Known Related Effects of Nutrition on Aging Muscle Function

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Introduction

Nutritional surveys in elderly populations have pointed to low energy and nutrient intake. This is of particular concern among the homebound or frail population groups [1–5] as reflected by considerable involuntary weight loss, including net protein loss [6, 7] leading to muscle wasting [8]. Inadequate intake of a number of nutrients has been associated with decreased body strength, lower resistance to infection and poorer indicators of quality of life [9–11]. Both an inadequate body weight for height and weight loss are associated with hip fractures, reduced autonomy, early institutionalization and increased mortality rates [12–21]. Low muscle mass was shown to be a significant independent risk factor for falls in elderly women after adjustment for age, balance and gait, medications, physical activity, proportion of body fat, and health status [22]. Preservation of muscle function is paramount for the maintenance of autonomy until advanced age. Since age-related decreases in functional ability are neither inevitable nor uniform [23], efforts have been made to identify factors associated with muscle function or functional status in general in many studies over the last decade. Two candidates for modifiable determinants, nutrition and physical activity, have been consistently studied in the context of observational and experimental designs.

This chapter will focus on the manner in which nutritional status contributes to the preservation or deterioration of muscle function in the elderly. For this purpose, an epidemiological perspective rather than a mechanistic one will be adopted. Results from cross-sectional and longitudinal observations as well as from experimental studies will be presented and
discussed. Finally, physical activity will be brought into the discussion, owing to its major impact on both nutritional requirements and muscle function. Indeed, daily energy intake is, in part, a function of the level of physical activity [24]. Inactivity leads to a low intake of energy and protein, reduced whole-body protein turnover, and a resulting net loss of body protein [25], while exercise activates a series of immune-related reactions which leads to increased skeletal muscle protein metabolism [26], higher energy requirements and, consequently, energy, protein and other nutrient intakes. Furthermore, a recent study showed that strength training in very elderly frail institutionalized people is a feasible and effective means of counteracting muscle weakness and physical frailty by improving muscle function [27].

**Muscle Function**

For this review of relationships between nutrition and muscle function in the aging individual, muscle function was defined either as (1) muscle strength measured by handgrip, knee extension, elbow flexion, or other muscle group strength, or (2) functional capacities measured using performance tests such as the Timed Up & Go [28], walking speed, chair stand [29, 30], balance and gait [31, 32]. We also report some studies where subjective measures were used to assess physical function since self-reported disability was the outcome of interest of many longitudinal studies investigating the impact of nutrition.

**Nutritional Status**

Nutritional status indicators include energy, protein and, in some instances, micronutrient intake, body mass index \((\text{BMI} = \text{weight (kg)/height (m)}^2)\) weight loss, fat mass and lean body mass.

Body mass is heterogeneous and includes both fat and fat-free components in different proportions. Variations in BMI among individuals reflect differences in both fat mass and fat-free mass, and age further limits the sensitivity of BMI to classify obesity [33, 34]. In the general population, fat mass is generally considered to have a negative impact on health and longevity while increased fat-free mass is hypothesized to enhance health and longevity [35]. This leads to considerable misclassification of body fatness and fat-free mass when individuals are categorized by BMI values. However, this index was used in many studies in relation to muscle function since weight and height measurements are practical and readily available in large population-based studies. Body weight loss is a precise nutritional marker that has been consistently associated with increased disability, morbidity and mortality even after
controlling for coexisting diseases [18, 20, 21, 36]. Weight loss may be a better predictor than BMI or energy intake because it really represents an imbalance between energy intake and expenditure and exacerbates loss in muscle mass [37]. In the Framingham participants, the greatest loss in lean body mass over a 2-year period was observed in those who lost weight during the same period [Payette et al., unpublished data]. Body composition should be taken into account when discussing nutritional status and muscle function in the elderly. On the one hand, body fat mass was investigated as a potential predictor of subsequent disability [38]. On the other hand, skeletal muscle mass obviously appears to be a major determinant of muscle function [39]. Furthermore, involuntary loss of skeletal muscle mass or sarcopenia is observed with aging even in generally healthy elderly people, in the absence of weight loss [37, 40] or in the presence of obesity [41]. Until recently, definitions of sarcopenia were based on a quantitative decline in muscle mass. However, it appears that qualitative changes occur as well in the aging muscle resulting in an even greater than expected effect on muscular force production and endurance [42, 43]. Nevertheless, specific issues pertaining to the changes in muscle quality with aging will not be discussed in this review.

**Conceptual Framework of the Relationships between Nutrition and Muscle Function in the Aging Individual**

In the definition of the clinical syndrome of frailty, the majority of the symptoms pertain to nutrition (anorexia, undernutrition, weight loss, weakness, fatigue) while the signs (or characteristics) include some physiological changes such as decreased muscle mass and bone mass, and muscle function such as muscle strength, balance or gait abnormalities [44]. Nutrition factors are consistently associated with muscle function in the development and evolution of frailty in the aging individual. Moreover, a hypothesized model of physiological contributors to the onset or progression of frailty [44] closely resembles the model suggested for sarcopenia [45].

Chronic undernourishment as a result of low energy and protein intake or prolonged consumption of a diet high in carbohydrates and low in protein may lead to protein energy malnutrition in the elderly. Protein energy malnutrition is characterized by a loss of body energy stores and loss of protein mass. Muscle is the largest protein reservoir of the body; therefore, the gradual and inevitable loss of body protein as a result of a long-term dietary protein deficit is primarily a loss of skeletal muscle protein. More than a decade ago, Jeejeebhoy [46] reported muscle abnormalities in fasted obese young adult subjects and untreated primary anorectic patients. Recovery of muscle function was achieved upon refeeding these subjects an adequate diet in
Known Related Effects of Nutrition on Aging Muscle Function

terms of energy and nutrients. Malnutrition may be one of the major contributors to the decline in muscle function with age [46] along with chronic diseases and medications [47–50], atrophy of disuse [51, 52] and changes in neuromuscular tissue [53].

Due to a variety of reasons, the elderly are particularly prone to protein energy malnutrition. Inadequate energy intake is frequently observed and their choices of foods tend to exclude protein dense foods (i.e. meat) because of lack of appetite, difficulty digesting, high cost or preparation time or fear of cholesterol even without any medical indication. Physiological factors such as reduced sense of smell and taste [54], decreased visual acuity [55] and abnormalities in the regulation of appetite by regulatory peptides [56–58] also contribute to reduced food intake. Moreover, secondary protein energy malnutrition may be the result of other diseases that lead to low food ingestion, inadequate nutrient absorption or utilization, disregulation of the appetite in relation to energy expenditure or energy needs [59], increased protein requirements [60] or increased nutrient losses.

Therefore, it was suggested that protein energy malnutrition, coupled with physical inactivity in a dynamic relationship, would lead to loss of skeletal muscle mass resulting in impaired muscle function in the elderly.

Observational Studies

Cross-Sectional Design

The quantity of fat-free mass was shown to be linearly and positively related to muscle strength. In small samples of frail though not undernourished elderly persons, fat-free mass measured using the Bioimpedance Spectrum Analyzer [61] or computed tomography of the thigh [62] was strongly correlated to handgrip strength ($R^2 = 0.38; p = 0.0005$), knee extension ($R^2 = 0.20; p = 0.02$) [61] and $(r = 0.73; p < 0.01)$ [62]. Significant relationships were also observed between muscle strength and dietary intakes of vitamin B$_6$ ($r = 0.745; p < 0.01$), magnesium ($r = 0.792; p < 0.01$), and potassium ($r = 0.745; p < 0.01$) [62] as well as time to rise from a chair ($r = −0.63; p < 0.05$) and time to walk 6 m ($r = −0.75; p < 0.01$). In contrast, the Timed Up & Go test, a measure of global function, was not associated with fat-free mass [61].

In a large relatively healthy elderly population, lean body mass was shown to be strongly correlated with a cumulative index of muscle strength, including elbow and knee flexor and extensor as well as ankle dorsiflexor [63]. Furthermore, it was suggested that muscle mass (measured from urinary creatinine excretion) was the major determinant of age- and gender-related differences in muscle strength [39]. In a cross-sectional analysis of apparently healthy elderly male participants in the Baltimore Longitudinal Study of Aging, grip strength was strongly related to both indices of muscle mass, namely creatinine...
excretion and forearm circumferences [64]. However, changes observed in
grip strength over a 5-year period were not correlated with muscle mass
dcline [64] suggesting that other factors, such as pain, motivation or qual-
tative changes in aging muscle, could explain losses in muscle strength with
aging.

Correlates of performance-based measures of muscle function were iden-
tified among The Cardiovascular Health Study participants [50]. Anthro-
metric indices of nutritional status, such as waist circumference and weight,
were consistently associated with grip strength, timed chair stand test and
gait speed.

Sarcopenia, defined as appendicular skeletal muscle ≥2 SD below sex-
specific values observed in young adults, was shown to be associated with a
3–4 times greater risk of disabilities [41], 2–3 times increased risk of falls
among very old individuals [65], and with an increased probability of mobility
disability and osteoporotic fractures [66]. However, when a sub-group of
sarcopenic obese individuals is studied [67], it appears that a combination
of sarcopenia and obesity has the greatest association with grip strength
adjusted for body weight (p < 0.01), physical disabilities (OR = 4.12; 95% CI
1.24, 15.5), balance (OR = 6.36; 95% CI 2.25, 19.9), gait (OR = 3.21; 95% CI
1.39, 7.69), and falls in the previous year (OR = 3.34; 95% CI 1.37, 8.26) as
compared to nonobese sarcopenic individuals or nonsarcopenic individuals.
On the other hand, energy or protein intake was not different between groups
classified according to the presence or absence of sarcopenia, obesity or both,
despite the fact that decreased energy needs were reported in association
with sarcopenia [68, 69].

Recent cross-sectional studies in two cohorts of free-living elderly
persons [70, 71] showed that the significant relationship observed between
low muscle mass and poor lower-extremity performance disappears after
adjustment for behavioral, physiological and psychological variables [70] or
muscle strength [71]. These results suggest that, although muscle mass and
strength are correlated, muscle mass per se is not an independent contributor
to muscle function when these relationships are examined in a cross-sectional
fashion.

**Longitudinal Design**

These studies investigated to what extent nutritional status influences
subsequent functional dependence in the elderly. A number of well-controlled
longitudinal studies have shown that low and high BMI as well as loss
of body weight increase the incidence of subsequent perceived functional
impairment [13, 16, 72], mobility disability [18] and hip fractures [36, 73].

Incident disability over a 3-year period in men and women aged 65–100
years was shown to be predicted by greater fat mass (BIA) at baseline (women:
OR = 2.83; 95% CI 1.80, 4.46, and men: OR = 1.72; 95% CI 1.03, 2.85) after
adjustments were made for age, physical activity level, chronic disease and
other potential confounders. In contrast, a protective effect of fat-free mass on incident disability was not noticeable [38]. One possible interpretation could be that a high percent body fat may mask muscle atrophy, and that a combination of both obesity and sarcopenia could place the elderly individual at an even greater risk of disability [67].

In a relatively high-functioning cohort of men and women aged 70–79 years in the MacArthur Studies of Successful Aging [23], declines in physical performance (integrated measure of hand, trunk and lower extremity movements including balance and gait) were more likely to occur over a 3-year period among those with a higher BMI, even after adjusting for baseline functional status, physical and mental health conditions and sociodemographic characteristics. In the context of a longitudinal study of aging and Alzheimer’s disease, women with an annual percent weight loss of 3% or more had 2.5 times more risk of becoming dependent in one or more activities of daily living over a 2-year period, compared to those with no weight change [72].

In the context of a systematic review of longitudinal studies of predictive factors for functional status decline, defined as difficulty doing activities of daily life or physical function limitations, the authors reported, with strong evidence, that a high or low BMI or weight loss were significant risk factors for subsequent functional decline [74]. The relative complexity of dietary intake assessment and the lack of validated instruments for detecting early nutritional risk factors in the elderly might explain why we could not find any study reporting on the relationships between energy, protein or nutrient intakes and muscle function.

**Experimental Studies**

Experimental designs provide the most convincing evidence of the impact of nutrition on muscle function in the elderly. If it could be demonstrated that nutritional supplementation reverses malnutrition and improves muscle function, this would allow effective prevention interventions to be developed and implemented.

Ambulatory patients with chronic obstructive pulmonary disease had increased respiratory muscle strength, handgrip strength and general well-being after refeeding [10], although such effects were not shown in another study [75].

Castaneda et al. [8] showed that elderly women fed a low protein diet (0.45 g/kg body weight) over a 9-week period remained in negative nitrogen balance and accommodated to the low protein intake with losses of muscle mass and muscle function (measured by adductor pollicis muscle, i.e. neuromuscular muscle function, and muscle strength using leg extension and handgrip). No such changes were observed in a control group fed an adequate
known related effects of nutrition on aging muscle function

protein diet (0.92 g/kg body weight). This suggests that chronic dietary protein deficiency may accelerate sarcopenia and loss of muscle function in the elderly.

In a small sample \((n = 11)\) of sedentary men aged 61–72 years undergoing a 12-week resistance training program, half of them were offered a daily nutrient-dense oral supplement that significantly increased their total energy intake and affected body composition without changing the rate of strength gain [76]. However, the design of the study precluded any clear conclusion with respect to the independent effect of strength training and nutritional status improvement on muscle mass or strength. Furthermore, one cannot exclude a lack of statistical power for the negative results regarding strength gain. Nevertheless, this study suggested that a change in total intake in elderly subjects beginning a resistance training program can affect muscle mass in contrast to an earlier study by Jeejeebhoy [46] where changes in muscle function as a result of refeeding were observed in the absence of a concomitant increase in the quantity of lean body mass. Similar observations were made with respect to the effects of resistance training [77].

A recent study showed that strength training and nutritional supplementation in very elderly frail institutionalized people is a feasible and effective means of counteracting muscle weakness and physical frailty [27]. In contrast, multinutrient supplementation without concomitant exercise did not improve strength or autonomy. In this study, subjects, although frail, were not undernourished at baseline (mean \(BMI = 25 \text{ kg/m}^2\)) and supplementation did not result in a net increase in total energy intake. This suggests that without exercise there was no drive to increase energy intake in generally well-nourished individuals; indeed, subjects who received the supplement alone reduced their \textit{ad libitum} dietary intake accordingly [78]. Selection of subjects suitable for evaluating the benefits of nutritional intervention should therefore be carefully considered in order to avoid a ‘ceiling effect’, that is a plateau where no further linear relationship can be observed [79].

We recently showed little effect on functional status in a randomized clinical trial designed to investigate the effect of a 12-week nutritional supplementation program in a free-living undernourished frail elderly population [80]. The duration of the study as well as the reliability and validity of the functional outcome measures in this specific population were challenged. A subsequent validation study led to identification of the functional measures most suitable for field nutritional intervention studies in the free-living frail elderly [61]. A 16-week intervention controlled study was designed to evaluate the impact of nutritional supplement on muscle strength and lower extremity function (Timed Up&Go) [81] in free-living frail elderly at high risk of undernutrition as indicated by low BMI \((20.1 \pm 2.8 \text{ kg/m}^2)\) and high prevalence of weight loss (15%). Although supplemented subjects gained significantly more weight than the controls, this gain did not translate into a significant improvement in muscle strength or functional performance.
Discussion

It appears that the conceptual framework where protein energy malnutrition in combination with inactivity results in decreased muscle mass leading to muscle weakness and loss in optimal muscle function could be an oversimplification. Relationships among these variables could be nonlinear and more complex than hypothesized.

Firstly, the energy requirements for tissue accretion have been shown to increase substantially with age [82, 83]. It may be that the weight gain observed in undernourished elderly subjects as a result of nutritional supplementation does not produce a significant increase in muscle mass, or at least not enough to translate into muscle function improvement. Furthermore, as suggested earlier, muscle quality could be the variable of interest [67]. Indeed, it was shown that, after adjustment for muscle strength, low muscle mass was no longer associated with poorer physical performance [70, 71]. However, assessment of muscle quality requires sophisticated techniques not readily applicable in field settings to the frail undernourished elderly. Finally, a decline in muscle mass with age is multifactorial including inactivity, neurological, hormonal and immunological determinants along with nutritional factors.

Although some cross-sectional observations showed correlations between muscle strength and performance tests [62, 70, 71, 84, 85], an increase in muscle mass or muscle strength is not always reflected in improved functional capacities as measured by performance tests [50, 61, 86]. Indeed, besides nutrition, many factors are known to markedly influence the functional performances and capacities of an older person including medical conditions, physical and mental health status, psychological well-being, life habits and socioeconomic status. Furthermore, these factors are interrelated and most likely associated with food intake and nutritional status as well. For instance, recent analyses of the EPESE data [87] suggested that depression per se increases the risk of mobility disability independent of its effect on physical activity and social interactions. Now, depression is a strong determinant of food intake [88, 89].

Measurement of functional performance with respect to sensitivity to change is still a challenge among elderly persons with a low functional level. The volitional problem of subject performance, compounded by arthritis or other degenerative diseases or conditions, limits function in the limb being tested [90]. Pain strongly interferes with strength and functional performance measurements [61] and could preclude detection of a significant change following nutritional intervention. In order to overcome volition and pain interferences, an alternative could be measurement of the abductor pollicis, although its application in field settings remains to be tested.

A nonlinear relationship between muscle strength and functional performance has been suggested [70, 91–93]. Indeed, analyses of these relationships in population-based samples showed that linearity was observed only in very
weak individuals. Above a very low threshold in muscle strength, a ceiling effect was observed. It could be that a gradual loss in strength is not apparent until the loss reaches a threshold at which the person is no longer capable of performing a test as he or she was before. It follows that, in a large proportion of individuals participating in clinical trials where strength is above this threshold, an increase in strength resulting from nutritional supplementation could not result in concomitant improvements in functional performance tests.

**Conclusion**

There is some supporting evidence to suggest that nutrition is involved in the preservation or deterioration of muscle function in the elderly. Nevertheless, further research is needed to clarify the relationships between the various components linking diet to functional capacities. Longitudinal studies including precise and exhaustive measurements of nutritional status in aging individuals are necessary in order to provide clear answers in this regard. Finally, a better understanding of the refeeding process in the undernourished frail elderly is required in order to determine which nutritional intervention might restore muscle strength and function.

**References**


Known Related Effects of Nutrition on Aging Muscle Function


**Discussion**

*Dr. Kehayias:* As you drew a clear distinction between muscle mass and function, what would be a realistic way to evaluate the efficacy of nutritional or other interventions in the nursing home? You can, for example, improve muscle function just by exercise, without any improvement in nutritional status – you make the muscles move better and faster without changing their quality, just by recruiting more neurons. So what tests can we apply to separate nutritional and training effects?

*Dr. Payette:* If we are unable to show that nutritional supplementation in frail undernourished elderly people is an efficient way of improving muscle function it is because we have problems with the methodology. First of all, it is essential to select the right subjects to study; thus in order to replenish nutritional status you have to start with a state of undernutrition to be able to show any benefit. We also need studies of longer duration, though of course longer term studies in frail elderly people are associated with large losses in follow-up because of death or illness. In addition, we need to improve our ways of measuring muscle function, particularly its sensitivity to change.

*Dr. Bunout:* Maybe you can confirm this, but I am not aware of any study in which nutritional supplementation alone has been shown to increase muscle strength. If we want to gain strength we always have to combine nutritional supplementation and training, because nutritional supplementation alone does not achieve that result.

*Dr. Payette:* There are a few studies – like the COPD one I referred to [1] – which show increased strength following nutritional supplementation alone, but I agree there are not many. It seems clear that the best way forward is to combine increased physical activity with nutritional supplementation. The problem when you are working with free-living, frail, undernourished, elderly people is what to start with. These people are very frail, and home-based strength-training programs are not yet well developed, but it is also difficult to apply nutritional supplementation programs under such conditions and ensure correct balance and good compliance. However, I agree that any program of this kind must combine strength training with nutritional supplementation.

*Dr. Burckhardt:* We have had problems with grip strength in frail elderly people because of arthritis in the hands.
Dr. Payette: You have to use a Martin dynamometer in such patients. This is a pear which you grab. It is much easier for frail hands.

Dr. Jensen: I was pleased that you took time to highlight the concept of sarcopenic obesity. In the USA, and apparently also in Chile amazingly enough, obesity among home-living elderly people has become a growing concern, literally and figuratively. A few years back we published a letter in the *Annals of Internal Medicine* [2] where we described the obesity/failure-to-thrive syndrome, which was characterized by functional limitation, especially mobility limitation, in grossly obese people trapped in their homes. They are unable to dress themselves and are highly dependent. One of the real challenges has been the assessment of body composition and measurement of muscle function. We have conducted a series of body composition investigations with MRI and DEXA and found tremendous variability in appendicular lean mass and thigh muscle mass in these obese elderly people. We have also applied a battery of modified physical performance tests on them, but it has proved very difficult to relate muscle mass measurements to objective measurements of physical performance. We desperately need better ways of looking at body composition in the field, not to mention muscle quality and function as you mentioned.

Dr. Heseker: Is there an association between muscle mass and appetite? Can we increase appetite by increasing muscle mass?

Dr. Payette: Not to my knowledge – I’m not aware of any studies where muscle mass has been measured directly and related to appetite. We often talk about the ‘anorexia of malnutrition’, so it may be that there is a relation. When we are refeeding frail undernourished people we have to implement a very intensive supplementation program to get over this anorexia problem, but once that is achieved the supplementation becomes much easier.

Dr. Morley: We did a study where this was looked at, as part of an investigation of hormones in the elderly. We found that food intake and physical activity, as well as testosterone and IGF-1, were related not only to muscle mass but also to muscle strength. There was not always, as you said, a one-to-one relation between the physical activity and muscle mass, and we still don’t know the reason for this mismatch. On a separate issue, do you know whether anyone has tried to measure myostatin as a proxy for dying muscle?

Dr. Payette: Not that I’m aware of.

Dr. Bellever: You mentioned the key importance of protein and energy in restoring the nutritional status of these elderly people and regaining muscle strength. Beyond protein and energy, what other nutrients or components might usefully be added to an oral supplementation regimen to improve muscle function?

Dr. Payette: I believe in complete nutritional supplementation. We need to give an increased energy intake that is also rich in macronutrients and micronutrients. We are still at the stage of trying to get enough energy into these old people. We have no basis for any magic vitamin or mineral supplements on their own.

Dr. Cottrell: Do you think it is mainly lack of exercise or poor nutrition that is the main cause of muscle loss in the elderly?

Dr. Payette: Muscle loss is observed in all aging people. This kind of muscle loss is not particularly related to nutritional problems or lack of activity. Even athletes lose muscle with age.

Dr. Cottrell: We have looked at changes in muscles in normal elderly people and we found the same phenomenon as we showed in the brain – there are COX-deficient muscle fibers in normal elderly patients. But we also looked at a group of octogenarian athletes and those mitochondrial abnormalities weren’t seen. There were no COX-deficient muscle fibers in those people, and there was a decrease in mitochondrial DNA mutations.
**Dr. Kehayias:** From epidemiological data and from the potassium data we know that we all lose muscle as we age. I would like to use osteoporosis as an example. In osteoporosis we know that if you enter late middle age with a high baseline level of bone calcium you can afford to lose a good deal of calcium without weakening the bone enough to cause fractures; therefore it is a good thing to take exercise and enter the menopause with a high bone calcium. We do not have any epidemiological data to support a similar story for potassium and muscle, although it is a very nice hypothesis. Dr. Cottrell’s comment suggests that there may be benefits of being an athlete, but there is no clear evidence of this yet.

**Dr. Cottrell:** Biochemically there does seem to be a significant difference in the muscle of elderly people who exercise vigorously.

**Dr. Kehayias:** However, we know that maintaining physical activity throughout life gives clear benefit.

**Dr. Payette:** And being sedentary and undernourished exacerbates the losses.

**Dr. Lesourd:** The group from Clermont-Ferrand showed that if you change the protein intake regimen you can reverse the decline in muscle mass in healthy elderly people. They did this in two different ways: first, by using protein that was rapidly absorbed, as opposed to protein that was slowly absorbed, and second, by changing the meal format, so that all the day’s protein was taken at lunch time instead of divided between the meals. The work was published in the *American Journal of Clinical Nutrition* [3]. Do you think this could be applied to the management of frail elderly people to improve their muscle function?

**Dr. Payette:** Was it a randomized trial?

**Dr. Lesourd:** Yes, and it also included a comparison of young people and elderly people of around 60–75 years of age.

**Dr. Payette:** And the regimen restored muscle mass?

**Dr. Lesourd:** Yes. It increased muscle mass, measured in various different ways including protein anabolism measurement.

**Dr. Payette:** Those sound like very interesting results. They need careful consideration as a possible way toward providing optimal supplementation in frail elderly people.

**Dr. Bunout:** In relation to attempts to increase muscle mass by nutritional supplementation, when you work in a hospital you normally don’t have enough time to see an increase in muscle mass, and when you work in the outpatient setting you have enough time but you normally spend it dealing with complaints about the nutritional supplementation, so it is also very difficult to assess any changes in muscle mass! It is possible that the study referred to by Dr. Lesourd was one in which they showed highly unphysiological changes in muscle mass, and I remember being worried about it at the time, on the grounds that there could have been a measurement error. What changes in muscle mass can you expect with nutritional supplementation over time? Is there a linear relationship? How much protein do you have to give to obtain a measurable change? These are the issues you have to deal with when you are planning a nutritional supplementation program.

**Dr. Payette:** At present I don’t think we can state the amount of protein needed to increase muscle mass, because we still don’t know exactly how the refeeding should be done in various at-risk groups: elderly hospital inpatients, those with acute disease, those with chronic disease, frail elderly people living in the community, and so on. We are not yet able to recommend the amount of protein needed to increase muscle mass, and we don’t have many studies measuring muscle mass directly and precisely. Muscle *quality* may be the variable of interest. Dr. Kehayias showed that this is an outcome variable that may respond to nutritional supplementation.
Known Related Effects of Nutrition on Aging Muscle Function

**Dr. Roubenoff:** I think that the problem between protein and muscle is not necessarily one of intake but one of partitioning, and unless you are below the RDA, where quantity of protein is clearly limiting, the issue is how to drive the protein into muscle. There are several ways, as the French group has shown. You can manipulate the timing of the food (there are several studies showing that feeding within an hour after exercise increases amino acid intake into muscle [3]), and you can use anabolic agents such as growth hormone, testosterone, and so on. I think the challenge is not only understanding the weaknesses of our measurements but also the weaknesses of our approach in general – we really have to think about the anabolic drive as well as about the anabolic material.

**References**