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Distribution of daily protein intake across meals and all-cause mortality in community-dwelling older adults

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Abstract

Recent findings suggest that the distribution of protein intake throughout the day has an impact on various health outcomes in older adults, independently of the amount consumed. We evaluated the association between the distribution of dietary protein intake across meals and all-cause mortality in community-dwelling older adults. Data from 3225 older adults aged ≥ 60 years from the Seniors-ENRICA-1 cohort were examined. Habitual dietary protein consumption was collected in 2008–2010 and in 2012 through a validated diet history. Protein distribution across meals was calculated for each participant as the coefficient of variation (CV) of protein intake per meal, in sex-specific tertiles. Vital status was obtained from the National Death Index up to 30 January 2020. Cox proportional hazards regression was performed to determine the hazard ratios (HR) and their 95 % CI for the association between the distribution of daily protein intake across meals and all-cause mortality. Over a median follow-up of 10·6 years, 591 deaths occurred. After adjustment for potential confounders, the CV of total protein intake was not associated with all-cause mortality (HR and 95 % CI in the second and third tertile *v.* the lowest tertile: 0·94 (0·77, 1·15) and 0·88 (0·72, 1·08); $P_{trend} = 0·22$). Similarly, the HR of all-cause mortality when comparing extreme tertiles of CV for types of protein were 0·89 (0·73, 1·10) for animal-protein intake and 1·02 (0·82, 1·25) for plant-protein intake. Dietary protein distribution across meals was not associated with all-cause mortality, regardless of protein source and amount, among older adults. Further studies should investigate whether this picture holds for specific causes of death.

Key words: **Dietary protein: Animal protein: Plant protein: Older adults: Mortality: Cohort study**

Poor dietary habits are associated with several unfavourable health outcomes and specific adjustments in diet may contribute to halt and reverse these outcomes. In particular, protein intake source is a modifiable nutritional factor for mortality risk[1–8]. Several prospective cohort studies have found that habitual intake of animal protein was positively associated with all-cause mortality[1–3], whereas plant protein showed an inverse association[1,3–5]. Focusing on more specific protein sources, higher intake of fish[6], eggs[7], nuts[3,8] and whole grains[9] were associated with decreased risk of all-cause mortality, while higher intakes of red meat and processed meat were associated with increased risk of all-cause mortality[3,10,11].

An adequate protein intake is critical in older adults, who are at higher risk for sarcopenia[12] and loss of appetite[13]. In addition, not only the amount of protein but the distribution in the intake may be relevant for health. It has been hypothesised that 30 g of protein per meal is required to stimulate muscle protein synthesis, so that an even distribution of protein intake during the day might help maintain an optimum level of muscle formation for longer periods, while an uneven distribution might result in a waste of protein[14–16].

Recent studies have associated an even distribution of protein intake with various health outcomes in older adults, including lower risk of frailty, lean mass loss, and physical impairment and with a higher muscle strength[17–20]. However, other studies have not found a benefit[21–23]. Beyond functional outcomes, to our knowledge, there is no evidence on the effect of mealtime distribution of protein intake on hard outcomes such as total mortality, which would be a surrogate of overall health status. If an even distribution of protein intake has a beneficial effect on health status of older adults, we would expect observing a decreased risk of mortality among those with this type of diet pattern. We evaluated the prospective association between the distribution of dietary protein intake (both animal- and

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plant-based) across meals and all-cause mortality in community-dwelling older adults in Spain.

Materials and methods

Study design and participants

Baseline data were taken from the Study on Nutrition and Cardiovascular Risk in Spain (ENRICA), whose methods have been reported elsewhere[24]. In brief, the cohort was established in 2008–2010 among 12 948 individuals representative of the non-institutionalised adult population of Spain (ClinicalTrials.gov NCT02804672). The study participants aged 60 years or older comprised the Seniors-ENRICA-1 cohort (n 3518). The information was collected by trained personnel in three sequential stages: (1) a telephone interview on socio-demographic variables, lifestyle, health status and morbidity; (2) a first home visit to collect blood and urine samples and (3) a second home visit, to perform a physical examination, obtain a diet history and gather other questionnaire data. In 2012, a new wave of data collection was performed to update information. Study participants were followed until January 2020 to determine vital status. The study was approved by the Clinical Research Ethics Committee of '*La Paz*' University Hospital in Madrid (Spain). Study participants and their relatives provided written informed consent in all phases.

Study variables

Diet. At baseline and in 2012, habitual food consumption was collected through a validated computer-based dietary history[25]. This instrument collects food consumption by occasions of intake throughout the day and accommodates habitual diet information to a 24-h format, by asking participants to indicate the time in which they usually had their meals, including snacks, during a typical week. This week represents the annual consumption since seasonal foods are included by using coefficients of ponderation. The daily food consumption was distributed in sixteen intake occasions, which were grouped in four blocks: breakfast, lunch, dinner and snacks. The first three intake occasions were defined as breakfast and included the first food consumed after waking up, breakfast and mid-morning food consumption. Lunch was defined as the next six intake occasions, incorporating the entrée or appetiser, first main course, second main course, side dish (e.g. salad, potatoes, rice, etc.), dessert and bread, wine and coffee. The last six intake occasions were defined as dinner and included supper, entrée or appetiser, first main course, second main course, dessert and bread, wine and coffee. Snacks included the food consumed after dinner and before breakfast, as well as the food consumed between breakfast, lunch and dinner (e.g. sweets, cookies, juices, caramels, etc.), and night out drinks (Methodological appendix)[25].

Energy and nutrient intakes were estimated using standard food composition tables for the Spanish population[25], and the latter were adjusted for energy intake using the residual method[26]. The validity and reproducibility of the diet history were evaluated by comparing its results against seven 24-h recalls over a 1-year period: the energy-adjusted Pearson's correlation coefficients ranged between 0·27 and 0·71 across nutrients (total protein, $r = 0{\cdot}50$; animal protein, $r = 0{\cdot}59$ and plant protein, $r = 0{\cdot}60$)[25].

Total protein intake distribution was assessed with a coefficient of variation (CV) calculated as the SD of grams of total protein per meal divided by the mean of grams of total protein per day (excluding snacks since they accounted for < 3 % of total protein intake)[17]. Similarly, we assessed animal and plant protein CV, by replacing total protein intake with animal or plant protein intake (animal/plant protein CV = SD of grams of animal/plant protein per meal divided by the mean of grams of animal/plant protein per day, excluding snacks). Lower values of CV indicate greater evenness of total-, animal- and plant protein intake across meals[17].

The Mediterranean Diet Adherence Screener was also calculated to assess overall diet quality[27]. This score ranged from 0 to 14, and higher scores indicated higher adherence to the Mediterranean diet and reflect better diet quality.

Mortality. Vital status was ascertained by a computerised search of the Spain's National Death Index, which contains information on the vital status of all residents in Spain[28]. In total, we identified 591 all-cause deaths from baseline to the latest update on mortality information on 31 January 2020.

Other variables. At baseline, data on participants' age, sex, education (≤ primary, secondary or university level), smoking status (never-, former or current smoker) and sedentary behaviour (self-reported hours/week spent watching TV) were collected. Physical activity during leisure time (metabolic equivalent hours per week) was ascertained with the European Prospective Investigation into Cancer and Nutrition study questionnaire, validated for the Spanish population[29]. Weight and height were measured under standardised conditions, and BMI was calculated as weight (kg) divided by height squared (m^2) and classified as < 25, 25–29·9 or ≥ 30 kg/m^2. The presence of clinician-diagnosed diseases was self-reported by participants and included musculoskeletal disease, CVD, cancer, chronic lung disease and depression requiring medical treatment.

Statistical analyses. From the 3518 study participants aged ≥ 60 years at baseline, we excluded 242 participants without diet history, implausibly energy intake (outside the range of 800–5000 kcal/d for men and 500–4000 kcal/d for women) or those with extremely high-protein consumption (above the 99·5th percentile of total protein intake) to account for unrealistic values. Also, thirty-one individuals without data on potential confounders were excluded. Finally, to lessen the chances of reverse causation, we excluded twenty participants who died within the first 2 years of follow-up. Thus, the analyses were finally conducted with 3225 individuals (online Supplementary Fig. S1).

Continuous variables were presented as means ± SD and categorical variables as percentages. The χ^2 test was used to analyse differences across sex-specific tertiles of the CV of protein intake for categorical variables, while the ANOVA test was applied to analyse differences for quantitative variables.

A Cox proportional hazards regression was performed to determine the hazard ratios and their 95 % CI for the association between the distribution of daily protein intake across meals and all-cause mortality. Person-years were calculated from baseline until the occurrence of death or the end of the study period, whichever came first. To consider variations in diet intake during the follow-up, we used the cumulative average of protein CV for participants with diet information at baseline and at a 3-year follow-up; for 1180 participants lacking follow-up diet information, we used baseline protein CV. Participants were classified into sex-specific tertiles of protein CV[30], using the first tertile (more even distribution) as the reference category. Three Cox models were built: the first model included age, sex and total protein intake; the second one was additionally adjusted for educational level, smoking status, alcohol consumption, sedentary behaviour, physical activity, BMI, energy intake and the Mediterranean Diet Adherence Screener score and the third model was additionally adjusted for prevalent morbidity (musculoskeletal disease, CVD, cancer, chronic lung disease and depression) and incident morbidity in 2012, 2015 and 2017 (CVD, cancer and chronic lung disease). All animal-protein models were additionally adjusted for plant protein CV, while all plant-protein models were additionally adjusted for animal protein CV. Additionally, to assess linear dose–response relationships ($P_{\text{for trend}}$), we modeled sex-specific tertiles of total-, animal- and plant-protein CV as continuous variables. To test non-linear risk trends, we used three knot-restricted cubic splines (in percentiles 25, 50 and 75) for the distribution of daily protein intake across meals and the risk of all-cause mortality. The proportional hazard assumption of the model was tested through visual examination of the Schoenfeld residuals; no violation of the assumption was observed. In stratified analyses, we assessed whether the association was similar among individuals younger than 75 years than among those of 75 years and more.

Statistical significance was set at two-tailed $P < 0{\cdot}05$. Analyses were conducted using STATA (version 15.1; Stata Corp).

Results

Participants with the highest total protein CV had a consumption of 54 % of daily total protein in a single meal (lunch total protein, g/d (47·9) × 100/total protein, g/d (88·6)). Table 1 shows the baseline characteristics of the study participants according to sex-specific tertiles of the total protein CV. Of the 3225 participants, 1747 (54·2 %) were woman. Compared with participants with a more even distribution of total protein intake, those with a less even distribution were younger, more likely to be current smokers, with higher alcohol intake and higher prevalence of obesity; in this group, CVD and cancer prevalence were lower. Total protein intake, breakfast total protein intake, dinner total protein intake, total energy, fat and carbohydrate intake were lower among those individuals in the highest tertile of total protein CV, while lunch total protein intake and Mediterranean Diet Adherence Screener score were higher. Participants with a less even distributed total protein intake had a higher animal-protein intake and lower plant-protein intake. The mealtime with the highest total protein intake was lunch, in all tertiles, whereas the lowest total protein intake was in breakfast (online Supplementary Fig. S2, and online Supplementary Fig. S3).

There were some differences in the baseline characteristics of the study participants across sex-specific tertiles of the total protein CV compared with the sex-specific tertiles of the animal and plant protein CV (online Supplementary Tables S1 and S2). When participants were divided into categories of animal-protein CV, the differences found in smoking status, alcohol intake and BMI across sex-specific tertiles of total protein CV were lost. When participants were divided into categories of plant-protein CV, participants with a less even plant-protein intake had a lower physical activity compared with those with a more even plant-protein intake. We also found that the differences in CVD prevalence across sex-specific tertiles of the total protein CV were lost in the animal and plant protein CV sex-specific tertiles. Additionally, despite not finding differences across sex-specific tertiles of the total protein CV on incident morbidity, participants with a less even animal-protein intake had a lower CVD incidence compared with those with a more even animal-protein intake. On the other hand, participants with a less even plant-protein intake had a lower chronic lung disease incidence than those with a more even plant-protein intake.

During a median of 10·6 years of follow-up and 32 838 person-years followed up, 591 deaths occurred. The cumulative average of the CV of total protein intake across meals was not significantly associated with the risk of death in the models (model 3 hazard ratio (95 % CI) for the second and third tertiles were 0·94 (0·77, 1·15) and 0·88 (0·72, 1·08), respectively, considering the first tertile as the reference category; $P_{\text{trend}} = 0{\cdot}22$) (Table 2). Similar results were found in the animal-protein CV models (model 3 hazard ratio for highest *v.* lowest tertile: 0·89; 95 % CI 0·73, 1·10; $P_{\text{trend}} = 0{\cdot}29$) and in the plant-protein CV models (model 3 hazard ratio for highest *v.* lowest: 1·02; 95 % CI 0·82, 1·25; P trend = 0·87) (Table 2). The spline for the non-linear risk trends on the association between total protein CV and all-cause mortality did not show a significant result (Fig. 1). Sensitivity analyses among participants < 75 years compared with those ≥ 75 years and according to the level of protein intake (total-, animal- and plant-protein) yielded similar associations (online Supplementary Tables S3 and S4). Finally, we could not find any suggestion of an increased risk of death by not reaching a minimum of protein intake per meal (0·4 g of protein/kg/meal or 30 g of protein intake per meal) (online Supplementary Tables S5 to S8).

Discussion

In this prospective study of community-dwelling older adults, mealtime distribution of daily total protein intake was not associated with all-cause mortality after 10·6 years of follow-up, independently of total protein intake, overall diet quality, other lifestyles and morbidity. Analysing mortality risk by specific source of protein, all-cause mortality was neither affected by animal-protein or plant-protein mealtime daily distribution. To our knowledge, this is the first study assessing the relation

Table 1. Characteristics of the study participants by sex- specific tertiles of the CV of protein intake across meals (*n* 3225)

	CV of protein intake across meals									
	Tertile 1 (More even distribution)			Tertile 2			Tertile 3 (Less even distribution)			
	%	Mean	SD	%	Mean	SD	%	Mean	SD	*P*-value*
n participants	1076			1075			1074			
Men, range of protein CV	0·04–0·51			0·52–0·65			0·66–1·29			
Women, range of protein CV	0·05–0·48			0·49–0·63			0·64–1·53			
Age, year		69·6	6·9	68·8		6·3	68·8		6·5	0·004
Sex, men %	45·8			45·9			45·8			1·00
Educational level, %										
≤ Primary	59·7			57·2			55·5			0·33
Secondary	22·1			23·0			25·1			
University	18·2			19·8			19·4			
Smoking status, %										
Current smoker	10·3			10·5			14·5			0·01
Former smoker	29·7			30·1			29·9			
Never smoker	60·0			59·4			55·6			
Alcohol intake, g/d		8·6	14·7		9·8	17·6		11·6	19·9	0·003
TV watching, h/week		18·6	11·5		17·9	11·1		18·4	11·8	0·35
Physical activity, METs-h/week		21·4	15·4		21·5	15·0		21·2	15·3	0·89
BMI, categories, %										
Normal weight	21·8			18·8			18·4			0·03
Overweight	48·7			48·4			46·2			
Obesity	29·5			32·8			35·4			
Baseline diagnosed morbidity, %										
Musculoskeletal disease†	50·0			51·2			49·9			0·81
CVD‡	7·3			4·6			5·1			0·01
Cancer	2·5			3·3			1·0			0·002
Chronic lung disease	7·0			8·4			7·6			0·47
Depression	8·2			8·2			10·0			0·24
Incident diagnosed morbidity, %										
CVD‡	10·6			9·5			7·6			0·06
Cancer	5·7			5·1			4·9			0·73
Chronic lung disease	10·3			11·6			10·0			0·42
Total protein, g/d		90·0	24·9		93·0	24·8		88·6	25·2	0·002
Total protein, g/kg/d		1·24	0·4		1·28	0·4		1·21	0·4	0·001
Breakfast total protein, g/d		20·7	9·6		13·2	6·5		9·2	6·0	<0·001
Lunch total protein, g/d		34·7	12·5		43·2	14·4		47·9	15·8	<0·001
Dinner total protein, g/d		31·8	10·9		33·7	13·3		28·7	17·0	<0·001
Snack total protein, g/d		2·8	4·8		2·9	4·6		2·8	5·0	0·96
Animal protein, g/d		58·2	20·4		62·0	20·0		60·5	21·3	0·001
Plant protein, g/d		31·8	10·2		30·9	10·7		28·1	10·0	<0·001
Energy, kcal/d		2063	580		2020	581		1910	551	<0·001
Fat, g/d		83·1	31·4		81·5	30·3		77·0	29·0	<0·001
Carbohydrate, g/d		223	66		211	65		194	60	<0·001
MEDAS score		6·7	2·0		7·3	1·7		7·3	1·7	<0·001

MET: metabolic equivalent.
For continuous variables, mean and SD are reported.
* ANOVA test was used for quantitative variables and the χ^2 test for categorical variables.
† Osteoarthritis, arthritis and hip fracture.
‡ Ischaemic heart disease, stroke and heart failure.

between mealtime protein intake distribution and all-cause mortality in older adults.

Most of the studies about daily protein intake distribution have investigated muscle- and weight-related outcomes, with inconsistent results[17–20,23]. A cross-sectional study among older adults found that frail, pre-frail and non-frail participants presented different protein CV values ($P < 0{\cdot}05$)[17]. In addition, participants with a low walking speed and exhaustion had a less even distribution of protein intake throughout the day compared with participants without these limitations ($P < 0{\cdot}05$)[17]. Also, prospective analyses from the NuAge study found that, after a 3-year follow-up, a more evenly distributed protein intake across meals was associated with higher lean mass and muscle strength in men and women but not with mobility[18,19]. In that study, mean protein CV did not differ in men and women at baseline ((0·55 ± 0·24 and 0·54 ± 24, respectively ($P = 0{\cdot}31$)) and after follow-up[19]. Additionally, three recent studies among older adults examined the association between mealtime protein distribution and physical function, as assessed with the Short Physical Performance Battery, and found no association[20,23,31].

In older adults, reaching or exceeding the current recommended dietary allowance of 0·8 g of protein/kg/d[32] is relevant as it lowers the risk of age-related sarcopenia and the risk of hip fractures, helps to maintain physical function, and promote recovery from illnesses, some of which are associated with increased mortality[33,34]. In our study, participants in the less

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Table 2. Hazard ratios (95 % confidence interval) for the association between sex-specific tertiles of the cumulative average of the CV of protein intake across meals and all-cause death during 10·6-year follow-up (*n* 3225)

	CV of protein intake across meals					
		Tertile 2		Tertile 3 (Less even distribution)		
	Tertile 1 (More even distribution)	Hazard ratios	95 % CI	Hazard ratios	95 % CI	P_{trend}
n	1076	1075		1074		
Total protein						
Person-years/*n* cases	10836/227	11033/188		10969/176		
Model 1	1·00	0·93	0·76, 1·12	0·87	0·71, 1·06	0·15
Model 2	1·00	0·94	0·77, 1·15	0·86	0·70, 1·06	0·16
Model 3	1·00	0·94	0·77, 1·15	0·88	0·72, 1·08	0·22
Animal protein						
Person-years/*n* cases	10828/225	10990/195		11020/171		
Model 1*	1·00	0·96	0·79, 1·16	0·86	0·70, 1·05	0·15
Model 2*	1·00	1·01	0·83, 1·23	0·88	0·72, 1·08	0·24
Model 3*	1·00	0·99	0·81, 1·21	0·89	0·73, 1·10	0·29
Plant protein						
Person-years/*n* cases	10905/200	11036/183		10897/208		
Model 1†	1·00	1·03	0·84, 1·26	1·12	0·91, 1·36	0·28
Model 2†	1·00	0·98	0·80, 1·21	1·02	0·83, 1·26	0·82
Model 3†	1·00	0·97	0·79, 1·20	1·02	0·82, 1·25	0·87

Model 1: Cox regression model adjusted for age, sex and protein (quintiles of g/kg/d).
Model 2: additionally adjusted for educational level (≤ primary, secondary or university), smoking status (never, former and current smoker), alcohol intake (quintiles of g/d), sedentary behaviour (tertiles of h/week watching TV), physical activity (quintiles of MET-h/week), BMI (normal weight, overweight and obesity), energy intake (quintiles of kcal/d) and for MEDAS score (tertiles).
Model 3: additionally adjusted for baseline morbidity (musculoskeletal disease, CVD, cancer, chronic lung disease and depression) and incident morbidity in 2012, 2015 and 2017 (CVD, cancer and chronic lung disease).
* Aditionally adjusted for the CV of plant-protein intake across meals.
† Additionally adjusted for the CV of animal-protein intake across meals.

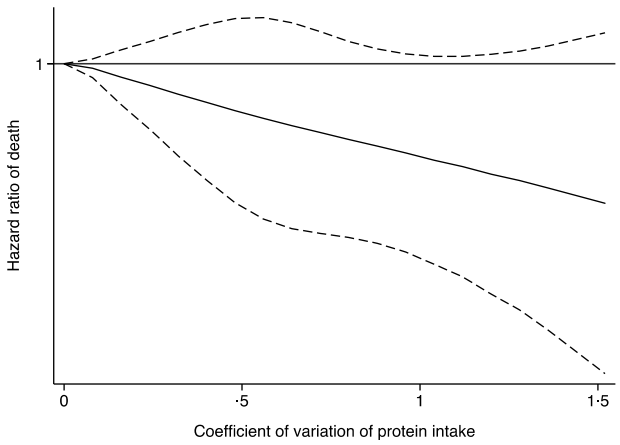

Fig. 1. Multivariable-adjusted spline curve for the association between the CV of total protein intake across meals and risk of all-cause death. Hazard ratios (95 % CI) from a Cox proportional hazards model adjusted for sex, age, protein (quintiles of g/kg/d), educational level (≤ primary, secondary or university), smoking status (never, former and current smoker), alcohol intake (quintiles of g/d), sedentary behaviour (tertiles of h/week watching TV), physical activity (quintiles of MET-h/week), BMI (normal weight, overweight and obesity), energy intake (quintiles of kcal/d), Mediterranean Diet Adherence Screener (MEDAS) score (tertiles), baseline morbidity (musculoskeletal disease, CVD, cancer, chronic lung disease and depression) and for incident morbidity in 2012, 2015, and 2017 (CVD, cancer and chronic lung disease). Dashed lines: 95 % CI.

even total protein intake distribution had the lowest mean total protein intake (1·21 ± 0·4 g/kg/d) and still it was above the recommended dietary allowance. While the total quantity of daily proteins is important, recent findings suggest that the distribution of these proteins is just as important. The biological mechanism that supports this hypothesis is that there is a maximum amount of protein that can be used in a single meal for the stimulation of muscle protein synthesis; this amount has been suggested to be about 25–30 g of high-quality protein per meal. Since the body has no capacity for protein storage, the exceeding number of amino acids can undergo oxidative degradation in different metabolic circumstances or results in urea synthesis[14–16].

Another study suggests that to determine the upper limit of protein in a meal, the individual body mass is also relevant and proposed a value of 0·4–0·6 g of protein/kg/meal as the necessary amount to stimulate muscle protein synthesis[35]. However, most studies about protein distribution differ on their methodology and alternate a host of factors that can influence protein metabolism such as protein source (e.g. whey and casein), the amino-acid composition of the protein, amount of protein, meal macronutrient combination and fasting time, among others. It has not been possible to reach a conclusion as there are studies that have found that ingesting most of the proteins of the day in a large meal does not affect muscle mass[21,36]. In our study, participants in two of their three main meals consumed nearly 30 g of proteins across all total protein intake distribution categories, which is in line with a recent study that found that distributing total protein intake over 1–2 meals of 30–45 g of protein each was enough to increase and/or maintain lean body mass and muscle strength[21].

Unlike most of the studies about daily protein intake distribution that had their highest protein intake at dinner[18–21,37,38], we found that in our study, it was at lunch. We believe that our

finding of a higher adherence to the Mediterranean diet in the intermediate and less even distributed protein intake groups may partially explain the null association found. Interestingly, this dietary pattern does not seek the evenness of nutrient intake throughout the day, instead, it focuses on the consumption of high amounts of fruits, legumes, vegetables, fish, white meat, olive oil and nuts. In other populations, consuming the biggest meal at dinner and not adhering to a good-quality dietary pattern might be the reason for the associations between an evenly distributed protein intake and positive health outcomes, since there is some evidence that a high energy intake at dinner is associated with several health problems[39–41].

We did not find a statistically significant association between animal and plant protein intake distribution with all-cause mortality. We had previously found that a higher intake of plant protein, but not animal protein, was associated with a lower risk of frailty[42] and that replacing animal protein with plant protein led to less unhealthy ageing[43]. As opposed to other studies[38,44], we did not use arbitrary cut-off points to calculate total protein CV, but instead, we opted to categorise total protein CV as a continuous variable, which allowed us to calculate animal and plant protein CV likewise; however, we could not compare our results with other studies, since to our knowledge, this is the first study that investigates animal and plant protein CV.

The strengths of the study are the large sample of the Seniors-ENRICA cohort and its prospective design with a large follow-up. Also, the estimation of protein intake through a validated diet history that included the habitual mealtimes and food intake occasions to help participants remember all the food ingested. Additionally, our analyses were adjusted for numerous potential confounders, although unmeasured confounding cannot be completely ruled out. A limitation in this study was that measurement error of dietary intake may exist and misclassification could occur. To lessen this limitation and to consider variations in diet intake during the follow-up, we averaged diet information at baseline and at follow-up for all the participants with this information available and excluded participants with implausible protein or energy intake. In addition, we performed analyses adjusting our models for incident comorbidity to also address a plausible change in dietary habits with the diagnosis of a chronic disease. Lastly, we excluded participants who died within the first 2 years of follow-up to avoid subclinical morbidity, although the possibility of reverse causation cannot be totally discarded.

Conclusions

In conclusion, among community-dwelling older adults in Spain, an uneven mealtime distribution of daily protein intake was not associated with all-cause mortality. Similar results were obtained for animal and plant protein intake mealtime distribution. Despite the fact of a lack of association with total mortality, the possibility of association with cause-specific mortality or with some relevant morbidities remains, and thus further studies are needed to shed light on these issues in older adults. Meanwhile, our findings support current dietary recommendations, which do not consider the mealtime distribution of protein intake.

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The authors' responsibilities were as follows: D. B. E-L., E. A. S. and E. L-G.: designed the research; D. B. E-L., F. F. C.: performed the statistical analyses; D. B. E-L., E. L.-G.: drafted the manuscript. E. L-G.: supervised the conduct of research and had primary responsibility for final content and all authors: read and approved the final manuscript.

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Supplementary material

For supplementary material/s referred to in this article, please visit https://doi.org/10.1017/S0007114522003695

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