Impacting Outcomes With Nutrition

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A recent survey has shown that geriatricians have good awareness of the relevance that nutritional status has on clinical outcomes, but that their knowledge and identification of malnutrition and nutritional intervention remains suboptimal.[1] In a recent satellite symposium held during the 6th Congress of the European Union Geriatric Medicine Society (EUGMS), leading experts discussed a validated screening tool for early detection of malnutrition. The experts advocated for routine screening for nutritional status as part of Comprehensive Geriatric Assessment, and that nutritional intervention must become a part of standard comprehensive treatment of geriatric patients. This is based on evidence that shows that intervention with oral nutritional supplements in malnourished elderly can decrease mortality, and that specific nutrients (such as protein and vitamin D) are important in optimizing musculoskeletal health and its important clinical outcomes including muscle strength, falls and fractures.

The Mini-Nutritional Assessment (MNA®): A Fast, Valid Tool

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Poor nutritional status linked with decreased functionality

Malnutrition is common in the elderly population, and predisposes these older individuals to functional decline and increased mortality. The prevalence of malnutrition in the elderly diagnosed by the Mini-Nutritional Assessment (MNA®) was 23%, with variations observed in different care settings (51% in rehabilitation, 39% in hospital, 14% in nursing home and 6% in community).[2] Taking into account the "at risk" group with a prevalence of 46%, approximately two-thirds of the elderly are at nutritional risk or frankly malnourished.

Weight loss in the elderly is cause for clinical concern. The European SENECA (Survey in Europe on Nutrition and the Elderly: a Concerted Action) study in a group of independently living elderly individuals has shown that subjects with weight loss (>5 kg) had higher mortality than those with stable or increased weight.[3] Similarly, in a group of elderly individuals residing in nursing homes, mortality was highest in those with body mass index (BMI) under 20 kg/m^2 at 1 year (58.8%).[4]

Occurrence of three or more of the following characteristics supports a diagnosis of frailty – unintended weight loss, self-reported exhaustion, weakness measured by hand grip strength, slow walking speed and low physical activity.[5] Sarcopenia – referring to the selective loss of skeletal muscle and decreased functionality[6] – should be regarded as part of the frailty syndrome of the elderly. In the clinical assessment of malnutrition, muscle loss and functional decline are important factors to consider.

Assessment of malnutrition in the elderly

A standard protocol for screening, assessment, intervention and monitoring of nutritional risk in elderly persons should be part of geriatric care and driven by a multidisciplinary team.

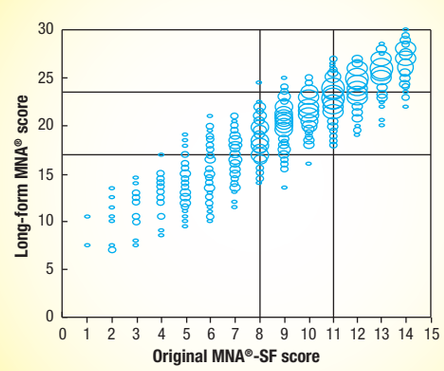
The MNA® is a screening tool developed for detecting the presence or risk of malnutrition in the elderly. Originally developed as a 30-point measurement, the MNA® has been modified into a short form (MNA®-SF) to provide a more practical tool while preserving the accuracy of the original.

The MNA® is the only nutritional screening tool specifically designed and validated for the elderly. As this target population is predisposed to depression, dementia and reduced mobility, there are specific questions on the MNA® that address these issues, and this makes the tool different from other nutritional screening tools.

At 3 years, the mortality rates of the subjects who met the criteria of "malnourished" and "at risk of malnutrition" in the MNA® were 50% and 40% respectively, which were significantly higher than 28% in the well-nourished group.[7] These findings are in line with the higher mortality rates observed in the frail and pre-frail elderly compared with the non-frail group,[5] and are suggestive of a close interrelationship between nutritional status and frailty.

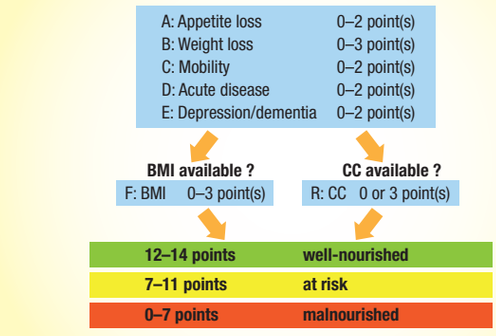
The classical MNA®-SF comprises six questions addressing food intake and appetite, weight loss, mobility, acute illness or stress, dementia or depression, and BMI. The classical MNA®-SF offers a rapid tool for screening out well-nourished older people, but does not differentiate between the nutritionally at risk and the malnourished as in the original MNA®. In 2009, the MNA®-SF was revalidated in a receiver operating characteristic (ROC) analysis of 12 databases involving 2,032 study

Figure 1. Bubble plot of revised MNA®-SF against full MNA®[8]



MNA®: Mini-Nutritional Assessment; MNA®-SF: Mini-Nutritional Assessment-Short Form

Figure 2. Classical MNA®-SF and new MNA®-SF[8]



BMI: body mass index; cc: calf circumference; MNA®-SF: Mini-Nutritional Assessment-Short Form

participants from around the world. Results showed that the new MNA®-SF score correlates strongly with the full MNA® score in this global data set (Figure 1).[8] This validates the new MNA®-SF as a stand-alone tool for nutritional screening of the elderly.

As BMI measurements may not always be available due to cultural reasons or immobility of the elderly, an alternative to applying the MNA® is to measure the calf circumference (CC). Comparison of the MNA®-SF using CC and the full MNA® again demonstrated a strong correlation.[8] Also using this ROC analysis, the three categories from the full MNA® (ie, well nourished, at risk and malnourished) were confirmed to be applicable to the new MNA®-SF, using either the BMI or CC version (Figure 2).

BMI alone is not necessarily the best predictor of health-related events in the evaluation of older persons. Functionality, the cornerstone of frailty, has been shown to be a better parameter. In a study of elderly patients attending a general practitioner's clinic, over 80% of frail persons displayed lower gait speed and approximately one-third of them experienced weight loss of over 5 kg.[9] Physical performance measure of the walking speed was well associated with mortality risk (hazard ratio [HR]=0.73; 95% confidence interval [CI]=0.60–0.88). A significant difference was observed between the low-speed and normal-speed group, independent of the BMI ($p<0.001$).[10] As sarcopenia, with its accompanying functional decline, is the correlate of nutritional frailty, the MNA®-SF and its questions pertaining to mobility mirror especially well the complexity of the nutritional state in the elderly.

Comparison of the MNA® with other nutritional screening tools

The Nutritional Risk Screening-2002 (NRS-2002) system was developed to assess the nutritional status of patients in acute hospital settings and identify those who would benefit from the improvement of their nutritional condition.[11] The tool queries the following: BMI <18.5 kg/m^2, recent weight loss, recent decrease in food intake and if the patient is severely ill.[12] The cut-off for BMI of <18.5 kg/m^2 is too low for an elderly population, Dr Sieber commented, as by this stage successful nutritional intervention is unlikely to be achieved. As the test is not specifically designed for an elderly population, one point should be added to the final score for patients over 70 years of age as compensation.

In acute hospital settings, the MNA® has been found to classify more geriatric patients as being at risk or malnourished than the NRS-2002 and, hence, is a more sensitive screening method.[12] For patients categorized as at risk for malnutrition according to the NRS-2002, there is an 85% concordance with those classified as at risk/malnourished according to the MNA®. However, 37% patients identified as normal according to the NRS-2002 were at risk or malnourished in the MNA®.

Conclusion

Screening for malnutrition should be part of Comprehensive Geriatric Assessment. The MNA® is the only screening tool specifically developed for those aged 65 years and older, who are especially prone to malnutrition. It has been used extensively across the world and is validated in various residential settings (community, rehabilitation, hospital and long-term care). The new MNA®-SF enables replacement of BMI with CC when BMI is not available, and clearly differentiates among the three categories of well nourished, at risk for malnutrition, and malnourished. It is easy to implement in clinical settings, taking less than 4 minutes to complete.

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The Value of Oral Nutritional Supplements

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Protein-energy malnutrition in the elderly – the paradox of the affluent society

Protein-energy malnutrition is a frequent condition in geriatric populations, which can be attributed to several mechanisms and comprises overlapping conditions like:

i. Cachexia, ie, disease-driven catabolism and anorexia
ii. Sarcopenia, related to ageing, disease, low activity and insufficient protein intake

iii. Frailty syndromes characterized by weight loss, muscle wasting and fatigue
iv. Starvation due to neurological and cognitive impairments which contribute to reduced food intake

Given the significant increase in the older segment of the population, improved treatment of chronic diseases and increased exposure to age-related catabolic conditions, protein-energy malnutrition will pose a challenge to many elderly individuals in the future.

Body Mass Index (BMI) is associated with function and survival in old age

BMI has been demonstrated to be related to functionality and survival in older individuals. In an analysis of five longitudinal cohort studies involving 12,725 subjects aged 65 years or older, the lowest hazard risk (HR) for mortality was seen among subjects with BMI of 25–30 kg/m^2 – with drastic increases in risk at higher or lower BMIs.[1] A similar trend was observed for disability, with the lowest HR for disability at a BMI of 24 kg/m^2. According to *NutritionDay* 2006 – a multinational, one-day, cross-sectional survey of nutritional factors and food intake in hospitalized patients, those who ate a quarter of their meal had a more than 2-fold increase in risk of 30-day mortality, which rose to 3-fold for those who ate nothing.[2] Another study further supports BMI to be the strongest predictor of mortality, among other relevant factors, including gender and Katz Index of Independence in Activities of Daily Living (ADL) Index.[3]

Nutritional treatment options

A multitude of treatment options are available for protein-energy malnutrition (Table 1). The oral nutritional supplements (ONS) commonly used in practice are usually rich in energy (carbohydrate and fat) and protein. The nutritionally complete formula can be used as a sole source of nutrition but is usually used as a supplement to food intake, while the nutritionally incomplete one should only be used as a supplement.

Table 1. Treatment options for protein-energy malnutrition

Nutrition	• Fortified regular food • Oral supplementation (energy rich, protein rich and micronutrient fortified) • Enteral nutrition (nasogastric tube, PEG) • Parenteral nutrition
Anabolic treatment	• BCAA, leucine • Growth hormone, nandrolone • SARMs
Reduce catabolism	• Myostatin inhibitors - decoy receptors • Megesterol acetate • Proteasome inhibitors • ACE inhibitors
Immunomodulation	• n-3 fatty acids • Arginine • Glutamine • Antioxidants
Physical activity Resistance training	

PEG: percutaneous endoscopic gastrostomy; BCAA: branched-chain amino acids; SARMs: selective androgen receptor modulators; ACE: angiotensin-converting enzyme

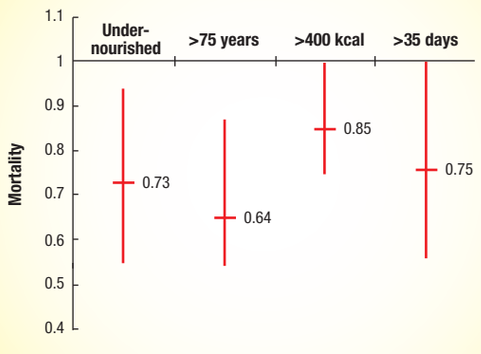
Evidence of benefit of oral nutritional supplements

In a prospective randomized study, elderly patients with hip fractures receiving oral nutritional supplementation (250 mL, 20 g protein, 254 kcal) displayed significant improvement in clinical outcomes compared with controls (56% vs 13%, $p<0.05$).[4] The rates of complications and 6-month mortality were substantially lower in the supplemented group (complications: 44% vs 87%; 6-month mortality: 40% vs 74%).[4] Hence, dietary oral supplementation is effective in improving clinical outcomes in elderly patients with hip fractures.

In the past two decades, a number of meta-analyses have consistently shown the beneficial effects of ONS in prolonging survival of undernourished elderly patients in the hospital.[5] In more recent updates,[6,7] the mortality by the end of follow-up in supplemented patients, overall, was not significantly different from that of control (relative risk[RR]= 0.92; 95% confidence interval[CI]=0.81–1.04). The discrepancy is largely attributed to the inclusion of the Feed or Ordinary Diet (FOOD) trial into the meta-analyses. The FOOD Trial enrolled 4,023 stroke patients to evaluate the effects of ONS, in addition to hospital diet, on survival and clinical outcomes.[8] Since the vast majority of patients in the trial were well nourished at baseline, relatively young (mean age 71 years), without dysphagia (an exclusion criterion), and were treated for a short period of time (6 months), it is not surprising that ONS did not have a significant impact on mortality.[8]

Benefits of ONS have been consistently shown in those with poor nutritional status. Indeed, when the pre-specified subgroup analysis was performed in the 2006 meta-analysis,[6] improved survival with supplementation was again shown in undernourished persons (Peto odds ratio=0.66; 95% CI=0.49–0.90).[6] In addition to undernourishment at baseline, reduction in mortality was also observed for the subgroups who were aged 75 years or older, offered higher energy supplements (>400 kcal) and had continuous intake of supplements for over 35 days (Figure 3).[6]

Figure 3. Meta-analysis: Mortality by subgroup[6]



The updated 2009 review corroborated the findings in 2006, confirming that ONS reduced mortality in undernourished participants (RR=0.79; 95% CI=0.64–0.97) and in geriatric patients (RR=0.78; 95% CI=0.62–0.98), and lowered overall complications (RR=0.86; 95% CI=0.75–0.99).[7]

Functional benefits with nutrition interventions

In patients at risk of protein-energy malnutrition discharged from geriatric wards, nutritional intervention improved Katz ADL index and prevented weight loss.[9] For nursing home residents, in addition to weight gain, nutritional intervention combined with group exercise and oral care intervention also resulted in improved physical performance as assessed by 30-second chair stand at 11 weeks.[10]

The combination of ONS and the anabolic steroid nandrolone was shown to improve lean body mass and activities of daily living in lean elderly women with hip fractures compared with ONS alone or control.[11] Physical exercise combined with ONS significantly improved the results of muscle-strength tests and muscle cross-sectional area in frail elderly.[12]

Conclusion

Poor nutrition is not acceptable in the elderly given its potentially serious consequences; good nutrition is key to healthy ageing.[13] Nutritional intervention should be considered in cases of low BMI, weight loss, reduced food intake and catabolic conditions. ONS provides a useful and cost-effective means to improve nutritional status. Clear benefits of ONS on mortality and complications have been demonstrated in undernourished old-age subjects on prolonged intake of high energy supplements. Combining nutritional intervention with anabolic treatment or physical exercise may bring enhanced effects.

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Vitamin D and Protein: Impact on Musculoskeletal Health in Older Adults

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Bone fractures can result from mechanical incompetence (eg, osteoporosis) or mechanical overload (eg, falls). Dietary factors, especially vitamin D and dietary protein, contribute significantly to the etiology, treatment and prevention of bone fractures. Hip fractures, the most serious complication of osteoporosis, warrant special attention as they represent an extreme situation of vitamin D and protein deficiency. In these cases, nutritional supplementation can help attenuate bone loss and improve muscle strength.

Vitamin D deficiency: Prevalence and pathophysiology

The prevalence of severe vitamin D deficiency (ie, <30 nmol/L) ranges from 50% of hip fracture patients living at home, to 72% of patients in assisted living situations, to 76% of patients in nursing homes.[1]

The protective function of vitamin D on fractures can be explained by its synergistic role in modulating bone metabolism with calcium. Several factors contribute to the disturbance in calcium/phosphate/vitamin D homeostasis with advancing age. Among them are reduction in intake of calcium and vitamin D, decline in intestinal calcium absorption and renal tubular reabsorption, and a lower capacity of the skin to synthesize vitamin D. An inadequate intake of calcium and vitamin D, in turn, leads to a reduction in circulating calcium concentration and increased parathyroid hormone secretion. These changes in the long term cause an increase in bone turnover and steady loss of bone mass, resulting in an increased risk of fractures.

Vitamin D also influences muscle strength. There are specific vitamin D receptors in human muscle tissue,[2] which decrease in number with ageing. Low vitamin D levels are associated with reduced neuromuscular function in ambulatory older persons.[3]

Preventing fractures and falls with vitamin D supplementation

A meta-analysis showed that supplementation with doses of vitamin D of 700–1,000 IU reduced the risk of falling by 19% (relative risk[RR]=0.81; 95% confidence interval[CI]=0.71–0.92, p=0.12).[4] No fall reduction was observed for low-dose vitamin D supplementation (200–600 IU), with a pooled RR of 1.10 (95% CI=0.89–1.35, p=0.42).[4] Given the dose-dependent relationship between vitamin D supplementation and the extent of fall prevention, it is recommended to supplement vitamin D at a daily dose of 700 IU or more to reach 25-hydroxyvitamin D (25[OH]D) concentrations of >60 nmol/L.[4]

In terms of fracture prevention, results from another meta-analysis showed that doses of vitamin D higher than 400 IU reduced non-vertebral fractures by 20% and hip fractures by 18%.[5] Anti-fracture efficacy was again shown to increase with higher doses and higher blood 25(OH)D levels for both non-vertebral and hip fractures.[5] The effects of vitamin D supplementation are rapidly seen, with efficacy typically observed at 3–6 months.[6,7]

Annual supplementation with vitamin D

Annual administration of vitamin D offers great convenience but its efficacy is disappointing. In a randomized controlled study of 1,606 female elderly, a single annual dose of 500,000 IU vitamin D administered orally resulted in 15% more falls and 26% more fractures compared with placebo.[8] Hence, sustained daily administration of vitamin D is preferred.

Vitamin D plus calcium supplement reduces overall mortality

More recently, a meta-analysis of five European vitamin D fracture prevention trials involving 28,700 patients demonstrated a 12% reduction in mortality associated with vitamin D plus calcium, especially for patients under 75 years of age.[9] This study revealed that, in addition to prevention of fractures and falls, vitamin D supplementation with calcium can produce benefits on overall survival.

Dietary protein and musculoskeletal health

Patients with hip fractures are frequently malnourished, with lower intakes of energy, protein, calcium and vitamin D than non-fracture controls.[10,11]

The effect of dietary protein on muscle and bone metabolism is mediated though growth factors such as insulin-like growth factor 1 (IGF-1). IGF-1 is essential for bone anabolism as it exerts a stimulating effect on bone growth and, indirectly, intestinal absorption of calcium and phosphate.[12,13] The production and activity of IGF-1 is, in turn, tightly regulated by protein intake, especially aromatic amino acid precursors.[14]

A body of clinical evidence points to the adverse role of reduced protein intake in muscle and bone loss and fracture risk. Marginal protein intake has been demonstrated to reduce plasma IGF-1 levels and result in skeletal muscle fiber atrophy in elderly women (Table 2).[15] Baseline dietary protein intake was positively associated with lean mass and muscle size measured at 5 years in a cohort of community dwelling elderly women.[16]

In a longitudinal follow-up in the Framingham Osteoporosis Cohort, the rate of 4-year bone mineral loss was inversely correlated to dietary protein intake in elderly persons.[17] Further, cross-sectional surveys have revealed that 1–2% of bone mineral density variance can be attributed to protein intake.[18]

In a prospective study conducted in over 32,050 postmenopausal women, a higher intake of animal sources of dietary protein was associated with a 69% reduced risk of hip fracture.[19]

Benefits of protein supplementation on bone metabolism

Studies of protein supplementation in elderly women post-hip fracture clearly showed benefits in terms of bone mineral density. In a randomized, double-blind, protein supplementation trial of elderly Swiss patients with a recent hip fracture, supplementation with 20 g protein/day for 6 months reduced the rate of bone loss in the year after the fracture.[20] To maintain nitrogen balance in elderly hospitalized patients, a minimum protein intake of 1.1 g/kg body weight per day has been reported.[21]

The IGF-1 level appears to be an important marker of response to protein supplementation. In an exploratory study of hip fracture patients, a rise of IGF-1 level to a maximum level sustainable at 6 months was observed as early as 7 days after onset of protein supplementation.[22] A similar response kinetic was noted in frail elderly.[23]

Table 2. Low protein intake results in reduced plasma IGF-1 and skeletal muscle fiber atrophy[15]

	Changes (%)	
Protein intake	0.92 g/kg	0.45 g/kg
IGF-1	+19 ± 7 *	-30 ± 2 *
Type 1 fiber cross-sectional area (CSA)	+22 ± 7 *	-33 ± 8 *

Changes CSA vs Changes IGF-1: $r^2 = 0.70$, $p < 0.03$

Data from a 10-week study on 12 healthy elderly women (66-79 yrs), randomized to receive protein intake 0.45 g/kg vs 0.92 g/kg and weight maintaining diet.

Conclusion

Based on several nutritional requirement studies in elderly persons, a daily intake of 800 IU/day of vitamin D is recommended for prevention of falls and fractures in this population; a minimum protein intake of 1.1 g/kg body weight is needed to maintain optimal IGF-1 levels and sensitivity for positive effects on bone and muscle.

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