

## Sarcopenia and malnutrition: impact on the outcome in hospitalized patients

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### Abstract

Sarcopenia is a condition caused by a progressive loss of lean body mass and muscle strength, related to aging; this leads to a progressive decrease of physical performance. Sarcopenia is inherently connected with a major risk of disability, hospitalization and mortality. Prevalence of sarcopenia increases with increasing age, in particular among hospitalized geriatric patients, with male dominance. Malnutrition is also very frequent condition in elderly patients during hospital stay and it is involved in the development of sarcopenia. The most common therapeutic approach for both malnutrition and sarcopenia is an increased nutritional support with a protein-rich diet. This narrative review summarises the biological mechanism linking sarcopenia and malnutrition in older hospitalized patients and examines evidence supporting the use of oral nutritional support for the prevention and treatment of malnutrition and sarcopenia in acutely ill medical patients.

### Sarcopenia and malnutrition

Sarcopenia is a condition related to aging, characterized by loss of muscle mass and reduction of muscle strength and physical performance.<sup>1</sup> As demonstrated by the InCHIANTI study, Sarcopenia is associated with an increased risk of disability, hospitalization and mortality.<sup>2,3</sup> In particular, the loss of lean body mass is due to a both quantitative and qualitative reduction of muscle fibers: they become atrophic with a reduction in size and also decrease in number, with less fibers within a single motor unit (fibers of type 2); moreover, the deposition of intramuscular adipose tissue is also present, which replaces the muscle mass. In the general population, the prevalence of sarcopenia is growing up and, as mentioned, increases with increasing of age: in a recent Italian multicentre study the estimated prevalence of sarcopenia diagnosed with the EWGSOP criteria (European Working Group on Sarcopenia in Older People) was 36.4% in

hospitalized patients aged 65 years or older, with male dominance.<sup>4</sup>

In addition to age-related changes, it should be emphasized that lifestyle can contribute to the development of sarcopenia, in particular the most important risk factors are sedentary life-style and caloric-protein malnutrition. Malnutrition is a condition characterized by imbalance between the supply and the demand for a nutrient by the body. Older patients are particularly exposed to malnutrition, because of the increase in catabolic processes and the reduced anabolism of muscle tissue; moreover, a low protein intake, common in elderly, causes a minor bioavailability of amino acids that leads to a reduced muscle mass synthesis.

During the hospitalization, there are many other causes that might promote or aggravate malnutrition in elderly people, including: hypercatabolic status given by acute pathology, side effects and drug interactions, prolonged bedrest, unattractive food, rigorous meal time-schedules, prolonged but insufficient nutritional supplementation, lack of adequate assistance during meals for disabled patients, lasting parenteral nutrition and finally the frequent lack of assessment of nutritional status, caloric intake and nutritional needs of the patient (Table 1). The deleterious effects of progressive malnutrition are numerous, including decrease in muscle mass, suppression of immune response, delay in healing of skin wounds, multiple organ failure syndrome (MOFS) (Figure 1). The patient with malnutrition may complain asthenia, apathy, depression, and eventually might develop delirium.<sup>5</sup> Moreover, it has been shown that undernourished patients with long hospitalization have a doubled mortality at 90 days.<sup>6</sup> Also the CRIME study demonstrated that hospitalized elderly patients with sarcopenia have an increased short and long-term risk of death.<sup>7</sup> Other studies suggested that the presence of sarcopenia might predict the probability of hospital re-admission and, as previously demonstrated, the risk of mortality.<sup>8</sup>

With regards to diagnostic criteria, there is lack of agreement on a unique diagnostic definition of sarcopenia; therefore, in clinical practice the condition characterized by reduction of muscle mass associated with reduction of muscular strength or physical performance is identified as sarcopenia. There are several tools that are used to measure the above parameters and to support the diagnosis. In particular, for the measurement of muscle mass, the gold standard is represented by Computed Tomography (CT) and Magnetic Resonance (MR), but in clinical practice they are not commonly used because of the high cost and the exposure to ionizing radiation. The

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Key words: Malnutrition; sarcopenia; hospital.

Received for publication: 26 July 2018.  
Revision received: 23 September 2018.  
Accepted for publication: 1 October 2018.

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*Geriatric Care* 2018; 4:7723  
doi:10.4081/gc.2018.7723

Dual Energy X-ray Absorbance (DXA) is very effective: it is able to define the density of the analysed tissues, exposing to a low dose of ionizing radiation, but it is rarely used in everyday clinical practice. The use of bioimpedentiometry (BIA) is very common, because of the easy transportability of the instrument and the simple execution of the method and because it is cheap. This technique uses an alternating current created between two transcutaneous electrodes, which, according to the resistance encountered through the body tissues, is able to estimate the percentage of muscle body mass. To evaluate muscle strength (usually hand grip strength) is commonly used a portable dynamometer; grip strength correlates with the strength of other muscle groups of the body and it is able to predict the likelihood of walking recovery in patients with a femoral fracture and age 70 years or older.<sup>9</sup> Finally, concerning the measurement of physical performance, the most used tool is the four meters walking test at usual pace. It is important to underline, however, that the lack of defined diagnostic criteria leads to an important variability in prevalence estimates across the studies carried out so far.

Prevention and treatment of sarcopenia are basically based on three options: physical exercise, drugs and nutritional support. Exercise, the most effective intervention, reduces the loss of muscle mass and strength of skeletal muscles during aging. Especially, anaerobic exercise seems to have major effectiveness in the prevention of sarcopenia; in fact, it is observed an increase in the size of muscle fibers, a reduction in intramuscular adipose deposition and in insulin resistance of fibers, which increase muscle strength and func-

tional performances. Nevertheless, physical exercise is seldom feasible in the acute care setting. Concerning the pharmacological approach, there is still no strong evidence in terms of efficacy and no single drugs are approved by international pharmaceutical regulatory agencies for prevention and treatment of sarcopenia in older people. Among the tested drugs, supplementation of vitamin D, often deficient in elder people, has been associated with both a reduction in loss of muscle mass and strength and with a protective effect on the bone fragility, and therefore, in turn, also with a reduction of the risk of falling and fracture. Vitamin D supplementation should be always performed in case of deficiency for more than one reason.

Several studies have investigated the effect of caloric and protein or amino acids supplementation on clinical outcomes in older hospitalized patients. Globally taken the results of these studies have yielded mixed results. A systematic review and meta-analysis published in 2016 highlights how a program of oral nutritional support, despite increasing caloric and protein intake and body weight, did not have significant effects on overall clinical outcomes including mortality, intra-hospital infections, length of stay, and physical performance at discharge, except for rate of urgent re-admission.<sup>10</sup> Nevertheless, other studies, not included in the meta-analysis, showed that the administration to elderly hospitalized and malnourished patients of oral supplements rich in amino acids, particularly containing hydroxymethylbutyrate (HMB), was associated with a lower 90-day mortality risk.<sup>11</sup> To further investigate the effect of nutritional supplementation on the health status of older medical inpatients, we have performed a multicenter study to determine if nutritional supplementation with amino acids (Aminoglutam®: 96 kcal, 12 g amino acids, 0.18 g fat, 11.6 g carbohydrates, vitamin B1, B6 and C) was associated with improvement in overall health status, assessed with the multidimensional prognostic index (MPI). This double blind placebo controlled study was performed on 126 hospitalized patients older than 65 years, recruited from six Italian geriatric wards. MPI assessment was performed at baseline and after 4 weeks of treatment with nutritional supplementation or placebo twice a day. At the end of the follow-up both the experimental and the placebo group had lower MPI score compared to baseline value, suggesting improvement in health status, without significant difference between groups. Subgroup analyses demonstrated a significant increased probability of MPI improvement among men but not among women.

In line with previous studies, our results demonstrate that oral amino acid supplementation is more effective in old male patients compared to old female patients to improve their health status, assessed with MPI. According to the literature,<sup>12</sup> we suppose that it might be due to the established sexual dimorphism between men and women in mass muscle and its age-related changes: a healthy adult man has more lean body mass and less fat than a woman, but the age-related loss in muscle mass is faster in male than in female.<sup>13,14</sup> The reason is still controversial, but the most accepted hypothesis is linked to sexual hormones:<sup>15,16</sup> testosterone has a strong anabolic effect on muscle tissue, while estrogen and estradiol have anti-anabolic properties; the decrease of sexual hormones' levels might justify the different muscle proteins metabolism among male and female patients over 65. Particularly, the inhibitory effect of female sex steroids

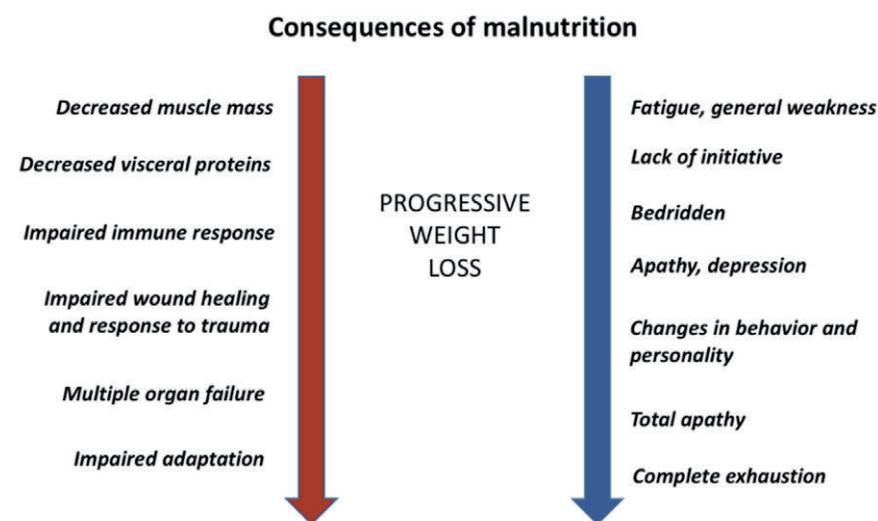
seems to be stronger than the anabolic capacity of testosterone on muscle mass metabolism, acting on the gene expression of inhibition muscle mass factors.<sup>17</sup> Consequently, there might be a different biological and clinical response to a protein-rich diet, that results most effective on old male patients.

Therefore, further studies are needed to confirm the related gender effect of amino acid supplementation on MPI in geriatric patients.<sup>18</sup>

In conclusion, sarcopenia and malnutrition are common problems among hospitalized elderly patients and have independent negative effects on hospital and post-discharge clinical course. Nutritional support leads to increase in caloric intake and body weight, but the effect on clinical outcomes is currently controversial. Hence the need to carry out additional high quality randomized trials.

**Table 1. Causes of intra-hospital malnutrition.**

Effects of acute diseases
Drugs side effects and drugs interactions
Food with unpleaseant tasting
Prolonged debridden
Lack of nutritional status assessment
Lack of appropriate evaluation of nutritional requirements
Strict meals schedules
Prolonged fasting and unsufficient nutritional supplementation
Lack of adequate assistance for disabled patients during meals
Prolonged intravenous artificial nutrition



**Figure 1. Schematic representation of malnutrition consequences in older acutely ill patients.**

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