The Role of Nutrition and Functionality in Ageing

Chair: Professor Cornel Sieber

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The Role of Nutrition and Functionality in Ageing

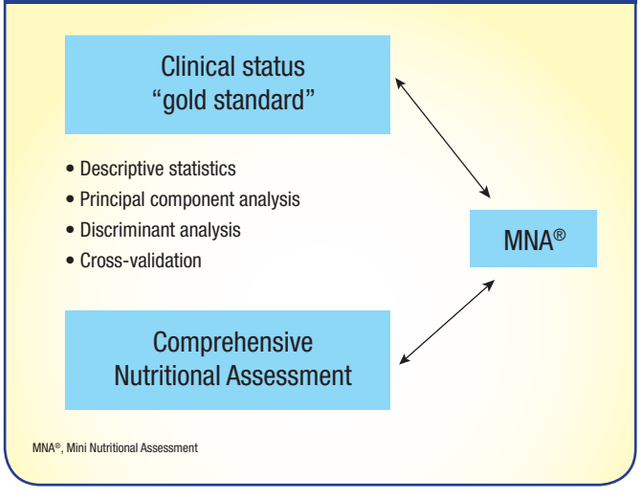
The Nestlé Nutrition Institute was proud to host the satellite symposium "Nutrition and Functionality: Key Partners in Ageing" at the 2009 ESPEN Congress. The objective of the symposium was to highlight the importance of good nutritional status, in older adults. In this population, adequate nutrient intake is essential for good nutritional status, which ultimately impacts functionality and independence. With the high prevalence of malnutrition in the older population and its link to poor outcomes and dependence, assessment of nutritional status should become a standard of care for all older adults. In the first presentation, Dr Juergen Bauer profiled the findings of a new international study on the Mini Nutritional Assessment (MNA®), which has again proven its validity in elderly persons living in different settings. Dr Bauer's presentation set the scene for the two other presentations focusing on the role of nutrients. In one, Professor Heike Bischoff-Ferrari discussed the role of vitamin D in minimising the risk of falls and fractures. In the other, Dr Luc van Loon discussed the merits of combining well-balanced nutrition with physical exercise.

The MNA® — New Insights from an Internationally Pooled Database

Dr Juergen M Bauer
Assistant Medical Director
Department of Geriatric Medicine
University of Erlangen-Nürnberg
Nürnberg, Germany

Malnutrition affects a large number of older individuals across all settings and has significant detrimental impact with respect to functionality, morbidity and mortality. Routine nutrition screening must therefore be considered a diagnostic standard for all those involved in the care of older persons. The original 18-item MNA® was specifically developed for application in the elderly and, since its first publication in 1994, has been established as one of the most valid and frequently used nutrition screening tools in older persons.[1-4] The questionnaire comprises anthropometric, global, dietary and self assessments. Originally, the MNA® was validated against clinical evaluation by two physicians with considerable expertise in the field of nutrition in older persons and also against extensive laboratory testing (Figure 1).[4] The nutritional screening provided by the MNA® offers a reliable scale with clearly defined thresholds and can be used by a generalist assessor with little opportunity for bias introduced during data collection. The tool is acceptable to patients and is inexpensive.[5-7] The general acceptability of the MNA® as a research and clinical tool is evidenced by its high publication numbers.

Figure 1. The original 18-item MNA® was validated using two principal criteria[4]



MNA®, Mini Nutritional Assessment

The MNA® Internationally Pooled Database Initiative

The MNA® International Initiative was a recent worldwide database study conducted with several aims in mind:

- Provide information on the prevalence of malnutrition in different settings across the world;
- Examine the relationship between MNA® results and external parameters of nutrition and inflammation;
- Test the validity of the original MNA® short form (MNA®-SF) in this large international data pool;
- Develop an alternative MNA®-SF for application in individuals where body mass index (BMI) is not available; and
- Create two cut-offs for the MNA®-SF for identical categorisation as provided by the full MNA®

Using PubMed searches, studies on nutrition in the field of geriatrics, published since 2000, were identified for inclusion in the database. Studies that provided data based on MNA® results, and on additional biochemical, anthropometric, functional and dietary assessment parameters of nutritional status were selected. Studies had to provide a clear definition of setting. Authors were requested to submit their original data together with a checklist for each dataset. Following a review of data quality and consultation with the authors, the data were merged into a single database. Twenty-four investigators submitted a total of 27 datasets that included 6,257 subjects (mean age 82.3 years) from 13 countries. Subjects came from a variety of settings, including hospital (n=2,579), nursing home (n=2,045), community (n=1,009), rehabilitation (n=384), and not specified (n=240).

Subject characteristics and MNA® correlations with serum albumin and CRP

When age was compared across settings, a lower age distribution (≤80 years) was observed in the community setting than in the hospital, nursing home and rehabilitation settings. There was a large variation in the prevalence of nutritional deficit across settings, with the rehabilitation setting providing the highest prevalence, followed by the hospital, nursing home, and community settings. There was a clear correlation between MNA® category and serum albumin level across all settings, with the lowest mean albumin level associated with malnourished subjects. This correlation was especially apparent in the nursing home setting, but was less clear in the hospital setting. C-reactive protein (CRP) levels were also correlated with MNA® category, with median CRP levels higher in malnourished subjects than in either at-risk or well-nourished subjects.

Testing the original MNA®-SF and alternatives

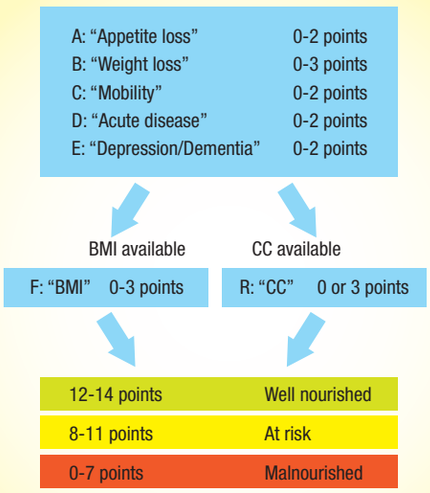
The original MNA®-SF questionnaire comprises six of the 18 items included in the full MNA®. For the MNA® Internationally Pooled Database Initiative, investigators conducted an analysis on a subgroup of 2,032 study subjects with complete information on all 18 MNA® items.[8] Through combination analysis and receiver operating characteristic (ROC)-based derivation of classification thresholds, various adaptations of the current MNA®-SF were proposed and tested on the database. When compared with the full MNA® instrument, the original MNA®-SF was ranked second for highest sensitivity out of 5,577 possible combinations of the 6-item questionnaire.[8] This finding confirmed the original MNA®-SF as a reliable screening tool.

However, the investigators wished to evaluate an alternate short form instrument for use in those geographic regions where weight measurement is uncommon for cultural reasons, and for those cases where subject immobility complicates any measure of weight and height. An alternative short form version that also provides easy and quick assessment was therefore developed based on calf circumference (CC) as a substitute for BMI. This CC-MNA-SF was found to perform equally well to the original MNA®-SF, achieving the highest ranking for sensitivity out of 4,290 possible combinations.[8] A further aim was to develop a MNA®-SF with three result categories. This was done for three reasons: firstly, to mirror the categorisation used in the full 18-item MNA®; secondly, to increase the focus on malnourished elderly subjects from that of the MNA®-SF; and finally, to increase the usefulness of MNA®-SF as a stand-alone tool for nutritional screening. Using a dichotomised full MNA® as reference, ROC analysis of the original MNA®-SF established an upper cut-point optimised for sensitivity of 11 points to separate well-nourished subjects from at-risk and malnourished subjects. A lower cut-point optimised for specificity of 8 points was similarly established. Based on this method, the original MNA®-SF incorporating BMI assessment was shown to achieve 79.9% correct classifications compared with the full MNA® and no complete misclassifications by two categories. Similarly, when compared with the full MNA®, the CC-MNA-SF achieved 72.9% correct classifications and no complete misclassifications by two categories.[8] Thus, the revised three-category scoring classification for the MNA®-SF using either BMI or CC was found to have good sensitivity compared with the full 18-item MNA®. The cut-points for the MNA®-SF and the alternative CC-MNA-SF are summarised in Figure 2.

Conclusions

The MNA® has gained worldwide acceptance with its utility further supported by the findings of the MNA® Internationally Pooled Database Initiative. Being malnourished or at-risk of malnutrition were shown to be highly prevalent conditions in older individuals, with the highest prevalence rates found in hospitalised subjects and those undergoing rehabilitation. Serum albumin and CRP levels were closely correlated with MNA® category, particularly for assessment of serum albumin in nursing home subjects. It was reconfirmed in the present large dataset that the MNA®-SF in its original form is a strong and reliable nutritional screening tool. When

Figure 2. Items, scoring and cut-points for the MNA®-SF (BMI available) and the alternative CC-MNA-SF (BMI unavailable)



MNA®, Mini Nutritional Assessment; BMI, body mass index; CC, calf circumference

weight and/or height measurements cannot be taken, the revised CC-MNA-SF is a valid alternative and offers practitioners the option of using calf circumference and further increases the applicability of the rapid screen in clinical practice. Due to its specific geriatric focus, the MNA® should be recommended as the basis for nutritional screening in older people.

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Minimising Falls and Fractures — What Role Does Nutrition Play?

Professor Heike Bischoff-Ferrari
Director, Centre on Aging and Mobility
SNF-Professor, Department of Rheumatology
University Hospital Zurich
University of Zurich
Zurich, Switzerland

Impaired functionality in the elderly predisposes the frail to falls and subsequent fractures. Among those aged 75 years and older who live in the community setting, an estimated 32% experience at least one fall each year with 6% sustaining a fracture.[1] Elderly individuals who sustain a fracture have a significantly increased risk of a subsequent fracture, with a similar relative risk (RR) for men and women.[2] Today, evidence-based data on nutrition and fall and fracture prevention is limited to vitamin D and calcium supplementation. Other nutrients, such as vitamins B12 and C have been associated with improved bone health, whereas a higher protein intake has been associated with muscle mass benefits and possibly better function. However, trial data for these nutrients are lacking for fall and fracture endpoints. This presentation summarises the state of the art with respect to vitamin D supplementation with or without calcium supplementation as a dietary intervention for fall and fracture prevention.

Early intervention with vitamin D: sources and insufficiency in the elderly

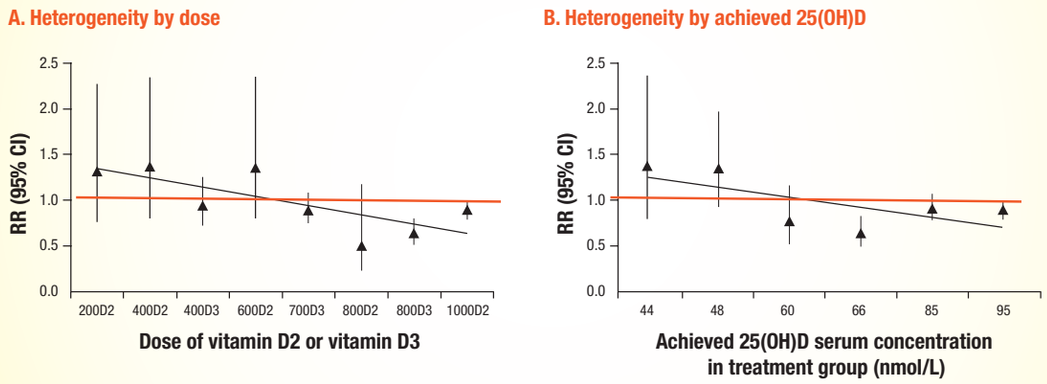
Successful fracture prevention in the elderly requires a dual strategy based not only around improved bone health, but also fall prevention through increased muscle strength. Vitamin D fulfils both criteria with a large body of evidence to show that its supplementation improves bone mineral density and contributes to fracture reduction, whilst also improving muscle strength and therefore reducing the risk of falling.[3] Although the sun and non-supplemental nutrition are both potential sources of vitamin D, the reality is that older persons in most geographical regions retain a high prevalence of vitamin D deficiency. Use of sunscreen, advancing age and concomitant aversion to direct sun, darker skin tone, latitude, winter season and institutional living are all risk factors for not receiving sufficient UVB exposure for the cutaneous synthesis of vitamin D.[4] On the other hand, nutritional sources of vitamin D are rare and largely limited to fatty fish.[4] In a Swiss survey of hip fracture patients aged 65 years and older (mean age 86 years), severe vitamin D deficiency was observed in 60%, with less than 4% achieving a desirable 25-hydroxy-vitamin D level of at least 75 nmol/L.[5] Just 10% of these patients had any vitamin D supplementation on admission to adult care, with significantly higher 25-hydroxyvitamin D levels reported among those whose diets were supplemented with 800 to 880 IU/day (63.5 nmol/L).

Impacts of vitamin D supplementation on muscle tissue

Vitamin D receptors (VDR) are expressed in human skeletal muscle tissue.[6] Intriguingly, increased age is associated with decreased VDR expression independently of muscle type.[6] Preclinical experiments with VDR knockout mice showing small and variable muscle fibres in hind limb skeletal muscle suggest that VDR plays an important physiological role in normal muscle development and provide a rationale for vitamin D supplementation.[7] The physiologic explanation for vitamin D supplementation is that 25-hydroxyvitamin D binding to the VDR in muscle tissue may lead to de novo protein synthesis, positively affecting muscle cell growth.[8] Conversely, muscle weakness may be a sign of severe vitamin D deficiency. In a population-based survey of 4,100 ambulatory older persons (aged ≥60 years) living in the community, two functional tests were used to demonstrate an association between 25-hydroxyvitamin D level and

Figure 3. Meta-analysis of fall prevention studies of vitamin D: heterogeneity between studies according to dose (A) and achieved 25-hydroxyvitamin D level (B)[3]

8 double-blind, randomised, controlled trials were included in the primary analysis (n = 2,376 individuals): pooled RR = 0.87 (95% CI, 0.77-0.99) — significant heterogeneity by dose and achieved 25(OH)D



RR, relative risk; 25(OH)D, 25-hydroxyvitamin D

musculoskeletal function.[9] In both active and inactive ambulatory seniors, lower extremity function improved with higher 25-hydroxyvitamin D levels; this was most pronounced when comparing seniors with very low levels with those with serum levels of up to 60 nmol/L, with a further but less pronounced improvement thereafter.

Fall prevention with vitamin D

The findings of clinical trials for fall prevention with vitamin D have been mixed, with several studies using low doses of vitamin D or with inadequate design and fall event ascertainment failing to establish a significant benefit. Given this background and the observation from two epidemiological studies showing a significant dose-response association between higher serum 25-hydroxyvitamin D levels and better lower extremity function, a meta-analysis was conducted to assess the efficacy of vitamin D supplementation for the prevention of falls among older persons.[3] The meta-analysis considered the role of calcium supplementation and also the efficacy of active forms of vitamin D compared with supplemental vitamin D in the same setting.

Eight high-quality, double-blind, randomised, clinical trials that enrolled 2,376 subjects were included in the primary analysis. The primary outcome measure was the RR of having at least one fall among subjects receiving vitamin D with or without calcium compared with the risk among those subjects receiving placebo or calcium supplementation alone. The pooled RR for any dose of vitamin D preventing a fall was 0.87 (95% CI 0.77, 0.99), indicating a 13% reduction in the risk of falling. However, significant heterogeneity between trials was detected both in terms of dose and achieved 25-hydroxyvitamin D level (Figure 3). This larger than expected variation indicated a need to stratify the studies according to dose (<700 IU versus 700 to 1,000 IU). Based on this stratification, the pooled RR for the 7 studies (1,921 subjects) with 700 to 1,000 IU of supplemental vitamin D per day was 0.81 (95% CI 0.71, 0.92) indicating a 19% risk reduction for falling in subjects given a high dose of vitamin D (Figure 4). In contrast, the pooled RR for the two studies with a dose of less than 700 IU of vitamin D per day was 1.10 (95% CI 0.89, 1.35), indicating that the daily dose for fall prevention begins at 700 IU per day. Achieved serum 25-hydroxyvitamin D levels of ≥60 mmol/L resulted in a 23% fall reduction (RR=0.77; 95% CI 0.65, 0.90), whereas lower concentrations had no effect on fall reduction (RR=1.35; 95% CI 0.98, 1.84).

In a primary subgroup analysis of trials assessing high supplemen-

Figure 4. Meta-analysis of fall prevention studies of vitamin D: higher dose vitamin D (700 IU to 1,000 IU per day) reduces the relative risk of a fall by 19%[3]

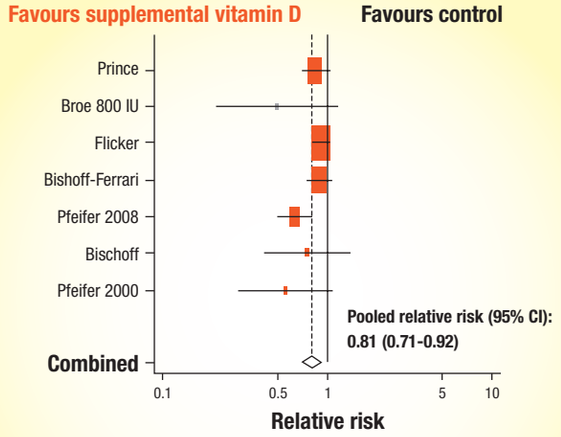


Table 1. Meta-analysis of fall prevention studies of vitamin D: subgroup analysis[3]

	Risk reduction
Primary analysis of higher dose randomised controlled trials	-19%*
Primary subgroup analysis D3 only D2 only	 -26%* -12%*
Age 65-79/community-dwelling Age 80+/institutionalised	-23%* -14%
Less than 12 months treatment duration At least 12 month treatment duration	-38%* -17%*
Main effect vitamin D Vitamin D plus calcium (1 trial)	-23%* -11%

*significant

tal vitamin D doses, the pooled risk reduction was 12% for vitamin D2 compared with 26% for vitamin D3, indicating potentially greater benefits for vitamin D3 in fall prevention. In contrast, active forms of vitamin D did not appear to be more effective than 700 to 1,000 IU of supplemental vitamin D. The findings of the primary subgroup analysis are summarised in Table 1 and suggest that the benefits of vitamin D supplementation on fall reduction were maintained independently of treatment duration. The combined effect of vitamin D plus calcium compared with placebo in one study showed a risk reduction of 11%. However, the main effect of vitamin D (administered alone and compared with placebo or administered together with calcium and compared with calcium) assessed in six studies was associated with a pooled risk reduction of 23% (RR 0.77; 95% CI 0.65, 0.92). This finding suggests that the main effect of vitamin D may be independent of additional calcium supplementation provided the nutritional needs for calcium are met.

Nonvertebral and hip fracture prevention with vitamin D

A second recently published meta-analysis examined the effect of oral vitamin D supplementation on fracture prevention in older subjects (≥65 years) in 12 double-blind, randomised, controlled trials for nonvertebral fractures (n=42,279) and eight similar trials for hip fractures (n=40,886).[10] The meta-analysis specifically addressed anti-fracture efficacy by received dose (dose x adherence) and in pre-defined subgroups including concomitant calcium supplementation. The pooled RR for prevention of nonvertebral fractures was 0.86 (95% CI 0.77, 0.96) and 0.91 (95% CI 0.78, 1.05) for prevention of hip fractures, with significant heterogeneity for both endpoints. Explaining the source of heterogeneity, anti-fracture efficacy increased significantly with a higher dose and higher achieved 25-hydroxyvitamin D level. When trials with a higher received dose of more than 400 IU/day were pooled, the RR was 0.80 (95% CI 0.72, 0.89) for nonvertebral fractures and 0.82 (95% CI 0.69, 0.97) for hip fractures. Moreover, the effect of vitamin D supplementation was independent of additional calcium supplementation.

Conclusions

Vitamin D modulates fracture risk in two ways: by decreasing falls and improving bone density. Data from two recently published meta-analyses suggest there is a dose-dependent benefit for vitamin D supplementation both in terms of preventing falls and fractures. For fall prevention, a **treatment** dose of 700 to 1,000 IU/day is required. For fracture prevention at the hip, a minimal **received** dose of more than 400 IU/day is required (about equivalent to a treatment dose of 700 to 800 IU/day). Thus, strong evidence from robust meta-analyses of double-blind, randomised, clinical trials suggests that older adults who are given vitamin D supplementation at a dose of 700 to 1,000 IU/day are at reduced risk of falling and a reduced risk of sustaining a nonvertebral or hip fracture.

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Nutritional and Exercise Interventions to Augment Muscle Mass in the Elderly

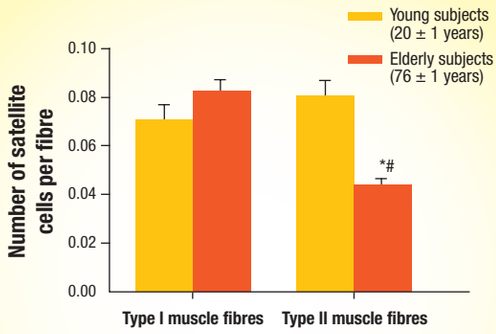
Professor Luc JC van Loon
Medical Physiologist
Department of Human Movement Sciences
Maastricht University Medical Centre
Maastricht, The Netherlands

Muscle mass in ageing and its relationship to strength

Ageing is accompanied by a progressive loss of skeletal muscle mass and strength — or sarcopenia — leading to the loss of functional capacity and an increased risk of developing chronic metabolic disease.[1] This loss of muscle tissue or atrophy is related to a reduction in the overall number of muscle fibres and a specific decline in type II fibre size in the elderly (Figure 5).[2] In addition, the number of satellite cells is reduced, which is thought to be an important factor in the aetiology of type II muscle atrophy accompanying age-related muscle loss.[2]

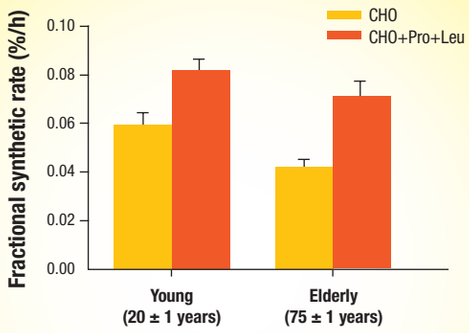
This age-related loss of skeletal muscle mass is attributed to a disruption in the regulation of skeletal muscle protein turnover, resulting in an imbalance between muscle protein synthesis and degradation.[1] As basal (fasting) muscle protein synthesis rates do not appear to differ substantially between the young and elderly, current thinking is that the muscle protein

Figure 5. Atrophy of type II muscle fibres in the elderly but not the young[2]



*Significantly different compared with the young (p<0.01).
#Significantly different compared with the type I muscle fibres (p<0.01).

Figure 6. Protein and leucine co-ingestion with carbohydrates stimulates muscle protein synthesis in young and elderly men[4]



CHO, carbohydrate; Pro, protein; Leu, leucine
Age group effect, p<0.05; treatment effect, p<0.001; interaction of age group and treatment, p=0.583.

synthetic response in the elderly is less responsive to the main anabolic stimuli of food intake and physical activity. The blunted muscle protein synthetic response to food intake is believed to be a key factor in age-related decline in skeletal muscle mass.

Impacting muscle protein synthesis and degradation with nutrient intake

The blunted muscle protein synthetic response to food intake in the elderly may be explained by a number of different mechanisms, including changes in protein digestion and absorption, splanchnic extraction, postprandial hormonal response, muscle perfusion, impaired muscle protein signalling, and the inter-relationships between these physiologic activities. Thus, various approaches have been adopted to overcome the blunted muscle protein synthetic response to food intake in the elderly. Among these, the view that increasing dietary leucine content alone can overcome any blunted response could not be confirmed by a recent long-term intervention study in elderly men showing that 3 months of leucine supplementation (7.5 g/day) does not augment skeletal muscle mass or strength.[3] However, co-ingestion of protein and leucine with carbohydrate after activities of daily living has been shown to stimulate muscle protein synthesis rates to an equivalent extent in young and elderly men, suggesting that a balanced approach to nutritional supplementation can provide benefits (Figure 6).[4] In addition, ingestion of a protein hydrolysate was shown to improve digestion and absorption compared with intact protein in elderly men, and tended to increase the incorporation rate of dietary amino acids into skeletal muscle protein.[5]

Exercise and food intake

Prolonged resistance type exercise training represents an effective therapeutic strategy to augment skeletal muscle mass and improve functional performance in the elderly.[1] Benefits of resistance type exercise on skeletal muscle health in the elderly include a type II fibre-specific increase in satellite cell content,[6] and increased postprandial protein synthesis.[7] Although resistance type exercise training stimulates muscle protein synthesis, it also accelerates whole-body protein breakdown and the net protein balance will remain negative in the absence of food intake after exercise. Tipping this balance towards anabolism requires the timed administration of amino acids and/or protein, which has been shown to be optimal immediately after exercise.[1] However, in healthy elderly men who habitually consume adequate amounts of dietary protein, supplementation before and after each bout of exercise does not further augment skeletal muscle hypertrophy during prolonged resistance type exercise training.[8]

Conclusions

Ageing is associated with loss of muscle mass, strength and function. In addition to physical inactivity and a decline in dietary protein intake, this progressive loss might be attributed to alterations in the muscle protein synthetic response to the main anabolic stimuli. Exercise represents an effective interventional strategy to stimulate muscle protein synthesis. Further research is warranted to elucidate the interaction between nutrition, exercise and the skeletal muscle adaptive response, which will assist in defining more effective strategies for achieving clinical benefits.

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Nutrition screening

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Mini Nutritional Assessment
MNA®

Last name: First name: Sex: Date:
Age: Weight, kg: Height, cm: I.D. Number:

Complete the screen by filling in the boxes with the appropriate numbers. Total the numbers for the final screening score.

Screening

A Has food intake declined over the past 3 months due to loss of appetite, digestive problems, chewing or swallowing difficulties?
0 = severe decrease in food intake
1 = moderate decrease in food intake
2 = no decrease in food intake

B Weight loss during the last 3 months
0 = weight loss greater than 3 kg (6.6 lbs)
1 = does not know
2 = weight loss between 1 and 3 kg (2.2 and 6.6 lbs)
3 = no weight loss

C Mobility
0 = bed or chair bound
1 = able to get out of bed / chair but does not go out
2 = goes out

D Has suffered psychological stress or acute disease in the past 3 months?
0 = yes 2 = no

E Neuropsychological problems
0 = severe dementia or depression
1 = mild dementia
2 = no psychological problems

F1 Body Mass Index (BMI) (weight in kg) / (height in m²)
0 = BMI less than 19
1 = BMI 19 to less than 21
2 = BMI 21 to less than 23
3 = BMI 23 or greater

IF BMI IS NOT AVAILABLE, REPLACE QUESTION F1 WITH QUESTION F2. DO NOT ANSWER QUESTION F2 IF QUESTION F1 IS ALREADY COMPLETED.

F2 Calf circumference (CC) in cm
0 = CC less than 31
3 = CC 31 or greater

Screening score
(max. 14 points)

12-14 points: Normal nutritional status
8-11 points: At risk of malnutrition
0-7 points: Malnourished

For a more in-depth assessment, complete the full MNA®, which is available at www.mna-elderly.com

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