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REVIEW ARTICLE

The relationship between protein quantity, BMD and fractures in older adults

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Abstract

Background Previously, no large-scale literature reviews have focussed on the relationship between dietary protein and its impact on bone mineral density (BMD) and fracture risk—as measures of bone health—in older adults and its potential impact as a primary prevention tool.

Aims The aim of this study was to assess the impact of varying dietary protein levels on bone health.

Methods A literature review of trials concerning older adults' (>50 years of age) and animals' varying protein intake in the diet and its effect on BMD (human and animal) and fracture risk (human only) was carried out. Additionally, a review of dietary assessment tools used in these studies was also analysed.

Results Ten out of fourteen trials assessing BMD and dietary protein quantity in humans and 3/4 in animal trials found a positive relationship between these two parameters. Four out of seven trials investigating the relationship between dietary protein quantity and fracture risk displayed a positive, protective effect of dietary protein levels on fracture risk. Sixty-two percent of studies used the Food-Frequency Questionnaire assessment method.

Discussion Increased protein intake in the diet is beneficial to bone health and reduces morbidity and mortality. The importance of using dietary protein, along with calcium and vitamin D, as a primary preventative strategy should be stressed, given the health and cost benefits that this would deliver, with a possible need for a higher level of protein in the diet of an elderly person than what is currently recommended.

Key points

Summary-We found that a higher quantity of protein consumed in the diet of those >50 years resulted in a higher bone mineral density and therefore confers a protective benefit for the bone health of this population.-It was also found that a higher quantity of protein in this cohort also reduced their fracture risk, and therefore, their morbidity and mortality.-We recommend that a higher recommended daily amount of dietary protein should be instituted in those who are more at-risk of fractures due to declining bone health, including those >50 years of age. *Research questions*-Although protein quantity is well discussed in our paper, the importance of protein quality on the bone health of this population, either animal or vegetable, is also an important question to discuss in the future.-Further studies to determine more accurately the exact benefit that increased protein quantity in the diet would have on specific cohorts (i.e. 70–80 years of age etc.) would be most beneficial.-In our conclusions, we recommend a greater RDA of dietary protein in those >50 years than what is currently recommended. Greater discussion and debate on this topic would be most welcome in this regard.

Keywords BMD · Elderly · Fracture · Nutrition · Protein

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Introduction

Osteoporosis is a systemic skeletal system disorder, characterised by diminishment of both bone architecture and bone mass, precipitating in an increase in bone fragility, risk of fracture [1, 2] and increased hospital admission and co-morbidities [3]. There is a significant social cost associated with hip fractures in Ireland, with the total in-patient cost alone being €58 million per annum for those over 65 years, which is set to increase [4]. Bone mineral density (BMD) is an indirect measurement tool for diagnosing osteoporosis, which is itself routinely measured using dual-energy x-ray absorptiometry (DXA), with osteoporosis defined as a T-score ≤ −2.5 (2 · 5 standard deviations below the young adult's average) [5]. The fracture-risk assessment tool (FRAX) is used to judge an individual's 10-year risk of developing a hip fracture and/or major osteoporotic fracture [6].

Weight bearing exercise, genetic factors, tobacco smoking, alcohol intake, age, hormone levels, gender, race, and nutrition all contribute to bone health [7–13]. Nutrients, including micronutrients—calcium, vitamin D, phosphorous and magnesium—are key components in the process of bone formation. However, macronutrients such as protein are an often neglected bone element and contributor to bone health through muscle mass and falls prevention, and the quantifying of its consumption in the population is important to physicians when considering treatment bone-related diseases [13–20]. Furthermore, dietary protein may also influence bone mineral content and density through its contribution to greater muscle contractions [21–24].

Protein accounts for approximately 30% of the mass of bone tissue and 50% of its volume [25]. The RDA of dietary protein is 0.6–0.8 g/kg per day for adult males and females, although studies have suggested that this figure could be increased to 1.0 g/kg or higher, especially for elderly populations [26, 27]. Certain mechanisms have been postulated while others have been established in relation to the association of protein with calcium absorption and urinary secretion. Protein has been observed to increase insulin-like growth factor (IGF-1) hormone production and secretion [13]. IGF-1 contributes variously to bone growth, including triggering chondrocyte proliferation and differentiation in the epiphyseal growth plate, involvement in osteoblast proliferation, differentiation and mineralization, trabecular and cortical bone formation and collagen synthesis [28–30]. It has also been observed that a decreased concentration of IGF-1, which can result from reduced dietary protein intakes [31], can indirectly lead to a decrease in calcium and phosphorous absorption in the intestine [32].

Dietary protein intake and its influence on the body's calcium balance, and therefore bone growth, are complex. An increase in protein consumption has been associated with an increase in urinary calcium concentrations [33, 34]. It has been suggested that during the oxidation of sulphur-containing amino acids, protons are released, which increase renal acid excretion and acid production [35]. This translates to the oxidation process contributing to the body's net acid load, causing increased bone dissolution, with the overall acid-base balance of the body being an important contributor to bone health [36]. The increased bone resorption of calcium was thought to act as a buffer to this increased acid load, with increased renal acid excretion of calcium as a result [37–39]. But more recent studies using a much larger dataset contradicted this, showing no significant difference between the biochemical indicators of bone turnover or whole body calcium retention in high protein or low protein diets [40]. This contradiction could be explained, among others, by the fact that foods which contain protein also contain hypocalciuric elements such as phosphorous [41–43]. Kerstetter et al. reported a strong association between dietary protein intake and intestinal calcium absorption [44] while conversely, both Surdykowski et al. and Fenton et al. concluded that increased protein intakes in the diet are not associated with significant blood pH changes and dispute the acid-base hypothesis [45, 46].

This confusion may have been due to the assumption of some studies that an increase in urinary calcium related to changes in bone turnover or bone health generally. Gaffney-Stomberg et al. reported a net gain of calcium with a high protein diet in rats, even when the resultant increase of urinary calcium was taken into account, with no changes in indicators of bone turnover [47]. In human isotopic studies, this trend has been repeated [40, 44, 48].

Advances have been made in understanding the underlying mechanism to which protein, or more accurately, the amino acids can increase calcium absorption. It is possible that calcium and protein act synergistically at the level of the cell, with one relying on the other to exist for the maintenance and growth of bone [30]. The calcium-sensing receptor (CaR), which is present in multiple organs, has been shown to be significant in maintaining calcium levels as well as contributing to skeletal growth and maintenance. Amino acids can increase the sensitivity of these receptors to calcium, therefore resulting in an increased uptake of calcium through these cells [13, 30].

There is considerable debate on whether protein quality, either vegetable or animal protein, is an important contributor to protecting and enhancing bone health. In some studies, vegetable protein was found to confer a greater benefit when compared with animal protein [49]. There is a degree of inconsistency in studies exploring the superiority of protein from vegetable rather than animal sources [13]. Furthermore, a potential disadvantage of consuming protein from vegetable sources is that vegetables may not contain all of the essential amino acids, unlike animal sources.

There is much controversy on the ideal quantity of protein intake and type among different population groups (especially older adults), as well as the most accurate and efficient means of evaluating dietary protein intake. The "one size fits all" model of adequate dietary protein intake among all age and population groups is not appropriate and may have unintended consequences for the elderly population, who require more dietary protein [27].

Therefore, our aims are to (1) review the evidence of the relationship between BMD and protein quantity in animal subjects as well as assessing this relationship among those ≥50 years of age and (2) assess the association between the concentration of protein consumed in the diet and bone fracture (hip fracture).

Materials and methods

We searched studies on various databases, including ScienceDirect, PubMed and EBSCO. The search strategy involved using specific terms: "Protein, bone, elderly, BMD" and "Protein, bone, elderly, fracture risk". The reference list of each study and previous review articles was also examined. The search was not restricted regarding the date of the studies, with any articles meeting the inclusion criteria included in the review. The initial population was further narrowed, with any literature which included populations under 50 years of age being discounted. The majority of studies which assessed BMD utilised DXA scanning, with a small number of studies using single-photon absorptiometry or ultrasound technology [50–52]. One other study used dual photon absorptiometry for the baseline readings, with the 4-year follow-up using DXA [53]. Studies fit for qualification in the review process were also assessed by two reviewers with clinical and laboratory expertise. There was no journal article which posed a language restriction problem, and no authors had to be contacted for the literature review. All studies that were included in the main review had to be published, and reference was made to literature related to opinions in the discussion. A small proportion of unpublished literature was included only in the analysis of the conclusions of the studies, rather than the studies/trials themselves.

For assessing the relationship between protein quantity in the diet and BMD, we included studies which measured BMD using a DXA scan at sites such as the radius, femoral neck, total hip, lumbar spine, total hip and total body. For assessing the protein quantity and fracture risk/history association, publications which analysed hospital records were reviewed, depending on each individual study. Fractures caused by events such as road traffic accidents were discounted in many of the studies. The review of the assessment of dietary intake was carried out in the context of the studies assessing an individual's protein consumption and BMD and fracture risk/history, respectively. We reviewed all publications on patients older than 50 years which related to protein quantity and fracture risk as well as BMD. There was a requirement for the subjects to be greater than 50 years, with studies discounted even if the average age was above 50 years but the range included those under 50 years, e.g. Sahni et al. [54]. Studies which included a maximum of two variables were included in the study, with the review of the studies taking this into account in the conclusions that were reached. This exclusion criteria and the process of selection is displayed in the flowchart below **(**Fig. 1**).**

To identify the volume of protein consumed in an individual's diet, dietary assessment tools such as the Food Frequency Questionnaire (FFQ), dietary records and food diaries are used in the screening of large populations and to accurately identify those who are at risk due to their consumption patterns.

Results

BMD (Tables 1 and 2)

Of the 287 titles that we identified, 18 studies aimed to evaluate the relationship between protein quantity intake in the diet and BMD. Animal studies (Table 2) composed 4 of these, while 14 were on human subjects (Table 1). Of these studies, 13 found a positive correlation between protein and BMD, while 3 found either no relationship or possibly negative relationship. Two studies exhibited inconclusive results.

Regarding the animal studies, one of these displayed no association while the remaining three showed a positive correlation. All of the population in the animal studies were growing or adult rats, either male or female. None were ovariectomized. Of the positive results, the studies focussed on the low BMD effects of a low-protein diet, along with negative effects on cancellous bone mass and trabecular thickness in some instances also found [58]. A control was used in all the animal studies, which was 15% casein for 2 of the studies and 18% and 24% protein diet for the remaining studies, representing adequate levels of protein in the diet.

Of the 14 studies on human subjects >50 years, 10 found a positive association between protein quantity in the diet and BMD. Of these, eight had protein as an independent variable in their assessment. The two remaining studies had a variation in calcium or vitamin D intake. Aside from these, the remaining 8, some of which were wide-ranging epidemiological studies, do show a strong positive correlation, independent of other factors. There was a significant variation in the number of subjects in each of the studies. Chan et al. had the highest number of participants, with 1225 men and 992 women. Geinoz et al.'s study of 74 hospitalised patients had the lowest number of participants. In the studies which portrayed a positive correlation, a significantly higher BMD was found in the femoral neck and lumbar spine of the human subjects [50, 53, 57], as well as total hip [51, 55] and total body [27, 59] of those who were not protein malnourished.

Bone fracture

A total of seven studies were identified which aimed to evaluate the relationship between protein quantity and bone fracture risk in those over 50 years (Table 3). Of these, four studies found a positive correlation between dietary protein quantity and bone fracture risk. One study found no association, with two studies with mixed results, depending on the ratio of animal to vegetable protein consumed.

Wengreen et al. observed that those who consumed the highest quartile of protein (17.4–30.8% of total energy) had a 65% reduction in the risk of hip fracture. The study also reported that the association between protein consumption and its protective effects from fracture risk dissipated with increased age. The authors also observed that a higher protein intake conferred a protective effect from hip fracture in 50–69-year olds, with this protective effect disappearing in the 70–89-year age bracket [61].

Discussion

Protein quantity in the diet and BMD

The results from these studies convey the positive change in BMD with an increase in protein consumption, with 72% of the studies consistent with this finding. The majority of the studies in this review observed a positive relationship between protein consumption and BMD in older adults and the importance of the interaction between protein and calcium in bone formation and maintenance. This emphasises the need for adequate intake of all key nutrients in the prevention of bone-related diseases such as osteoporosis. However, not all studies were in agreement—2 of the 14 studies observed no association between consumption and BMD [21, 34].

For example, Kerstetter et al. in a combination of 13 younger and postmenopausal women observed no association between protein intake and femoral neck and lumbar spine BMD [44]. However, in this study, the relationship between a ratio of protein and calcium with bone was assessed, rather than protein on its own.

Importantly and as previous studies have suggested that although BMD is a good marker of bone strength, it is only one factor in the process, with bone mineral mass and architecture among other important contributors to bone strength [64]. Even with these, variance on the development of osteoporosis can occur. Therefore, assessing the role of intrinsic tissue quality may be a more accurate measure of the risk of osteoporosis developing [65]. Furthermore, the measurement and assessment of important structural proteins such as collagen and bone turnover (and the technical challenges that accompany this) in determining overall bone health should be considered for future studies.

Protein quantity in the diet and risk of fracture

The majority of studies reviewed displayed a positive relationship between protein consumption and fracture risk [59–62]. Many of the studies which displayed a positive correlation between protein quantity and fracture risk also emphasised the importance of correct calcium intake as well as protein intake in the diet [54]. However, this interdependent phenomenon between protein and calcium was not as evident among more elderly participants (aged >50 years [54]) which reinforces the

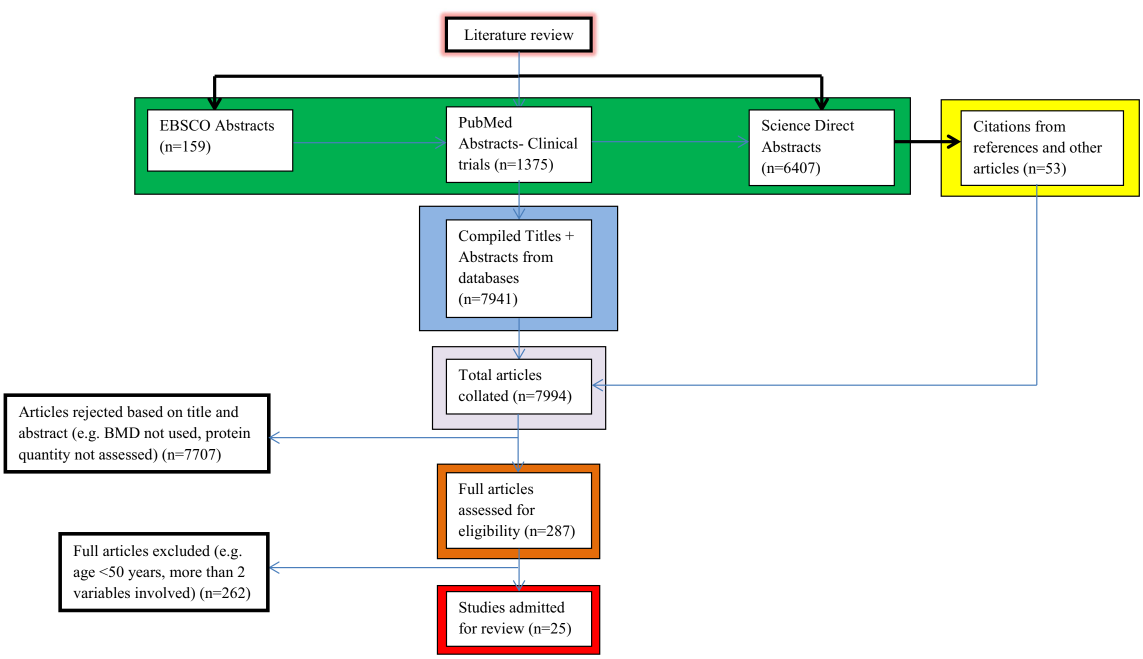

Fig. 1 Exclusion criteria and the process of selection

Table 1 Comparison of studies identified that evaluate the effect of protein quantity in the diet on bone mass (BMD)-human subjects

Study Reference	Subjects (community or hospital, ages, number)	Characteristics of trial	Outcomes	Type of questionnaire used
Thorpe et al. [55]	161 Postmenopausal women	Protein sulphur load included. 80% were taking supplemental calcium, 31% on hormone replacement therapy, 20% on osteoporosis medication. Observational study	Protein intake positively associated with aBMD.	United States Department of Agriculture multiple-pass 24-h recall.
Geinoz et al. [50]	74 hospitalised patients for various medical indications—48 women, (mean 82 years); and 26 men (mean 80 years)	Divided into 2 groups according to their intake of dietary protein while on a regular diet, assessed in the first 28 days in hospital. 1 group had equal to or greater than 1 g of protein per ideal body weight (kg). Other group had less than 1 g/kg protein in their diet.	Patients in the moderate/high protein intake group displayed higher BMD at the level of the femoral neck	3-day food diary
Dawson-Hughes et al. [81]	161 men and 181 women (≥65 years)	Protein intake was classed as tertiles as a % of total energy (1: 9.64–15.49 2: 15.53–18.15 3: 18.16–29.14). Protein quantity assessed within a randomised, placebo-controlled trial evaluating effects of calcium and vit D supplementation, 3-years in length	Positive assoc. between dietary protein consumption and change in BMD (total-body and femoral neck) in presence of calcium citrate malate and vitamin D supplementation.	126-item food-frequency questionnaire (Willett 1988 version).
Chan et al. [82]	1225 Chinese men and 992 women ≥65 years	Dietary intake evaluated at baseline over 2 years (2001–2003). Univariate associations first assessed, then multivariate regression model. Prospective cohort study	Association between lower protein intake in men and BMD loss in hip and femoral neck, but this diminished when adjusted for calcium and vit D.	FFQ, with assessment of mean nutrient quantitation/day using food tables from Chinese Medical Sciences Institute and McCance and Widdowson database.
Kim et al. [49]	134 osteoporotic and 137 non-osteoporotic postmenopausal women (52–68 years) recruited during a visit to a clinic.	Tertile classification for nutrient variables (values not given). Controls used (137 non-osteoporotic women).	Diets rich in animal protein or total protein are risk factors for osteoporosis, diets with low vegetable protein are protective	FFQ
Kerstetter et al. [83]	208 women (≥60 years) and men (≥70 years)—no further breakdown.	Subjects halved into 45 g whey protein group or isocaloric maltodextrin supplement (low protein) diet for 18 months. Randomised, double-blind, placebo-controlled trial.	No difference in BMD, but IGF-1 raised.	Does not specify- diet questionnaire and history used by dietitians
Devine et al. [51]	1077 women (75 ± 3 years)	Expressed in tertiles (<66 g, 66-87 g, >87 g). Regression analysis.	Positive association between protein intake and BMD after adjustment for co-variables.	Semi-quantitative FFQ
Zhu et al. [56]	219 healthy women aged 70 to 80 years	Randomization to either 30 g of whey protein drink or a placebo drink	No difference in protein concentration and BMD, although IGF-1 was raised	3-day weighed food record. FFQ was used to exclude the ineligible subjects

Table 1 (continued)

Study Reference	Subjects (community or hospital, ages, number)	Characteristics of trial	Outcomes	Type of questionnaire used
		containing 2.1 g of protein. Randomised, double blind, placebo-controlled prospective trial over 2 years		
Hannan et al. [53]	Framingham Cohort: 224 men, 392 women. Mean age-74.5 ± 4.4 years (range: 68–91)	Protein was expressed as a percentage of total energy as well as animal protein, protein in g/day and protein in g/kg/day. Divided into quartiles dependent on protein intake (0.21–0.71, 0.72–0.96, 0.97–1.23, 1.24–2.78).	Protein found to be protective against spinal and femoral bone loss. Animal protein also conferred a protective effect, even at quantities several fold greater than the RDA	Semi-quantitative FFQ
Kerstetter et al. [57]	1822 white women aged >50 years.	Protein levels divided into quartiles. Mean g/day- Q1: 31 ± 8, Q2: 50 ± 4, Q3:65 ± 5, Q4: 96 ± 22,	Women in the 1st and 2nd quartile had significantly reduced BMD values compared to the highest protein intake in the 4th quartile, even when the sample was restricted to women with adequate calcium.	FFQ
Ilich et al. [26]	136 generally healthy Caucasian women at least 5 years post-menopausal (68.7 ± 7.1 years)	Multiple regression models	Protein consistently showed a high correlation with bone mass in almost all skeletal sites measured. Low BMD associated with below-median intakes.	3-day dietary record (2 week and 1 weekend day.
Rapuri et al. [84]	92 women (65–77 years)	Quartiles dependent on protein intake as a percentage of total energy. Q1 (13.1 ± 0.12%), Q2 (15.1 ± 0.11%), Q3 (16.7 ± 0.12%), Q4 (19.8 ± 0.12%)	Increased intake of protein associated with higher BMD. But Vit D increased as protein increased in each quartile.	7 day food diaries
Thorpe et al. [55]	161 postmenopausal women (67.9 ± 6.0 years)	Intake of protein, minerals and sulphur containing amino acids assessed, plotted against BMD. Retrospective study	Protein intake positively associated with BMD, but benefit diminished by a negative impact of the protein sulphur acid load. But requires further research.	United States Department of Agriculture multiple-pass 24-h recall.
Wang et al. [85]	125 postmenopausal women. (59–84 years)	Multiple linear regression analysis.	Did not show a positive relationship. However, a combination of calcium and protein levels were used to come to this conclusion.	National Cancer Institute Food Questionnaire

hypothesis that the interaction of protein and calcium is complex in bone formation and stability [30].

The results of Wengreen et al. who investigated the different associations between protein intake and bone fracture risk between different age groups in the elderly population also requires further research. The renal tubular re-absorption and intestinal absorption of calcium are decreased among the elderly population, and as protein has been shown to potentially influence these mechanisms, the change in dietary protein would have to reflect this alteration in the elderly population [66]. This also emphasises the need for early intervention to maximise bone health before this life stage is reached, as previously stated by both Zhu et al. and Delmi et al. [56, 67].

Dargent-Molina et al. who observed a negative association between protein intake and bone health had calcium intakes which were designed to be low among the participants, while protein intakes were either moderate or high. The low calcium intake, rather than the moderate or high protein intake, could have contributed to the risk of the increased fractures. Interestingly, this study which looked at fracture risk of post-menopausal women (40–65 years) at baseline and 15 years later found that high animal protein intake actually conferred a greater fracture risk in the presence of reduced calcium intake whilst displaying a benefit in the presence of adequate calcium intake [36]. The complex interaction these two nutrients have is supported by Sahni et al. (which was not included in this review as the age range included subjects who were pre-menopausal), where there was a negative correlation between animal protein and risk of hip fracture in the presence of adequate calcium intake, as opposed to an increased risk of fracture associated with moderate to high intake of animal protein in the presence of low calcium intake in the diet [54].

As observed with BMD, the ratio of animal to vegetable protein may also play a role in the prevention of hip fractures. Sellmeyer et al. observed that elderly women with a high animal-plant ratio had a higher risk of hip fracture (relative risk = 3.7, $P = 0.04$) [63]. The acid-load hypothesis or a different, unknown mechanism may help explain this observed difference. However, this requires further exploration to elicit whether the issue is one of the animal protein vs plant protein or rather a question of macronutrients and micronutrients [13].

It has been observed that elderly fracture patients undergo deterioration in nutritional status during their hospital stay, with a negative association between low dietary protein intake and the risk of bone fracture and longer rehabilitation [61, 68, 69]. Furthermore, their functional outcome after bone fracture is well documented in literature [59, 60, 67, 70, 71]. Therefore, protein intake could also be a determinant of a patient's morbidity and mortality and the length of their stay in hospital [70, 72, 73]. For example, protein-energy malnutrition has been found to be an outcome determinant for the patient, affecting immune function, among others [74, 75]. In three studies, protein energy malnutrition was identified in a significant percentage of admissions to long-term care settings, an orthopaedic surgery department and a community resident home, respectively [76–78].

Table 2 Comparison of studies identified that evaluate the effect of protein quantity in the diet on bone mass (BMD)-animal subjects

Study reference	Details of study	Outcomes
Ammann et al. [31]	28 female rats (5.5 months old) divided into 4 groups of varying casein levels (2.5, 5, 7.5, and 15%) in isocaloric diets for 16 weeks. No other variables. DXA scans carried out on tibia and lumbar spine before intervention and at 7 and 15 weeks.	BMD was decreased in rats only in low protein diet groups after 16 weeks. Significantly decreased in 2.5% casein groups.
Bourrin et al. [58]	14 male rats (8 months old) divided into 2 groups and pair fed diets of 2.5% casein and 15% casein for 1 or 7 months. No other variables. DXA scans carried out on proximal tibia and its diaphysis.	Reduction in protein in diet associated with decreased BMD.
Orwoll et al. [86]	60 male rats (6 weeks old) fed a control (18% protein) diet for 7 days. Then divided into 2 groups, with 1 group now receiving a 5% protein diet only. No other variables. Single photon absorptiometry carried out on mid-shaft femur and tibia at 4, 6 and 10 weeks.	No change in BMD observed between the 2 groups.
Demigné et al. [87]	Female mice fed a westernised or standard diet before and during pregnancy, with their offspring fed the same. DXA was carried out on the offspring-whole body, caudal vertebrae and tibia at 30 weeks. Protein content was lower in westernised diet. But many other variables within the 2 groups, including minerals—likely affects the findings.	Reduction in BMD with Westernised diet (lower protein). But minerals were also reduced.

Table 3 Comparison of studies identified that evaluate the association between protein quantity in the diet and bone fracture risk/history

Study Reference	Subjects (community or hospital, ages, number)	Characteristics of the trial	Outcomes	Type of questionnaire used
Munger et al. [60]	32,050 women (55–69 years) randomly selected from driver's licence files of Iowa, USA	Information on incidence of hip fractures was collected using follow-up questionnaires 1 and 3 years following the FFQ. Quartiles of total protein (<9.56, 9.56–10.78, 10.78–12.05 and >12.05 g/MJ), animal protein (g/MJ) and vegetable protein (g/MJ)	Those in the hip fracture group had a lower intake of protein/day compared to those in the non-hip fracture group. Consumption of animal protein confers a protective effect.	FFQ
Wengreen et al. [61]	Hip fracture patients in Utah (50–89 years)—831 women, 336 men. Controls: 885 (f), 449 (m)	Case-control study. Quartiles of total protein (5.6–13.9, 14.0–15.5, 15.6–17.3, 17.4–30.8), animal and vegetable protein as a % of total energy	Significant negative association between protein consumption and risk of hip fracture in 50–69 year range. No association in 70–89 year range. Animal and vegetable sources have a protective effect**.**	Picture-sort FFQ
Misra et al. [59]	576 women and 370 men from Framingham study with no previous history of hip fracture (mean age 75 years). Interviewed in 1989, with final follow-up in 2005.	Energy-adjusted protein quartiles compared with hazard ratio and incidence rate. Protein levels not provided.	Lower risk of hip fracture with higher protein intake in elderly men and women. But was limited by relatively small number of fractures.	FFQ
Dargent-Molina et al. [36]	36,217 postmenopausal women (40–65 years), 15-year follow-up.	Calcium and protein consumption levels divided into quartiles (<40.75 40.75–45.16 45.16–50.11 > 50.11) (g/1000 kcal). Relative risk used.	No association between any forms of protein and fracture risk, although *p* value is 0.09. Increase in risk with high protein in the presence of low calcium.	French dietary questionnaire
Martínez-Ramírez [62]	167 subjects with 167 controls ≥65 years (80% women)	Case control study. Total protein (<85, 85–99, 100–117, >118) (g/day), animal protein and animal/vegetable protein also assessed	No difference in total protein consumption in cases and controls. Low protein diet linked with an increased risk of fracture. Subjects with a fracture history had a lower intake of animal protein.	136-item Harvard Willett semi-quantitative FFQ with colour pictures to show food portions
Sellmeyer et al. [63]	1035 white women (>65 years)	Prospective cohort study. Animal: vegetable ratios discussed.	Relative risk of hip fracture increased with high animal protein. Protective effect seen with vegetable protein	FFQ
Zhong et al. [88]	2006 postmenopausal women (≥50 years)	Retrospective cohort study. Mean, median and range of protein values1 included.	Statistically insignificant protective effect of increased dietary protein on fracture risk. However, high dietary calcium had an increased risk of fracture in t he presence of low protein.	24-h dietary recall from NHANES

Strengths and limitations of this review

From an initial literature review of 7941 papers, 25 were found to meet inclusion criteria. A total of 25 papers were assessed to examine the relationship between protein, BMD, and hip fracture, with reference to quantity rather than quality of protein. This review is one of the few studies that focussed predominantly on bone health in the over 50 age group. As there is a degree of variation within the FFQ format itself (with some FFQs going into more detail and using slightly different tools compared to others), the conclusions of this review had to reflect the degree of non-standardisation when deciding its effectiveness [79]. Furthermore, it was unknown if some of the studies included the impact of polypharmacy on absorption and utilisation of micronutrients which is a limitation of this paper.

Conclusions

The results of this review suggest that the quantity of protein consumed in the diet is associated with a greater BMD in the elderly. Furthermore, it was observed that protein bestowed a protective effect from the risk of fracture. These observations suggest that there is a need for a greater effort in ensuring that those >50 years meet their protein requirements as a means of bone protection [27]. Although there are weaknesses associated with the FFQ, the most common assessment tool in these studies, there are currently no equally alternative methods which have displayed greater utility in data attainment in this regard, in large studies. Ideally, the combination of biomarkers with BMD would yield the most accurate results by far, but there is limited cost and time, especially in the clinical environment. Improvements in the current FFQ model, such as creating a more detailed questionnaire, may prove to be more accurate in eliciting information [80]. As a result, the FFQ will continue to be the mainstay method of choice until further evidence suggests the need for a complete diet record of micro and macro nutrition.

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Compliance with ethical standards

Conflict of interest The authors declare that they have no conflict of interests.

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