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Original Article

Higher Animal-Derived Dietary Protein Intake is Associated with Lower Prevalence of Frailty

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SUMMARY

Background: It is accepted that malnutrition is involved in the pathophysiology of frailty. However, the relationship between dietary animal-derived protein (DAP) intake and the prevalence of frailty is still unclear. Using data from the FRAIL Project, we aimed to determine whether DAP consumption is associated with frailty in community-dwellers aged 65 years and older.
Methods: In this cross-sectional study involving only participants older than 65 years, DAP intake was evaluated through specific items of the Mini-Nutritional Assessment (MNA). Frailty status was assessed according to the Cardiovascular Health Study (CHS) model, which consists of five items (unintentional weight loss, weakness, slow gait speed, exhaustion, low physical activity). Frailty was defined as the presence of at least 3 criteria, and pre-frailty as the presence of 1 or 2.
Results: Among the 407 participants enrolled (mean age 77.9 ± 4.5 years; 51.6% women) the prevalence of frailty was 9.3%, and of pre-frailty 26.5%. Daily DAP consumption was reported by 206. Multinomial logistic regression analysis, adjusted for potential confounders, showed that higher DAP intake was associated with a significant reduction in frailty (odds ratio, OR = 0.41; 95% confidence intervals, CIs: 0.16–0.98) and pre-frailty (OR = 0.46; 95%CI: 0.27–0.79).
Conclusion: Daily animal protein intake is associated with a lower prevalence of frailty in community-dwelling older subjects, suggesting that a diet rich in animal proteins could be useful in preventing frailty. Simple specific questions drawn from the MNA may be an effective tool to gather useful information on protein consumption in elderly people and on their nutritional risk of being frail.

1. Introduction

Frailty, which is traditionally defined as "a state of increased vulnerability to stressors that results from decreased physiologic reserve in multiple organ systems that cause limited capacity to maintain homeostasis".[1] is a common condition in older people. Frailty has been associated with a higher risk of several deleterious outcomes in older people, such as disability, hospitalization and institutionalization. Recent evidence suggests that frailty may be regarded as a potential risk factor for cardiovascular[2] and metabolic[3] diseases, which could further worsen the typical transition from frailty to disability and from disability to death.

While numerous conditions are recognized as possible risk factors for frailty, diet might play a pivotal role in the development of this condition.[4] Of particular interest is the association between animal protein intake and frailty. An adequate intake of dietary proteins seems to be fundamental to maintaining muscle mass, since it ensures the provision of amino acids and stimulates protein synthesis, thereby preventing sarcopenia and frailty.[5] At the same time, older people, even if healthy, need to make up for age-related changes in protein metabolism, such declining anabolic responses to ingested protein. They also need more protein to offset inflammatory and catabolic conditions associated with chronic and acute diseases that occur commonly with aging.[6]

In a cohort of 1,345 older French participants,[7] the prevalence of frailty was significantly (59%) lower among those with a higher protein intake than those with a lower intake. These findings were prospectively confirmed in the Health, Aging, and Body Composition study, in which participants in the highest group of protein intake lost nearly 40% less appendicular lean mass than did those in the lowest quintile, after 3 years of follow-up.[8] Other studies substantially confirmed the association between low protein intake (particularly of animal origin) and frailty.[9,10] In order to confirm this association, however, further studies are needed for at least three reasons. First, higher protein intake seems to be associated with a higher cardiovascular mortality rate,[11,12] even if other works reported that higher protein intake is associated with lower cardiovascular risk.[13] Second, many older people suffer from renal failure, a condition in which the intake of proteins (particularly of animal origin) should be strictly limited.[14] Finally, higher protein intake seems to be associ-

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ated with a higher insulin sensitivity and lower glucose tolerance, also in the muscle mass,[15] suggesting that the appropriate intake of proteins in the elderly should be better defined.[16]

Given this background, our study aimed to investigate whether higher dietary animal protein (DAP) consumption is associated with a lower prevalence of frailty in a cohort of community-dwellers aged 65 years and older living in Genoa, Italy.

2. Subjects and methods

2.1. Data source and subjects

The present study used data from the ongoing FRAIL project, an observational cohort study on the Italian older population living in community in Genoa, a city in northern Italy. In Genoa, the aging index (i.e. the number of elders per 100 persons younger than 15 years old in a specific population) was 235.9 in 2013, compared with the Italian mean value of 152.7 and the European (EU28) mean value of 117.7 (https://open-data.europa.eu/en/data/publisher/estat). The main objective of the FRAIL project is to investigate the local prevalence of frailty, the associated factors (biological, lifestyle-related and socio-economic) and subsequent health outcomes.

No specific inclusion/exclusion criteria were adopted.

The local ethics committee approved our study protocol, and participants gave their written informed consent to the study.

2.2. Animal dietary protein intake (exposure)

Nutritional status was examined by means of the Mini-Nutritional Assessment (MNA®) tool, an internationally validated method consisting of 18 items covering anthropometric measures, health status, dietary patterns, and subjective assessments of an individual's nutritional and health status.[17] In this questionnaire, participants are asked about their protein intake, specifically: their daily consumption of dairy products (e.g. milk, cheese); their weekly consumption of legumes or eggs and their daily consumption of meat, fish or poultry.

As the main exposure variable, we considered the DAP intake, which was calculated on the basis of the consumption of dairy products plus meat/fish/poultry and categorized as lower DAP (not every day) and higher DAP (every day) consumption. Secondary exposure variables were: total protein intake and the daily consumption of meat/fish/poultry.

2.3. Frailty definition (outcome)

Fried defined frailty by using 5 measurable items (unintentional weight loss, low physical activity level, weakness, exhaustion, and slow gait speed).[18] In the present study, we used a slightly modified version of this definition, as follows:

1. Weight loss: unintentional weight loss of ≥ 5% of body weight in the previous year.
2. Weakness: grip strength in the lowest 20% of the study sample, adjusted for gender and body mass index.
3. Poor endurance and energy: self-reported exhaustion, identified by the same criterion used in the original description of the 'frail' phenotype.[18]
4. Slowness: gait speed below 0.8 m/sec in a 4-meter walk at usual pace.[18]
5. Low physical activity level: PASE score[19] (see below) in the lowest quintile of the study sample, adjusted for gender.

Participants were classified as: a) frail if they met 3 or more of the 5 modified Fried criteria; b) pre-frail if they met 1 or 2 criteria, and c) non-frail if they met none of the criteria.

2.4. Covariates

Participants were examined at a city hospital by trained physicians and nurses, who evaluated: 1) body weight, height and body mass index (BMI, kg/m^2); 2) disability level through the Barthel index, a common tool that measures disability or dependence in activities of daily living; 3) physical activity, evaluated by using the Physical Activity Scale for the Elderly (PASE),[19] a validated scale for assessing physical activity level in the elderly. This scale covers 12 different activities, including walking, sports and housework, and is scored from 0 upwards; 4) comorbidities, assessed by using the Cumulative Illness Rating Scale (CIRS),[20] a validated physician-rated index calculated by collecting the subject's medical history, conducting a physical examination, and reviewing the medical information available; 5) cognitive status, assessed by using the Short Portable Mental Status Questionnaire (SPMSQ);[21] 6) pressure sore risk, assessed by means of the Exton-Smith scale.[22]

2.5. Statistical analyses

For continuous variables, normal distributions were tested by means of the Shapiro-Wilk test. P values were calculated by using Student's t-test for independent samples for continuous variables and chi-square test for categorical ones, by DAP intake (higher vs. lower).

Known factors (i.e. age, sex, body mass index, cognitive status, Exton-Smith scale, disability, co-morbidity, education and number of drugs) associated with frailty and/or nutritional status were included in the analysis. The predictors included in the final model were all the variables that reached a $p < 0.10$ in the univariate analysis. As the outcomes of interest were two (frailty and pre-frailty), a multinomial logistic regression analysis was run. A backward model was applied in order to obtain the best set of factors associated with frailty and pre-frailty. Odds ratios (ORs) and 95% confidence intervals (CIs) were used to compare the prevalence of frailty and pre-frailty by DAP status, the subjects with lower DAP being taken as the reference. In secondary analyses, we explored whether daily total dietary protein (TDP) or meat/fish/poultry intake, instead of DAP, could change our findings.

All analyses were performed by means of the SPSS 21.0 for Windows (SPSS Inc., Chicago, Illinois). All statistical tests were two-tailed and statistical significance was assumed for a p-value < 0.05.

3. Results

The sample included 407 older participants with a mean age of 77.9 (4.5) years, mainly women (51.6%).

As shown in Table 1, 206/407 participants (= 50.6%) reported DAP intake every day. Compared with those with lower DAP intake, these subjects did not significantly differ in mean age, percentage of females, BMI, Barthel Index or self-reported physical performance levels. Similar findings emerged with regard to education and cognitive and nutritional status (Table 1).

In the sample as a whole, the prevalence of frailty was 9.3%, and of pre-frailty 26.5%. As shown in Fig. 1, the prevalence of frailty and pre-frailty was significantly higher in people with lower DAP intake ($p = 0.009$).

In the multinomial logistic regression analysis, in which subjects with a lower DAP intake were taken as the reference, and after adjustment for potential confounders (Barthel index, CIRS-SI, years of education and number of drugs), participants with a higher DAP

Table 1
Baseline characteristics according to dietary animal-derived protein (DAP) intake.

Variable	Lower DAP (n = 201)	Higher DAP (n = 206)	*p* value*
Age (years)	77.9 (4.5)	77.9 (4.5)	0.97
Females (n, %)	108 (53.7)	102 (49.5)	0.43
BMI (Kg/m^2)	28.5 (17.0)	27.5 (15.9)	0.55
Barthel index (points)	97.7 (7.0)	98.2 (5.9)	0.43
PASE (points)	103.5 (67.4)	1044 (54.3)	0.87
CIRS-SI	1.44 (0.30)	1.42 (0.28)	0.56
Number of drugs	4.0 (2.5)	4.3 (2.9)	0.22
Exton-Smith scale (points)	19.3 (1.5)	19.4 (1.3)	0.26
Education (years)	10.2 (4.9)	10.2 (4.9)	0.96
SPMSQ (points)	9.6 (1.2)	9.7 (0.9)	0.39
MNA (points)	26.8 (5.7)	27.6 (1.9)	0.08
Frail (n, %)	20 (10.0)	18 (8.7)	0.009
Pre-frail (n, %)	67 (33.3)	41 (20.0)	

Numbers are mean values (and standard deviations) or numbers (and percentages), as appropriate.
* Unless otherwise specified, *p* values are calculated by means of an independent Student T-test for continuous variables and a Fisher's exact test for categorical variables.
BMI, body mass index; CIRS-SI, Cumulative Illness Rating Scale-Severity Index; DAP, dietary animal-derived protein; MNA, mini-nutritional assessment; PASE, Physical Activity Scale for the Elderly; SPMSQ, Short Portable Mental State Questionnaire.

intake displayed a 59% lower prevalence of frailty (OR = 0.41; 95%CI: 0.16–0.98; p = 0.03) and a 54% lower prevalence of pre-frailty (OR = 0.46; 95%CI: 0.27–0.79; p = 0.005) (Table 2). The multivariate analysis suggests that Barthel index and years of education significantly reduced the odds of frailty, whilst comorbidity significantly increased the odds of frailty. Conversely, Barthel index and number of drugs were significantly associated with the presence of pre-frailty (Table 2).

In the sensitivity analysis, we explored whether the association between DAP and frailty/pre-frailty was exclusive; this was done by replacing DAP with daily TDP or meat/fish/poultry intake. TDP intake proved to be not significantly associated with the presence of frailty or pre-frailty (details not shown), whilst the daily consumption of meat/fish/poultry reduced the odds of being frail (OR = 0.39; 95%CI: 0.15–1.00; p = 0.05) and pre-frail (OR = 0.42; 95%CI: 0.25–0.72; p = 0.002).

4. Discussion

In this cross-sectional study, we found that higher dietary animal protein intake was associated with a 59% lower prevalence of frailty and a 54% lower prevalence of pre-frailty, after taking into account the role of potential confounders. Total dietary protein intake was not associated with the presence of frailty, whilst the daily consumption of meat/fish/poultry reduced the odds of being frail and pre-frail. Taken together, these findings suggest that animal proteins are essential to preventing frailty in older people.

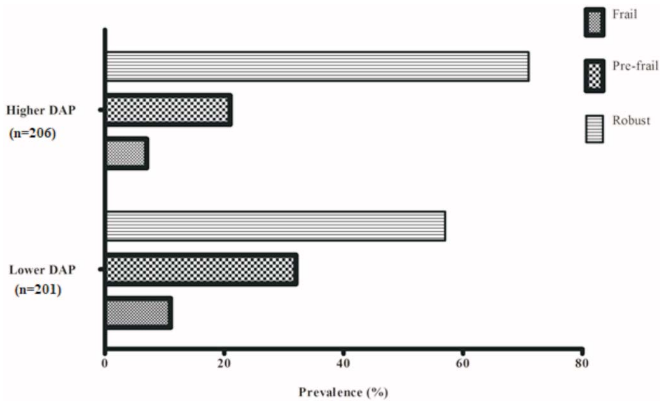

Fig. 1. Prevalence of frailty and pre-frailty by animal protein intake. Chi-square test: p-value = 0.009.

In our study, the prevalence of frailty and pre-frailty proved to be in agreement with the current literature data suggesting that frailty affects about 10% and that pre-frailty affects 25–50% of community-dwelling elderly individuals.[23]

It is of relevance that, after subjects had been divided on the basis of DAP intake, no significant differences emerged in terms of age, gender, co-morbidities or the number of drugs taken, all of which are well-known risk factors for the onset of frailty. These findings indirectly confirmed not only the importance of DAP in the development of frailty, but also a peculiar relationship between DAP and frailty. The criteria suggested by Fried et al. mainly highlight physical frailty, a condition that is often a consequence of sarcopenia,[24] that is probably early in the development of disability typical of older age. We can hypothesize that in this cohort of substantially healthy older people, the prevalence of disability and medical conditions is too low for detecting any difference by DAP intake contrary to frailty and pre-frailty that are present in a person over 10 and in one over four, respectively.

Animal protein intake, together with physical exercise, is one of the most important anabolic factors in the building/maintenance of muscle mass.[5] In this sense, our study further confirms that meat is an optimal source of high-quality proteins, which are essential for optimal muscle development. Indeed, meat contains a large quantity of essential amino acids, which are fundamental to the building and conservation of muscle mass, also in the elderly. Probably, other factors (such as creatine and carnitine)[25,26] and other nutrients (such as iron and cobalamin) positively contribute to the lower prevalence of frailty among people with a higher DAP intake.[27] Like other authors,[9,10] we found that higher animal (but not total) protein intake was associated with a lower prevalence of frailty, again underlining the importance of proteins of animal origin in preventing frailty. It should be observed that the consumption of animal proteins in older

Table 2
Factors significantly associated with frailty and pre-frailty in the multivariate analysis.

	Frailty odds ratio (95% CI)	*p*-value	Pre-frailty odds ratio (95% CI)	*p*-value
Higher DAP intake	0.41 (0.16–0.98)	0.03	0.46 (0.27–0.79)	0.005
Barthel index	0.50 (0.41–0.60)	< 0.0001	0.58 (0.49–0.70)	< 0.0001
CIRS-SI	6.87 (1.31–36.1)	0.02	2.60 (0.85–8.00)	0.09
Education (years)	0.82 (0.74–0.93)	0.001	0.95 (0.90–1.00)	0.06
Number of drugs	1.03 (0.84–1.25)	0.81	1.16 (1.04–1.30)	0.009

Unless otherwise specified, data are presented as odds ratios and 95% confidence intervals.
Age, sex, body mass index, short portable mental state examination and Exton-Smith scale were initially included, but they were removed from the final model, having a p-value > 0.20.
CIRS-SI, Cumulative Illnesses Rating Scale-Severity Index; DAP, dietary animal-derived protein.

people is often limited by several factors, including poverty, teeth and shallowing issues and difficulty to digest animal foods.[28]

Moreover, our study confirms that DAP should be recommended in some categories at higher risk of frailty, namely the disabled, the less educated and those with poly-comorbidities and/or on poly-medication. These categories comprise older persons at particularly high risk of both malnutrition and frailty. Among these factors, poly-medication probably merits some additional comment. The fact that many and various medications reportedly affect taste and smell is a testament to the complexity of the gustatory and olfactory systems. Older people who take many medications are at increased risk of developing malnutrition.[29] Indeed, drugs are able to modify several pathways involved in taste and smell, including the reception, transduction, propagation and perception of a chemical tastant or odorant.[30] Meat is probably one of the aliments most frequent subject to such alterations, particularly if eaten by individuals with other impairments, such as dysphagia or edentulism.[30]

The findings of our study should be interpreted within its limitations. The first is its cross-sectional nature, which does not permit us to determine whether lower DAP intake is predictive of frailty or vice versa. Secondly, the method of assessing dietary protein intake displayed some shortcomings, including its approximate quantification of protein intake and the lack of precise specification of the type of proteins; however, since it is difficult to get reliable information on the diet of elderly people (in particular if disabled or cognitively impaired),[31] our data suggest that it could be sufficient to ask elderly patients if they eat fish or meat every day, in order to gather easily obtainable information on their nutritional risk of being frail. Regarding this topic, further studies investigating the relationship between dietary proteins intake assessed with more detailed methods (such as food frequency questionnaire) with frailty are needed. Third, the sample size was small, particularly in comparison with the other studies present in the literature. Finally, we used a slightly different definition of frailty, and using different criteria could have added another bias to our findings.[32]

In conclusion, the daily intake of animal-derived dietary protein is associated with a lower prevalence of frailty and pre-frailty in community-dwelling older subjects, suggesting that a diet rich in proteins of animal origin is necessary in order to prevent or delay frailty in older people. Moreover, simple specific questions (like those we have drawn from the MNA) may be an easy and effective way to get useful information on protein consumption in the elderly. Our follow-up results and future studies, particularly with a longitudinal design, are needed in order to confirm these preliminary findings.

Conflict of interest

No potential conflicts of interest were disclosed.

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