NEW DEVELOPMENTS IN THE APPROACH AND DIAGNOSIS OF SARCOPENIA

Irina-Mihaela Crăcană¹, Ramona Ștefăniu¹, Veronica Mocanu²*, Ioana-Dana Alexa¹
University of Medicine and Pharmacy “Grigore T. Popa” - Iași
Faculty of Medicine
1. Department of Medical Specialties (II)
2. Department of Morpho-Functional Sciences (II)
*Corresponding author. E-mail: veronica_mocanu@yahoo.com

NEW DEVELOPMENTS IN THE APPROACH AND DIAGNOSIS OF SARCOPENIA (Abstract): Sarcopenia, the key point of frailty syndrome, leads to decreased physical activity, with important consequences upon the quality of life in elderly. The prevalence of sarcopenia is still uncertain because of the lack of homogeneity of the studied populations, and also because of the variety of techniques. The development of biological markers that can be used in a cost effective manner to guide diagnosis and facilitate monitoring patients with sarcopenia, would mark an important step in managing the care of geriatric patients. Nutrition combined with physical activity is the key component of the management of sarcopenia, with a synergistic effect that helps combat malnutrition and improve the quality of life. Keywords: SARCOPENIA, BIOMARKER, NUTRITION, VITAMIN D.

Sarcopenia is defined as the loss in muscle mass and strength that occurs with age, generating a decrease in physical activity. It causes a progressive decrease in muscle mass of about 8% per decade by age 40-70 years, and of 15% after the age of 80. This condition affects 30% of patients over 60 years of age and about 50% of those over 80 years old (1).

The factors that contribute to the development of sarcopenia are multiple: physical inactivity, vitamin D deficiency, chronic inflammatory status, hormonal changes (low testosterone levels) and neuromuscular changes (decrease in the number of muscle fibres and motor neurons). The consequences will be severe, as the decreased muscle mass and strength will lead to a decline in physical activity, increased body instability and risk for falls and ultimately depression, poor quality of life and disability.

The decline in physical activity due to sarcopenia leads to a decrease in physical strength and force and will eventually lead to sedentary life and dependency with direct implications on quality of life and an increased risk of disability (2).

Sarcopenia decisively influences the risk of falls and fractures in older people: nearly half of accidental deaths in people over 65 are related to falls and their consequences (prolonged immobilization, respiratory tract infection) (3).

Unlike cachexia, that occurs secondary to a chronic disease, usually neoplasia,
Sarcopenia refers to a decrease in muscle mass, not necessarily associated with weight loss (4). Thus, the concept “sarcopenic obesity” was introduced, where muscle tissue is infiltrated by fat tissue, in addition to excess subcutaneous fat, which translates to lower quality muscle fibre and muscle strength. Sarcopenia is a reliable marker of global presence of fragility syndrome (5). However, sarcopenia can lead to frailty, but not all sarcopenic patients are frail.

**DIAGNOSIS**

Decreased muscle mass makes the diagnosis of sarcopenia. The discrepancy between muscle mass and strength makes the assessment of muscle mass alone insufficient (6). Longitudinal studies have shown that the decline in muscle strength far exceeds changes in muscle mass, particularly in patients with constant body weight. In addition, preservation of muscle mass does not prevent the sensation of muscle weakness in the elderly (7).

The prevalence of sarcopenia is still uncertain because of the lack of homogeneity of the studied populations, but also because of the variety of techniques used to assess muscle mass. Full body scan by Dual X-Ray Absorptiometry (DXA) is currently considered the golden standard for assessing muscle mass (8). Other methods are bioelectrical impedance analysis, computed tomography (CT), magnetic resonance imaging (MRI), each of them providing objective and reliable information on muscle mass and fat (9). Unfortunately, such imaging equipment is not always available. In addition, MRI and CT examinations are quite expensive. Also, each of these techniques provides different estimates of body composition profile in terms of anatomical regions, making it difficult to compare the results (10). These and other drawbacks limit their use in routine practice. Muscle mass is only one dimension of sarcopenia. The functional decline arising from muscle coordination and balance disorders are clear signs of aging, which significantly affect the quality of life (11).

Muscle strength can be easily measured through performance tests: Short Physical Performance Battery (SPPB), 4-meter walk test, handgrip strength test. These tests can be significantly influenced by comorbidities that are often present in older people, mainly through inflammatory or degenerative ostearticular diseases (12). While assessing the combined muscle mass and strength is a prerequisite for identifying sarcopenia, one of the biggest current problems is to define thresholds to differentiate between "physiological” and "pathological" aging (13). This limits the applicability of imaging tests and biomarkers in clinical practice and research.

The development of biological markers that can be measured in body fluids, used in a cost effective manner to guide diagnosis and facilitate monitoring patients with sarcopenia, would mark an important step in managing the care of geriatric patients. Recent studies show that the combination of biochemical assays with imaging methods increase the accuracy of sarcopenia detection (12). However, the list of biomarkers proposed is very long and includes markers of inflammation (CRP, IL-6 and tumor necrosis factor TNF-alpha), urinary creatinine, hormone levels (testosterone, insulin-like growth factor 1, vitamin D), markers of oxidative stress. It was recently proposed a new set of serum markers directly associated with changes in skeletal muscle mass and function.
New developments in the approach and diagnosis of sarcopenia

N-terminal peptide of type III procollagen (P3NP) (10) seems to be correlated with muscle remodeling after lifestyle change, exercise done consistently (14) or after hormone therapy with testosterone or growth factor (15). Framingham Offspring study conducted on 687 people showed that P3NP levels were related to total muscle mass in postmenopausal women but not in elderly men, therefore this biomarker is highlighted as a gender restrictive one (16).

C-terminal Agrin Fragment (CAF) (17) seems to be a reliable marker in skeletal muscle mass assessment. Excessive cleavage of the native motor neuron-derived agrin by neurotrypsin into a C-terminal Agrin Fragment (CAF) leads to functional disintegration at the neuromuscular junction and may consecutively cause sarcopenia. Elevated plasma levels of CAF were correlated with impaired neuromuscular junction, which in turn is involved in fiber denervation, muscle atrophy and dysfunction (18).

Similar to CAF, plasma concentrations of extracellular heat shock protein 72 (eHsp72) were inversely related to muscle mass and function (19). Production of eHsp72 has been correlated with inflammation (20) and the phenomenon of apoptosis. However, its implication in the development of sarcopenia is currently unclear.

Listed parameters and their partial association with pathophysiological processes involved in the development of sarcopenia underline the idea that we cannot consider the existence of a single biomarker. Comorbidities (cardiovascular disease, chronic renal disease, diabetes, lung disease, cancers) can also influence the biomarkers.

In conclusion, a complex approach can provide useful information about the pathophysiological mechanisms that lead to frailty and sarcopenia, with further implications in prevention or therapeutic strategies.

**PREVENTION AND TREATMENT OF SARCOPENIA**

Screening elderly people in order to detect those at risk of malnutrition is the key point and involving geriatricians, nutritionists and physiotherapists is essential.

In 2008 the Society for Sarcopenia, Cachexia and Wasting convened an expert panel to develop a guide of nutritional recommendations for prevention and management of sarcopenia. It concluded that protein and calorie intake is key measures associated with appropriate resistance training and aerobic exercises. However, nutritional management for sarcopenia remains unknown, recommendation ranging from one study to another.

1. **PROTEIN INTAKE**

In 2015, Rizzoli reported their recommendations for optimal protein intake from 1.0 to 1.2 g / kg, with an equal distribution for each meal (21).

Paddon-Jones et al. have proposed a diet plan that includes 25 to 30 grams of high quality protein per meal. In addition, adding to the diet 15-20 grams of whey proteins has increased the effects of exercise on muscle (22).

The intake of proteins and amino acids remains the most important anabolic stimulus of lean muscle tissue. Previous studies demonstrated anabolic effect of essential amino acids, particularly the branched chain (leucine). The β-Hydroxy β-Methylbutyrate (HMB), is a metabolite of the amino acid Leucine that, along with KIC (α keto-isocaproate) and isovaleryl-CoA, mediate the effects of leucine. Approximately 5% of dietary leucine is oxi-
dized into HMB, and HMB appears to be the main metabolite of leucine that more effectively prevents the breakdown of muscle protein. HMB is proposed as a potential food supplement for patients confined to bed for a long period of time (23), but further studies are needed.

In addition, diets supplemented with amino acids and carbohydrates consumed one hour after physical exercise increase muscle protein synthesis.

2. PHYSICAL ACTIVITY

Exercise is another important aspect in the prevention and management of sarcopenia. There are four types of recommended exercise, depending on the particularities of each elderly. Endurance exercises have a positive effect on the cardiovascular system. Strength training increases muscle mass and combined with nutritional supplements, improve muscle strength. Complex or simple balance exercises standing on one leg with eyes closed and hand support may decrease the risk of falls. Flexibility exercises, such as yoga or stretching can help prevent or recover from falls (24). Regardless of the type of exercise, it is recommended practicing them at least three times a week.

Nutritional intake combined with exercise has a synergistic effect that helps combat malnutrition and improves the quality of life. Physical activity should be recommended but in different intensity and complexity depending on age and possibilities of travel. Patients should be evaluated by a physiotherapist in order to assess range of motion, strength and endurance and to determine the need of using assistive devices such as canes, grab bars, shower seats.

3. VITAMIN D

Vitamin D deficiency is also frequent in older people, regardless of race or ethnicity. The level of 25-hydroxy vitamin D (25) (OH) decreases with age and is associated with muscle weakness. Dosing of vitamin D should be made to all person with sarcopenia, followed by adequate treatment (doses sufficient to increase the level of over 100 nmol/L) (25). The effects were observed in postmenopausal women. Doses up to 50,000 IU of vitamin D2 or D3 per week are allowed. But recent studies show that increased doses do not provide additional benefits compared to usual doses (26).

CONCLUSIONS

The analysis of recent literature makes us conclude that sarcopenia is a fundamental element in the diagnosis of frailty syndrome. According to our results, the geriatric evaluation must include the evaluation of sarcopenia, in order to assess the response to treatment and the evolution of frailty. From our experience several nutritional supplements, such as whey protein, amino acids (leucine, glutamine), vitamin D appear to be beneficial in promoting healthy muscle mass.

REFERENCES

New developments in the approach and diagnosis of sarcopenia


---

**NEWS**

**ORGANOPHOSPHATE PESTICIDES DURING PREGNANCY AND NEUROLOGICAL DEVELOPMENT DURING EARLY CHILDHOOD**

The authors studied prenatal exposure to organophosphate pesticides, which are ubiquitous in the environment, and child's neurological development. The study was conducted between 2003-2006 on a sample of 327 pairs mother / infant in Cincinnati, Ohio, to determine if there are associations between prenatal exposure to organophosphate pesticides and neurodevelopment in children. In pregnant women, urinary concentrations of metabolites of organophosphate pesticides and non-specific concentrations diethylphosphates, dimethylphosphates and dialkylphosphate were measured twice. In children, Bayley Scales of Infant Development, Second Edition-Mental and Psychomotor Developmental indices at the age of 1, 2, 3 years, the Clinical Evaluation of Language Fundamentals-Preschool, Second Edition, at age 4, and the Wechsler Preschool and Primary Scale of Intelligence, Third Edition, at age 5. Mothers with higher urinary total dialkylphosphate concentrations reported higher levels of socioeconomic status and an increased fresh fruit and vegetable intake. The authors found no association between prenatal exposure to organophosphate pesticides and cognition in children aged 1-5 years. It is possible that higher socioeconomic status and a healthy diet protect the fetus from potential side effects of exposure of pregnant women to organophosphate pesticides or that dietary exposure to metabolites is harmless or not an ideal measure of exposure to the parent compound. (Donauer S, Altaye M, Xu Y, Sucharew H, Succop P, Calafat AM, Lanphear B, Yolton K. An observational study to evaluate associations between low-level gestational exposure to organophosphate pesticides and cognition during early childhood. *Amer J Epidemiol* 2016; 184, 5, 410-418)

*Alina Manole*