

Protein Effects on Bone and Muscle in Elderly Women

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2.1 Introduction

Fractures continue to constitute a major public health problem of aging despite recent evidence that the age-specific rate may be falling.¹ The facts that before dying at a median age of approximately 83 years, 50% of women would have sustained a fracture with its consequent morbidity, and health care costs give some idea of the magnitude of the problem. As with other common health problems such as atherosclerotic cardiovascular disease, a combination of the whole of the population public health approach with pharmaceutical intervention for those at highest risk is recommended. In this regard, increased calcium supplementation to counteract reduced intestinal calcium absorption and increased renal excretion due to the loss of the effect of estrogen on these two mechanisms² is now widely accepted as is vitamin D supplementation due to a reduction in skin exposure to sunlight. Interestingly this latter factor, which in the absence of adequate sunlight can be replaced in the diet, has also been shown to play a significant role in falls prevention which together with osteoporosis constitute the pathological basis for fracture.

In recent years, there has been an increased interest in other nutrient deficiencies that may play a role in the increasing risk of fracture with age. In this regard, a research group, The Protein Intake Metabolic Outcome Study Collaborators, was formed in 2005. The basis of our interest was stimulated by early evidence that increased protein intake may be beneficial rather than being deleterious to the skeleton may be beneficial. In addition, there is

some evidence that muscle function may be enhanced by increased protein nutrition. It is possible that the magnitude of the effect could play a role in falls reduction and thereby reduce fracture risk. This chapter reviews recent ongoing work undertaken by our group in relation to the substantial work done by others in the area.

2.2 The Epidemiology of the Effects of Aging on Nutrition (Table 2.1)

There is a relative paucity of data on the effects of aging on nutrient intake. Indeed, it is not infrequent to consider that there is a greater problem from overnutrition than undernutrition, often based on studies of younger individuals. We have therefore recently reviewed data from a longitudinal study of 954 free-living elderly women aged 70–85 years at baseline who survived 7 years from a cohort of 1,500 elderly women recruited in 1998³.

Compared to national data, this study population had a higher rate of overweight (44.2% vs. 35.6%), but a similar rate of obesity (21.9% vs. 22.9%).⁴ This suggests that the increase in body size seen in Australia extends to older adulthood (>70 years), where the prevalence of chronic disease is already high and overweight and obesity remain as strong determinants of chronic disease.⁵ The change in nutrient intake data is shown in Table 2.1. Over the 7 years, there was a reduction in energy intake and 68–76% of the population fell below the ideal Acceptable Macronutrient Distribution Range (AMDR) for energy intake⁶ possibly related to declining appetite.⁷ The reduction in energy intake extended to all three major classes of nutrients including protein, although protein intake was substantially above previously recommended levels.⁸ In addition, it is clear that over the 7 years, there was a gradual

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Table 2.1 Anthropometric measurements of elderly women in the CAIFOS CARES cohort from baseline to 84 months

	Baseline (<i>n</i> = 949)	60 months (<i>n</i> = 949)	84 months (<i>n</i> = 949)
Age (years)	74.9 ± 2.6	79.9 ± 2.6*	81.9 ± 2.6*
Weight (kg)	68.7 ± 11.9	67.9 ± 12.0*	66.8 ± 12.0***
Corrected tricep skinfold (cm)	0.86 ± 0.26	0.85 ± 0.25	0.70 ± 0.26***
Corrected upper arm girth (cm)	1.03 ± 0.12	1.02 ± 0.13*	0.92 ± 0.13***
Physical activity (kJ/day) ^a	498 (191, 866)	448 (122, 807)	382 (0, 782)****
Nutritional intake			
Energy (kJ/day)	7,206 ± 2,134	6,866 ± 2,307*	6,522 ± 2,150***
All fats (g/day)	65 ± 24	62 ± 26*	62 ± 24*
Protein (g/day)	81 ± 27	78 ± 31****	75 ± 28***
Carbohydrates (g/day)	193 ± 59	182 ± 61*	176 ± 59****

Results are mean ± SD unless otherwise stated

*Significantly different from baseline ($p < 0.001$)

**Significant differences between 60 and 84 months ($p < 0.001$)

***Significant differences between 60 and 84 months ($p < 0.05$)

****Significantly different from baseline ($p < 0.05$)

^aMedian (interquartile range)

reduction in weight, fat mass as shown by triceps skin fold and muscle mass as shown by corrected upper arm girth. Thus it is possible that at least a proportion of the aging population may benefit from an increase in protein nutrition. This concept has been pursued in two further studies of the relation between protein nutrition and bone and muscle mass and function.

2.3 Epidemiology of the Effects of Protein Nutrition on Bone and Muscle Structure

The data on protein effects on bone and muscle have been published in two recent papers, both of which utilized data from the longitudinal study of aging in women which formed the basis for the report discussed above.

The subjects were recruited from the Western Australian general population of women over 70 years of age for a 10-year cohort study, where the first 5-year study was a prospective randomized controlled cohort trial of supplemental oral calcium to prevent osteoporotic fractures³ and years 6–10 were a study of health outcomes with aging. Initially, a letter was sent to 24,800 individuals selected at random from the electoral roll,

which has the names and addresses of 98% of women of this age. Of the 4,312 women who responded to the letter, 34% joined the study. No subjects had any medical condition likely to influence the 5-year survival and subjects were not taking bone-related medication including calcium supplements, estrogen, bisphosphonates, and vitamin D at enrolment. Although women enrolled in this study were weighted in favor of those in higher socioeconomic categories, they did not differ from the whole population in health resource utilization.⁹ During the intervention phase of the study (first 5 years), subjects were randomized to receive 1.2 g of calcium carbonate daily or matched placebo. At the commencement of the study, each subject completed a self-administered semiquantitative food frequency questionnaire developed by the Anti Cancer Council of Victoria (ACCV)^{10–12}, from which the daily dietary intake of energy, carbohydrate, protein, fat, and calcium were derived. The dietary calcium was from food alone and did not include the amount from any supplement.

2.3.1 Study 1

The first report was of a cross-sectional study of protein intake effects on bone mass.¹³ The demographics

are shown in Table 2.2. Protein intake in Australian elderly women was found to be higher than previously recommended (0.94 g/kg). Furthermore, although there was a high correlation between protein intake and other nutrients, there was a low correlation with body weight emphasizing the fact that body composition is the result of past intake and not current nutrient intake.

Figures 2.1 and 2.2 show the relationship between protein intake in tertiles and bone structure at the heel site, measured by bone ultrasound attenuation (BUA) and hip areal BMD measured by DXA. After adjustment for age and BMI, individuals in the highest tertile of protein intake had the best bone structure at the heel and hip sites. Calcium intake was not significant in the model. A 50% increase in protein intake from the median 55 to 103 g was associated with a 2% increase

Table 2.2 Baseline demographics of subjects in the study of protein consumption and lower limb bone mass

Variable	Value
Number	1,077
Age (years)	75 ± 3
Weight (kg)	68.5 ± 1.9
BMI (kg/m ²)	27.1 ± 4.5
Protein (g/day)	80.5 ± 27.8
Protein (g/kg body weight/day)	1.19 ± 0.44 (range 0.31–4.51)
Protein (% of energy)	19 ± 2.9

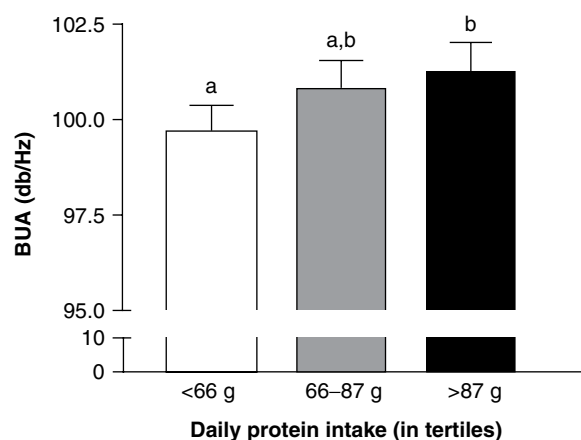


Fig. 2.1 Effects of differing habitual protein intake on heel ultrasound bone ultrasound attenuation (BUA). Results are mean ± SE heel ultrasound BUA corrected for age and BMI. Bars with different letters differ at $p < 0.05$ (reproduced from Devine et al¹³)

in bone structure. So, although the effect size was not large, nevertheless, it was possible to be demonstrate it in an epidemiological study.

2.3.2 Study 2

Next, we studied the protein intake effect on bone and muscle in a 5-year longitudinal design utilizing the data acquired as part of an RCT of calcium supplementation.¹⁴ The study sample consisted of 862 community-dwelling women who had their nutritional intake assessed at baseline as indicated above and had a measurement of whole body DXA composition at 5 years. The baseline data is shown in Table 2.3. It is evident that individuals with a high protein intake were physically more active and had a higher calcium intake.

The relationship between baseline protein intake and bone mass at 5 years is shown in Fig. 2.3. It is clear that similar to the cross-sectional data, high protein intake was associated with high total body bone mass. There were insufficient individuals for heel ultrasound and hip DXA at 5 years to examine these endpoints. These data are consistent with some^{13,15,16}, but not all¹⁷ studies that have shown that a high protein intake is associated with reduced bone loss, and reduced risk of hip fracture.¹⁸

In addition to studying the effects of protein intake on bone mass, we were able to study the effects on muscle mass and fat mass. There was no relation between protein intake and fat mass. On the other hand, there was a substantial positive effect of baseline protein intake on muscle mass (Fig. 2.4). Thus subjects consuming 20% of kJ as protein as opposed to 17% of their kJ as protein had a 5.3% higher whole body lean mass, and 6.6% higher appendicular lean mass independent of age, body size, energy intake, and physical activity level.

These findings are consistent with the results of the Health ABC study in the US,¹⁹ which showed that the community-dwelling older people in the highest quintile of protein intake lost 40% less lean mass and appendicular lean mass than did those in the lowest quintile of protein intake over a 3-year period, but are inconsistent with two cross-sectional studies.^{20,21} Interestingly, the beneficial relationship between protein intake and whole body bone mass disappeared after adjustment for muscle mass effects. This raises the interesting possibility that the bone effect is dependent on the muscle effect.

Fig. 2.2 Effects of differing habitual protein intake in DXA BMD. Results are mean \pm SE hip DXA corrected for age and BMI. Bars with different letters differ at $p < 0.05$ (reproduced from Devine et al¹³)

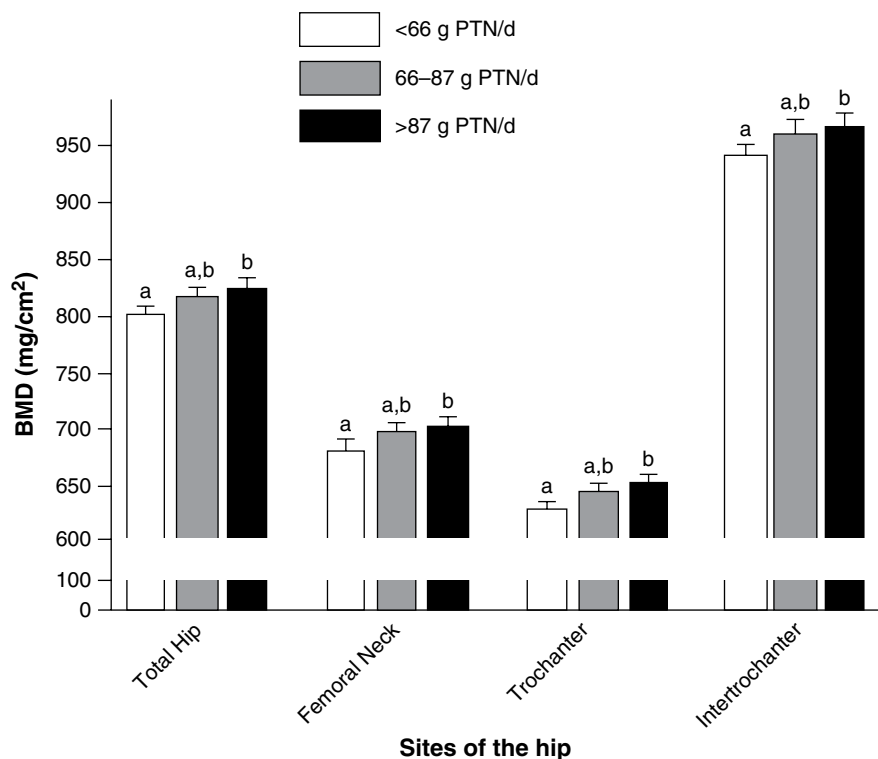


Table 2.3 Baseline demographics of a 5-year cohort study of the effects of high protein intake on lean mass and bone mineral content in elderly postmenopausal women

	First tertile protein <66 g/day (n=287)	Second tertile protein 66–87 g/day (n=287)	Third tertile Protein >87 g/day (n=288)
Age (year)	74.9 \pm 2.5	75.0 \pm 2.6	74.7 \pm 2.7
BMI (kg/m ²)	26.4 \pm 4.2	26.7 \pm 4.7	27.3 \pm 4.3*
Physical activity (kJ/day) ^a	466 (0–808)	530 (207–897)*	614 (237–1,002)*
Protein (g/day)	54.4 \pm 9.1	76.6 \pm 6.2*	110.9 \pm 23.4***
Protein (% of energy)	17.7 \pm 2.7	19.0 \pm 2.3*	20.4 \pm 3.2***
Calcium (mg/day)	704 \pm 202	973 \pm 243*	1,220 \pm 364***

Results are mean \pm SD

*Significantly different from the first tertile, $p < 0.05$

**Significantly different from the second tertile, $p < 0.05$ (ANOVA with Tukey's test)

^aMedian and interquartile range

2.3.3 Conclusions

The nutritional epidemiology of body composition is a difficult area of study for a variety of reasons. First, there are substantial cocorrelations between nutrient intakes

which make identification of a specific effect uncertain. Second, there are the problems of confounding of effects due to unrecognized baseline cocorrelates inherent in all epidemiological investigation. Third, there is the problem of the effects of nutrition on body size in cross-sectional

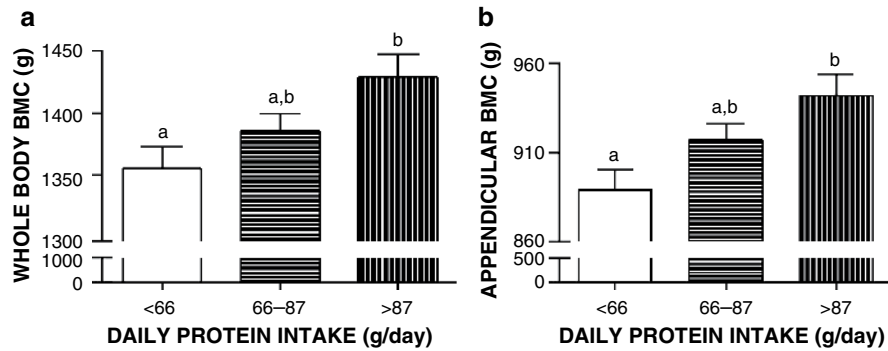


Fig. 2.3 Effects of baseline protein intake on DXA BMC of whole body and appendicular skeleton 5 years later. Results are mean \pm SE adjusted for baseline age, height, energy intake, physical activity, and calcium treatment. Groups with different

lower case letters are significantly different, $p < 0.05$ (ANCOVA with Bonferroni test) (reproduced from Meng et al¹⁴ with permission of the American Society for Bone and Mineral Research)

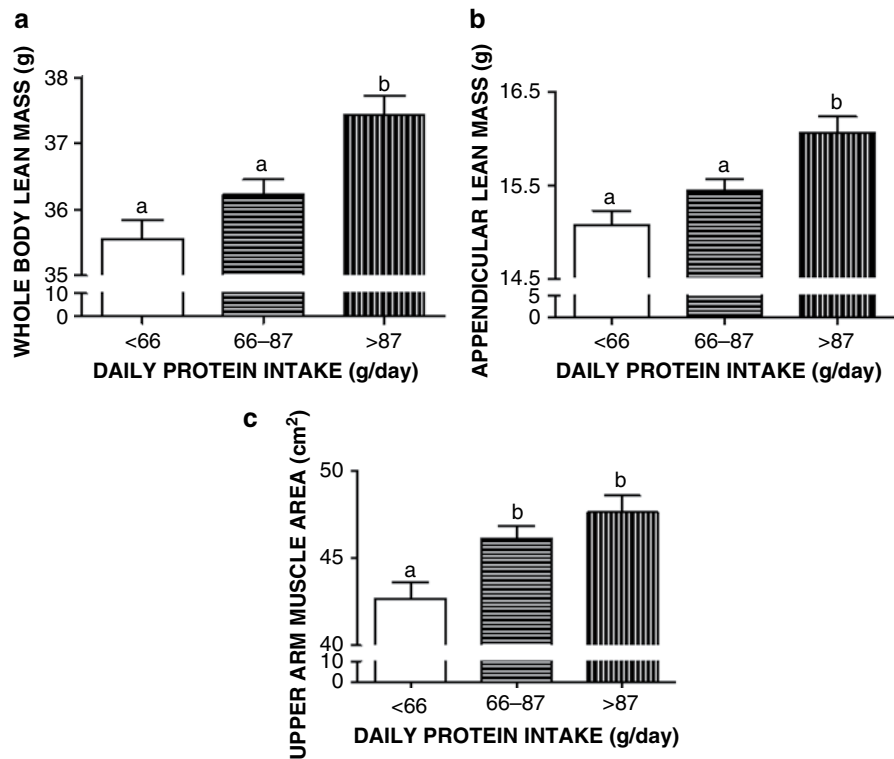


Fig. 2.4 Effect of baseline protein intake on DXA lean mass 5 years later. Results are mean \pm SE adjusted for baseline age, height, energy intake, and physical activity. Groups with different lower case letters are significantly different, $p < 0.05$ (ANCOVA with Bonferroni test) (reproduced from Meng et al¹⁴ with permission of the American Society for Bone and Mineral Research)

studies. This is because body size is determined by many long-term factors including genetic effects in childhood and adolescence and nutritional intakes in the past. Given this complexity, it is surprising that the relationships outlined above are evident. Nevertheless, it is essential to

subject observational studies of beneficial effects to controlled clinical trial interventions before cause and effect can be validly concluded. To this end, we have commenced a 2-year RCT of increased protein intake against identical placebo as outlined below.

2.4 A Population-Based, 2-Year Randomized, Double Blind and Placebo Controlled Trial of Protein Supplementation

In 2005, we commenced planning for an RCT of the effects of increased protein intake on body composition and metabolic outcomes, the PIMES (Protein Intake Metabolic Effect Study). Preliminary data on 1-year end points have been presented here.

The study design was to recruit community-dwelling ambulant women aged 70–80 years and offer them an intervention of a daily 250 mL drink. One contained a protein supplement group consisting of 30 g of whey protein isolate (Alacen 894, Fonterra NZ), 600 mg of calcium as calcium lactate, and 1,050 kJ of energy. The placebo contained 1.7 g protein, 600 mg of calcium as calcium lactate, and was isocaloric with the protein drink. Hundred women were recruited to the protein drink and 95 to the placebo drink. Body composition was measured at baseline and 1 year using whole body dual-energy X-ray absorptiometry and knee strength was assessed by isokinetic dynamometer.

The baseline demographics are shown in Table 2.4. There were no differences between the two groups for any of the factors assessed which were similar to the values obtained in the epidemiological studies. The effect of the intervention on lean mass, which is largely muscle mass in the appendicular regions including both arms and both legs and knee extensor and flexor strength is shown in Fig. 2.5. In essence, although there was an increase in lean mass and leg strength over 1 year there was no group difference.

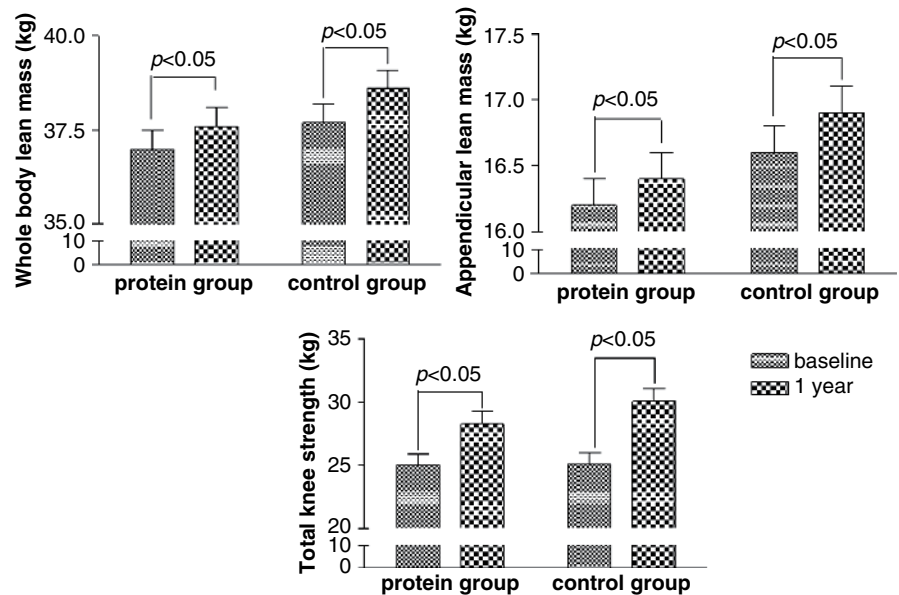
2.5 Conclusions

The lack of a protein treatment effect must be regarded as preliminary as the study was designed to be a 2-year intervention, because the time course of a protein nutritional supplement was considered to be a long-term effect. Nevertheless, an alternate hypothesis that may be worth considering is that the increased calcium and caloric intake in both the groups may have induced a beneficial effect on muscle mass and function. Clearly, this concept suggests that nutritional intake in the ambulant elderly may not be optimal to maintain skeletal function.

Table 2.4 Baseline characteristics of the two test drink groups

	Protein group mean \pm SD ($n = 100$)	Control group mean \pm SD ($n = 95$)	p value
Age (year)	74 \pm 3	74 \pm 3	0.80
Height (m)	159.8 \pm 6.3	159.8 \pm 5.7	0.86
Weight (kg)	66.8 \pm 11.1	69.6 \pm 11.3	0.09
Dietary intakes assessed by 3-day food record			
Energy intake (kJ/day)	7,074 \pm 1,595	7,307 \pm 1,456	0.29
Protein intake (g/day)	76.6 \pm 18.0	77.9 \pm 21.6	0.65
Fat intake (g/day)	60.7 \pm 19.6	64.0 \pm 18.9	0.24
Carbohydrate intake (g/day)	188.6 \pm 50.0	192.1 \pm 44.0	0.61
Energy intake from protein (%)	19.0 \pm 3.5	18.5 \pm 3.4	0.28
Body composition			
Whole body lean mass (kg)	37.0 \pm 4.7	37.7 \pm 4.7	0.29
Appendicular lean mass (kg)	16.2 \pm 2.4	16.6 \pm 2.4	0.27
Total knee strength (kg)	25.2 \pm 8.6	25.1 \pm 8.7	0.93

Fig. 2.5 Change from baseline to 1 year for whole body and appendicular lean mass and total knee strength (knee extension strength and knee flexion strength). Results are the mean (SE). Paired sample t-test for within group change from baseline to 1 year



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