CLINICAL

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THE ROLE OF NUTRITION, FOOD SUPPLEMENTATION AND PHYSICAL ACTIVITY TO COUNTERACT SARCOPENIA IN POST-MENOPAUSE AND AGEING

SUMMARY

The reduction of muscle mass during ageing and menopause is a fact; it is difficult to discriminate between the effects of one and the other. Low physical activity together with inappropriate nutrition are correlated with SCI and Sarcopenia. During the menopause, reduced Oestrogen is associated with increased oxidative stress. Insulin sensitivity, DHEA, GH, IGF-1, and Vitamin D3 levels all seem to be reduced after the menopause; these all correlate with reduced muscle mass. Strength training, appropriate nutrition, supplementation (Gunaminoformula) and the intake of Vit. D, Magnesium and Potassium are good tools for counteracting Sarcopenia.

KEY WORDS

SARCOPENIA, MENOPAUSE, AGEING, GUNAMINOFORMULA

BACKGROUND – MENOPAUSE

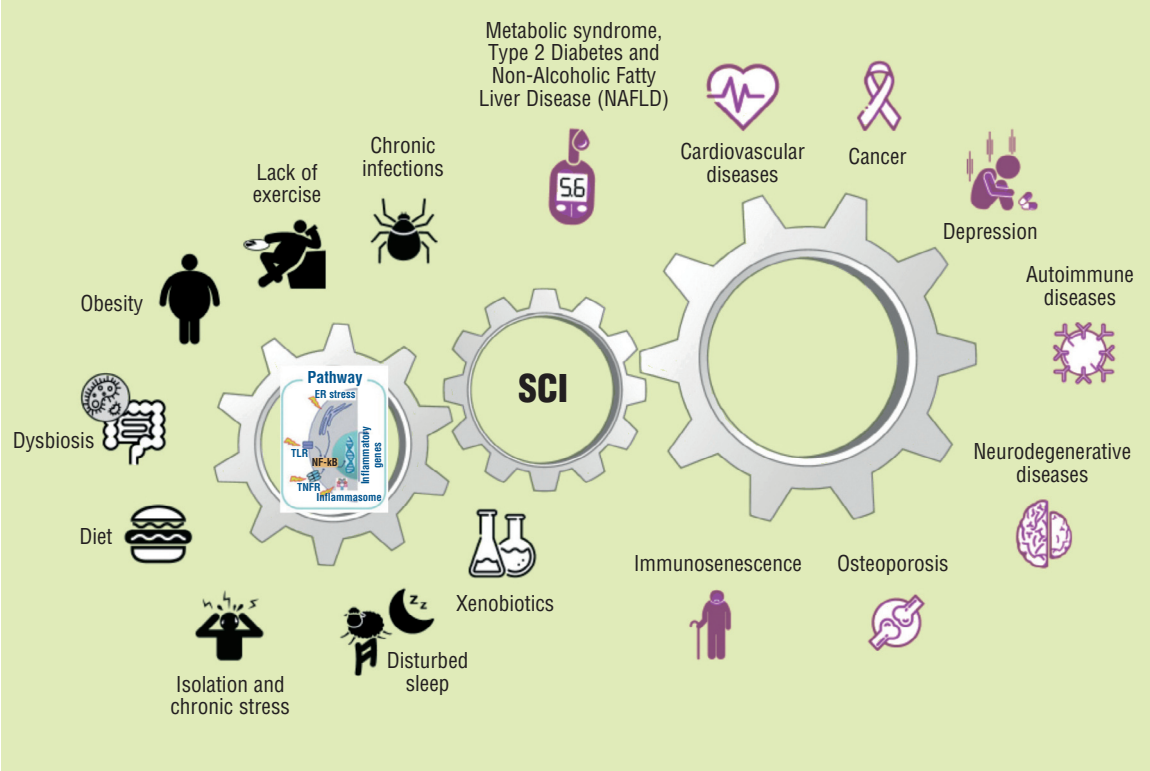
Menopause is a physiological process that generally occurs between the late forties and early fifties; the transition occurs over 5-8 years (climacteric).

Vasomotor signs and symptoms (flushes, palpitations), psychological (mood changes, irritability, anxiety, sleep disturbances, depression) and cognitive (memory and concentration problems), as well as vaginal atrophy, bladder inflammation, night sweats, headache, asthenia, reduced libido, itching, muscle aches and lower back pain can occur in this phase.

– Moreover, during the menopause and with advancing age, the risk of developing cardiocerebrovascular diseases, neoplasms, Type 2 Diabetes, autoimmune diseases and osteoporosis increases (1,2).

BACKGROUND – CHANGES IN MUSCLE MASS AND STRENGTH WITH AGEING

Ageing is associated with **Low Grade Systemic Chronic Inflammation (SCI)** and the natural decline of numerous physiological functions, as well as skeletal mineralisation, muscle mass and strength (3).



Low Grade Chronic Inflammation.
(revised from: Furman *et* Al., 2019).

Furman D. *et* Al. – Chronic inflammation in the etiology of disease across the life span. Nature Medicine, 25, 1822-1832; **2019**.

– This reduction does not occur in a linear manner and is different for both genders. For women it happens earlier than for men and the climacteric period is the most critical and significant one, making them weaker at 65-69 years old than men at 85-89 years old (4).

BACKGROUND – SARCOPENIA

Sarcopenia is clinically understood as a reduction in appendicular muscle mass by 2 standard deviations from the mean of the young adult reference population.

It is characterised by:

1) reduction in the quantity and quality of muscle mass
2) reduction in muscle strength
3) reduction in functional performance (in women more so than in men).

Baumgartner *et* Al. (5) report a prevalence of Sarcopenia for postmenopausal women (< 70 years old) of **23.6%** *versus* **15.4%** for men of the same age.

Rolland *et* Al. (6) describe an average reduction of 0.6% per year in muscle mass after the menopause.
The loss is more pronounced in the first three years, however, than in subsequent years.
Oestrogen reduction, which is related to menopause, is associated with reduced muscle mass and contributes to loss of skeletal mineralisation, the redistribution of subcutaneous fat in favour of visceral fat, increased cardiovascular risk and a lower quality of life (7).
– Since the average life expectancy of women is over 80 years, at least in the European Union, as many as 30 of these are experienced in the post-menopausal period.

CHANGES IN MUSCLE COMPOSITION AFTER THE MENOPAUSE

In the post-menopausal period, intramuscular fat significantly increases; it should be noted that, for energy purposes, women use lipid oxidation more than glucose oxidation.
Lipoprotein lipase (LPL) is the enzyme responsible for the metabolism of muscle triglycerides and their transportation.

Its activity decreases with age and reduced exercise.
LPL in pre-menopausal women causes fat accumulation in the gluteo-femoral regions, while inhibiting fat accumulation at the visceral level.
In post-menopausal women, this difference is no longer present, suggesting a specific relationship between Oestrogen and LPL.

Post-menopausal women who are not on Oestrogen therapy retain the ability to store fat in muscle tissue, and lose the ability to oxidise it for energy, resulting in an excessive accumulation of fat in muscle.
The protective effect of Oestrogen on abdominal fat deposition is impaired.
This results in a lower insulin sensitivity and a higher risk of developing Type 2 Diabetes (8).

FACTORS CONTRIBUTING TO THE REDUCTION OF MUSCLE MASS AFTER THE MENOPAUSE

The elements positively correlated with muscle mass that change with the menopause are **Oestrogen, Dehydroepiandrosterone (DHEA)**, **GH**, **IGF-1** and **Insulin**;
those correlated with Sarcopenia are exercise, dietary protein intake and oxidative stress;
lastly, the element correlated with muscle function is **vitamin D3**.

HORMONAL MODIFICATIONS THAT CONTRIBUTE TO THE REDUCTION OF MUSCLE MASS IN THE POST-MENOPAUSE

– DHEA (9) is a pro-hormone that can be transformed into both Androgen and Oestrogen; it is associated with increased muscle mass, improved Glucose and Insulin levels, lower fat mass and a reduced risk of breast cancer.
With age, especially during the menopause, its circulating levels decrease, leading to a reduction in muscle mass and physical performance.

– GH (10, 11) exerts an anabolic effect on skeletal muscle Tissue during growth; its levels remain stable throughout life with a decline in the post-menopause period.
Estradiol is correlated with GH levels; GH reduction likely correlates with loss of muscle mass and skeletal density; it appears to lead to accumulation of adipose tissue in the abdomen.

– IGF-1 activates synthesis and inhibits protein catabolism in the muscles. The reduction of Oestrogen and IGF-1 with menopause (Oestrogen is believed to exert its anabolic effect through the stimulation of IGF-1 receptors) correlates with an increase in pro-inflammatory Cytokines such as IL-6 and TNF-α (12). Sarcopenia correlates with increased levels of pro-inflammatory Cytokines that promote muscle catabolism, a loss of strength and physical performance.

– Insulin; reduced Insulin sensitivity could also be correlated with lower muscle mass in the post-menopause period.
Insulin is an anabolic hormone that increases protein synthesis and reduces catabolism. Chevalier *et* Al. (13) have shown that post-menopausal women have a lower capacity for anabolism due to increased Insulin resistance.

EXERCISE

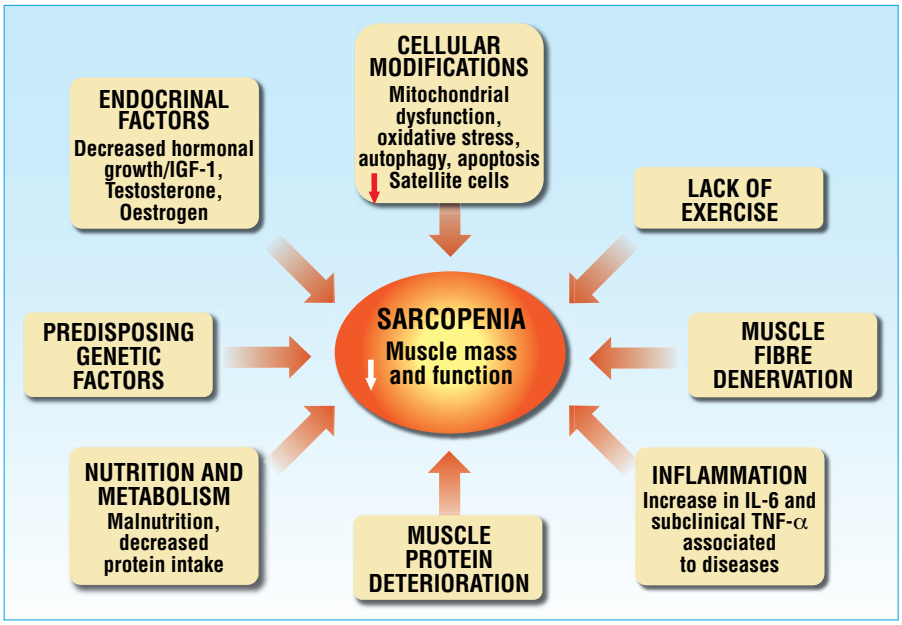
The absence of exercise is considered second only to cigarette smoking as a cause of disease, and is responsible for considerable economic costs in all countries.
– The short-term benefits of exercise include: **1)** increased stamina, energy metabolism and psycho-physical well-being; **2)** improved musculoskeletal health; **3)** reduced stress; **4)** improved cognitive abilities, and sleep.
Overall, regular exercise is associated with a better quality of life and a reduced risk of developing diseases, including neoplasms, cardio- and cerebrovascular diseases, Type 2 Diabetes, obesity, osteoporosis, etc.

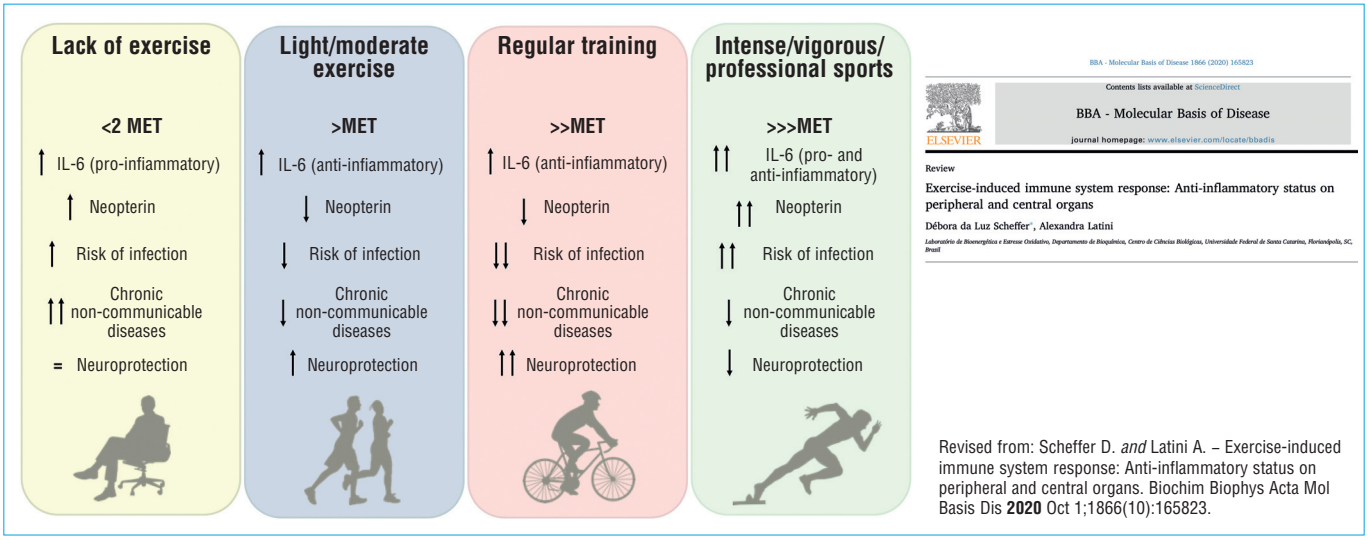
– Exercise, particularly strength training, is crucial for maintaining muscle mass and reducing the accumulation of fat.

Hughes *et* Al. (14), in a longitudinal study lasting over 9 years, report that exercise is crucial when it comes to lowering body weight and preventing muscle mass loss (although not completely).
– In this study, exercise was not distinguished between aerobic and strength activities; it appears that endurance exercises cannot prevent Sarcopenia, whereas strength exercises may be the key strategy for maintaining muscle mass (15).
– The WHO recommends at least 150-300 minutes of moderate-intensity aerobic exercise during the week, or at least 75-150 minutes of vigorous activity plus strengthening exercises of the major muscle groups at least twice a week.

DIETARY PROTEIN INTAKE – JUSTIFICATIONS AND DOSAGES

Protein is essential for optimising adaptation to training and improving performance (note that this is not simply a matter of nitrogen balance).





The effects of a lack of exercise and different exercise intensities on the inflammatory response (IL-6 and neopterin) and health outcomes (risk of infection, chronic non-communicable diseases and neuroprotection). MET = Metabolic Equivalent of Task.

If Carbohydrates correlate with the duration of exertion, Protein correlates with muscle mass, and consequently with the intensity of exertion.

– They are essential for post-menopausal women, especially in the form of essential aminoacids.

Gunaminoformula, a dietary supplement consisting of ultra-purified essential aminoacids already present in the product in adequate ratios and quantities to allow optimal utilisation, provides all the nutrients needed to counteract Sarcopenia.

Some authors believe that the recommended daily intake in this age group should increase from 0.8 to 1.2 g/kg (16-18).

Therefore, these recommendations do not only concern post-menopausal women. Body Protein synthesis increases with increasing daily intake (from 0.86 to 1.4 g/kg) in strength training subjects without increasing the rate of oxidation of aminoacids.

In contrast, consuming diets that provide 2.4 g/kg of Protein increases the oxidation of aminoacids without observing a greater increase in Protein synthesis.

DIETARY PROTEIN INTAKE: TIMING

With regard to the timing of the intake, the following points should be considered:

1) supplements should be phased over time and taken every 3-5 hours
2) recommended doses for each intake are 0.3 g/kg (700-3000 mg of Leucine and a balanced supply of essential aminoacids; approx. 10 g stimulate mTOR, p70s6k and Akt signal genes, necessary for muscle Protein synthesis)
3) take milk-derived Protein and Leucine in the evening before bedtime as it facilitates GH secretion with improved rest and increased muscle Protein synthesis
4) take between 0 and 2 hours after exercise in combination with Carbohydrates with a high glycaemic index (physiological increase in Protein turnover)
5) some authors propose intakes immediately before doing sport as an alternative to post-exercise administration
6) the administration of Protein during exercise at 0.25 g/kg/hr, at the same time as simple Carbohydrates, is useful for minimising the increase in CPK, muscle pain and increasing post-exercise muscle Protein synthesis
7) the administration of post-exercise Protein increases muscle Glycogen synthesis by between 40 and 100% in situations where there is a low Carbohydrate intake (< 1g/kg/h)
8) concerns regarding excessive Protein intake and renal health are completely without scientific basis up to more than 3 g/kg/day in healthy sporting individuals
9) the intake of doses exceeding 2 g/kg/day is unnecessary, except for extremely limited periods of time and in endurance sports.

THE ROLE OF DIET

It is known that inflammatory response is amplified when overeating: hyperlipidic diet, excess of saturated Fats and simple Carbohydrates, low intake of fibre, Vitamins and antioxidant compounds (19-21).

– *In vivo:* the relationship between SFAs (Saturated Fatty Acids) and biomarkers of inflammation has been demonstrated in overweight subjects, where the SFA: ω6-ω3 ratio is directly correlated with the concentrations of IL-6, CRP and adhesion molecules; furthermore, inhibition of IRS-1 (Editor's note: Insulin Re-

ceptor Substrate-1) and reduced Adiponectin levels induce Insulin resistance, increasing the risk of Metabolic Syndrome.

Index and glycaemic load are associated with increased plasma concentrations of PCR; the consumption of whole grains, due to increased fibre intake, is associated with reduced serum concentrations of inflammation biomarkers (PCR and IL-6).

Hyperglycaemia is associated with both a condition of oxidative stress and an inflammatory state.

Chronic hyperglycaemia, through the formation of AGEs (Advanced Glycation End-products) and the interaction with their receptors, leads to the activation of the polyol pathway; Glucose autoxidation results in the increased production of Oxygen-free radicals which induces the activation of certain transcription factors including NF-kB, which corresponds to the increase in inflammation biomarkers, such as PCR, IL-6, IL-8, TNF-α, matrix metalloproteins and endothelial dysfunction markers.

OXIDATIVE STRESS

Oxidative stress increases with menopause and is linked to an increase in the production of Reactive Oxygen Species in the mitochondrion/reduction in the buffering capacity of anti-oxidant systems.

Thus, a vicious circle is created with damage to the mitochondria DNA and a reduction in the ability to produce energy via the electron transport chain; this loss of energy production capacity makes the muscle cell more susceptible to apoptosis, resulting in muscle fibre atrophy and Sarcopenia.

– Signorelli *et* Al. (22) have shown that post-menopausal women have significantly higher levels of oxidative stress than women of childbearing age.

This increase could be related to:

1) significant weight gain in women during this period of life (women with a higher body weight have a higher level of oxidative stress)

2) lower Oestrogen seems to play a protective role against oxidative stress (although the related mechanisms are not yet clear).

VITAMIN D3

Vitamin D3 is known to play a key role in Calcium regulation and the development/maintenance of skeletal mineralisation (23, 24).

There is ample evidence supporting its role in maintaining muscle physiology (its receptors have been identified in the nuclei of muscle cells).
Vitamin D3 deficiency is related to:

– type 2 muscle fibre atrophy
– adipose infiltrate in muscle fibres
– increase in interfibrillar spaces.

Vitamin D3 (and Calcium) supplementation appears to be relevant not only to maintain bone density, but also for muscle function, strength, and reducing the risk of falls and loss of balance.

CONCLUSIONS

The reduction of muscle mass during menopause and ageing is a fact; it is difficult to discriminate between the effects of one and the other.

Low amounts of exercise together with inappropriate nutrition are correlated with SCI and Sarcopenia.

During the menopause, the reduction of Oestrogen is associated with increased oxidative stress.

Insulin sensitivity, levels of DHEA, GH, IGF-1 and vitamin D3 all seem to be lower after the menopause; all this correlates with reduced muscle mass in women.

- Strength training is of great help for a better quality of life during the menopause, as it delays Sarcopenia and the associated decline in physical performance.
- Appropriate nutrition and supplementation are important in order to maintain and prevent the loss of muscle strength associated with ageing and possibly the menopause.
  – In particular, the intake of Protein (or rather **essential Aminoacids**) is crucial for maintaining muscle mass (by stimulating Protein synthesis and reducing catabolism).
- **Vitamin D3**, **Magnesium** and **Potassium** are all good supplements. ■

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