <i>P</i> for trend       |                   | 0.13             |                                  | 0.24             |                                         | 0.02             |                          |
| <b>Vegetable protein</b> |                   |                  |                                  |                  |                                         |                  | .016                     |
| Tertile 1, lowest        | 190/822           | 1 (ref.)         | 169/772                          | 1 (ref.)         | 21/50                                   | 1 (ref.)         |                          |
| Tertile 2                | 160/822           | 0.86 (0.66-1.12) | 149/771                          | 0.86 (0.66-1.12) | 11/51                                   | 0.20 (0.05-0.74) |                          |
| Tertile 3, highest       | 172/820           | 0.91 (0.70-1.20) | 159/758                          | 0.91 (0.70-1.20) | 13/62                                   | 0.20 (0.05-0.84) |                          |
| <i>P</i> for trend       |                   | 0.38             |                                  | 0.68             |                                         | 0.02             |                          |

<sup>a</sup>According to tertiles of protein intake in the Seniors-ENRICA cohort study (N = 2464). Analyses were stratified by a weight loss ≥4.5 kg in the preceding year.

Note: Models were adjusted for sex, age, educational level, smoking status, alcohol intake status, body mass index, physical activity, time sleeping, time watching TV, cardiovascular disease, hypertension, diabetes, chronic pulmonary disease, arthritis or osteoarthritis, history of hip fracture, cancer, and/or depression (requiring medication), number of medications, sleeping treatment, hypertension treatment, energy intake, caffeine intake, calcium intake, vitamin D intake, Mediterranean diet, living alone, and dependence in performing instrumental activities of daily living. Animal protein and vegetable protein intake were adjusted for each other as appropriate.

Abbreviations: CI = confidence interval; OR = odds ratio.

improve dietary protein intake may prevent the development of sarcopenia and frailty.<sup>28,29</sup> Furthermore, a systematic review and meta-analysis associated frailty with the risk of falls,<sup>30</sup> and protein intake was related to a lower risk of frailty in the WHI-OS study.<sup>31</sup> Additionally, in a previous analysis of this cohort,<sup>29</sup> the intake of protein and monounsaturated fatty acids was strongly and inversely associated with frailty and more specifically with slow walking, considered a predictor of falls.<sup>32</sup> Similarly, Rahi et al found that a daily protein intake of 1 g/kg/d was associated with a lower prevalence of frailty in community-dwelling older adults.<sup>33</sup>

In the NuAge study,<sup>34</sup> a protein intake of more than 1.0 g/kg/d was found to protect against a 1-year weight loss of 5% or more. Additionally, protein intake may attenuate not only the age-related loss of skeletal muscle but also the development of sarcopenia,<sup>35</sup> an independent predictor of incident falls.<sup>36,37</sup> Interestingly, in participants in the Health ABC study who lost weight, higher protein intake was related to lower lean muscle loss, whereas in those with a stable weight, no association was found.<sup>35</sup> Similarly, some studies related unintentional weight loss to an increased risk of frailty fractures and falls.<sup>38,39</sup> Thus two of the frailty criteria, namely unintentional weight loss and muscle strength, were associated with protein intake. Moreover, frailty was associated with the risk of falls.<sup>30</sup>

Finally, laboratory analyses showed that some proteins may influence unintentional weight loss in older humans; some of these proteins (such as neuropeptide Y and peptide YY) are altered in both aging animals and aging humans.<sup>40</sup> Therefore, our results are consistent with existing biological and medical knowledge and emphasize the important role of dietary protein intake on sarcopenia prevention and muscle protein synthesis<sup>28</sup> mediated or not mediated by frailty.

Some authors suggest increasing the recommendations for the dietary allowance of protein that currently is 0.8 g/kg/d.<sup>41</sup> Additionally, a randomized controlled trial performed with malnourished older adults showed that an intervention consisting of a protein-enriched diet, calcium vitamin supplements, and telephone counseling by a dietitian decreased the number of patients who suffered falls,<sup>42</sup> emphasizing the protective effect of protein consumption in malnourished older adults.

Our results may be relevant in older adults because protein intake might decrease the risk of frailty syndrome and falls among individuals who lose weight. Of special interest are proteins from vegetables, since the consumption of fruit and vegetables was also associated with a reduced risk of frailty,<sup>43</sup> and fruits and vegetables seem to be especially beneficial for individuals who have lost weight.

A strength of this study is its prospective design. Additionally, the study results were robust because they did not change substantially across many sensitivity analyses. A relatively large number of events were included, and participants were an unselected sample of free-living community residents. However, limitations of the study should be noted. As in most nutritional epidemiology studies, diet was self-reported. The HD-ENRICA data were validated against seven 24-hour recalls collected every 2 months during the previous year.<sup>13</sup> However, recall bias cannot be totally ruled out when questionnaires are used to assess habitual dietary consumption. Additionally, the underreporting of falls is possible because of recall bias, thus leading to a misclassification bias toward the null value. Additionally, residual confounding cannot be ruled out because of the observational design. Finally, a survival bias could be present because hip fracture increases mortality, and participants lost to follow-up could be more likely to have

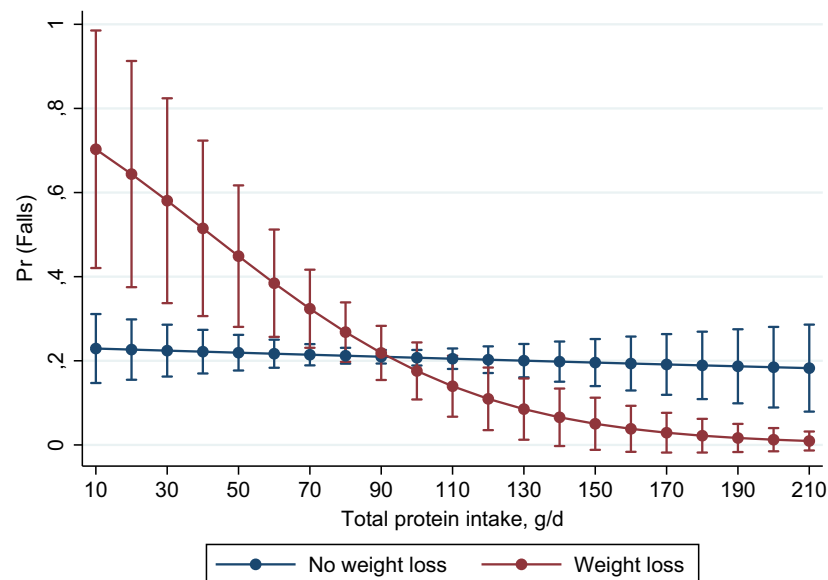


**Figure 1.** Adjusted predictive risk of falls with 95% confidence intervals, according to an unintentional weight loss of 4.5 kg or more in the preceding year, from the Seniors-ENRICA cohort study (N = 2464). Models were adjusted for sex, age, educational level, smoking status, alcohol intake status, body mass index, physical activity, time sleeping, time watching TV, cardiovascular disease, hypertension, diabetes, chronic pulmonary disease, arthritis or osteoarthritis, history of hip fracture, cancer, and/or depression (requiring medications), number of medications, sleeping treatment, hypertension treatment, energy intake, caffeine intake, calcium intake, vitamin D intake, Mediterranean diet, living alone, and dependence in performing instrumental activities of daily living.

experienced weight loss and falls. However, the effect of this bias is probably small because hip fracture occurs in only approximately 1% of falls,<sup>44</sup> and the baseline characteristics of the participants included in the analyses were similar to those of the participants lost to follow-up.

In conclusion, no protective association was found between protein intake and the risk of falling in older adults. However, participants who had experienced an unintentional weight loss of 4.5 kg or more in the preceding year benefited substantially from high protein intake. Consequently, a broad and integrative approach is needed to address the association between protein intake and fall prevention in older adults. Further studies should consider the influence of weight loss on this association.

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## SUPPORTING INFORMATION

Additional Supporting Information may be found in the online version of this article:

**Supplementary Table S1.** Unadjusted odds ratios (95% confidence interval) for the risk of falls according to tertiles of protein intake in the Seniors-ENRICA cohort study (N = 2464). Analyses were stratified by a weight loss of  $\geq 4.5$  kg in the preceding year.