Diagnosis, management strategies and research horizons in sarcopenia

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Abstract

Sarcopenia was first described by Rosenberg as the age-related loss of skeletal muscle mass. The early operational definitions of sarcopenia were based on low muscle mass alone. However, research has suggested a strong predictive relationship between measures of muscle quality i.e., strength and/or physical performance, and health outcomes. Therefore, the definition has been revised to "age-related loss of muscle mass and muscle function". The etiology of sarcopenia is multifactorial and diagnostic recommendations published to date have addressed the total or appendicular muscle mass. Measurement of anterior thigh muscle mass has better correlations with functional tests and all-cause mortality when compared with appendicular or total muscle mass measurements. The aim of this review is to highlight the importance of sarcopenia as an emerging public health issue, diagnostic evaluation with muscle mass and functional performance evaluations and appropriate interventions for management.

Keywords: Muscle mass, lean mass, geriatrics, rehabilitation intervention, muscle power.

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Introduction

Sarcopenia is an important public health problem as it causes physical frailty, mobility limitation and premature death.[1] The term "sarcopenia" was initially defined as "age-related loss of muscle mass"; however, with increasing awareness, its definition has been revised to "age-related loss of muscle mass and muscle function".[2] There are two core components for diagnosing sarcopenia. First is the loss of muscle mass, and second is loss of muscle function. To assess the former, different methods are used worldwide including appendicular (measured by dual X-ray absorptiometry) or regional (i.e. anterior thigh or psoas major measured by ultrasound, computed tomography or magnetic resonance imaging) skeletal muscle mass. The loss of muscle function is usually evaluated by grip strength, chair stand test (CST) and gait speed.[1]

There is still no consensus on the definition and diagnosis of sarcopenia and the evaluation methods to measure muscle mass and function are diverse. Different working groups are trying to establish algorithms to bring uniformity in diagnosis, assessment of severity and management strategies in sarcopenia.[1] The diagnostic recommendations published to date have addressed the total or appendicular muscle mass. However, the age-related loss of muscle mass is more evident in muscles rich in type II fibers (e.g. anterior thigh, abdominal and psoas major), and muscles rich in type I muscle fibers such as soleus, multifidus, tibialis anterior are relatively spared.[3] In this regard, ISarcoPRM algorithm — developed by the Special Interest Group on Sarcopenia of the International Society of Physical and Rehabilitation Medicine (ISPRM) — has been recently released.[1] It is based on regional muscle mass and functional evaluations of the anterior thigh muscle, which is the most commonly/initially affected area with ageing.[3]

The aim of this review is to highlight; the importance of sarcopenia, its diagnosis with simple (but vital) muscle mass and functional performance evaluations (preempting it in the aged population) and relevant interventions for prompt management. The need for future research especially regarding the association between sarcopenia and various/chronic disorders is also noted.

Understanding Sarcopenia

Muscle mass reaches its peak up to middle of the fifth decade and thereafter shows a steady decline with ageing.[3] This reduction in muscle mass may occur due to a combination of the atrophy and loss of muscle fibers preferentially in type II fast twitch fibers.[4] Denervation of fast motor units which is then reinnervated with slow motor units can lead to increased muscle fatigability.[5]

It is known that muscle mass and function are strictly dependent on the balance existing between the anabolic and catabolic processes of sarcomeric proteins, collagen fibers, and myocytes.[2] With ageing, a disruption of balance between the anabolic and catabolic processes leads to loss of muscle mass and function, i.e., sarcopenia. The renin angiotensin system (RAS) modulates these

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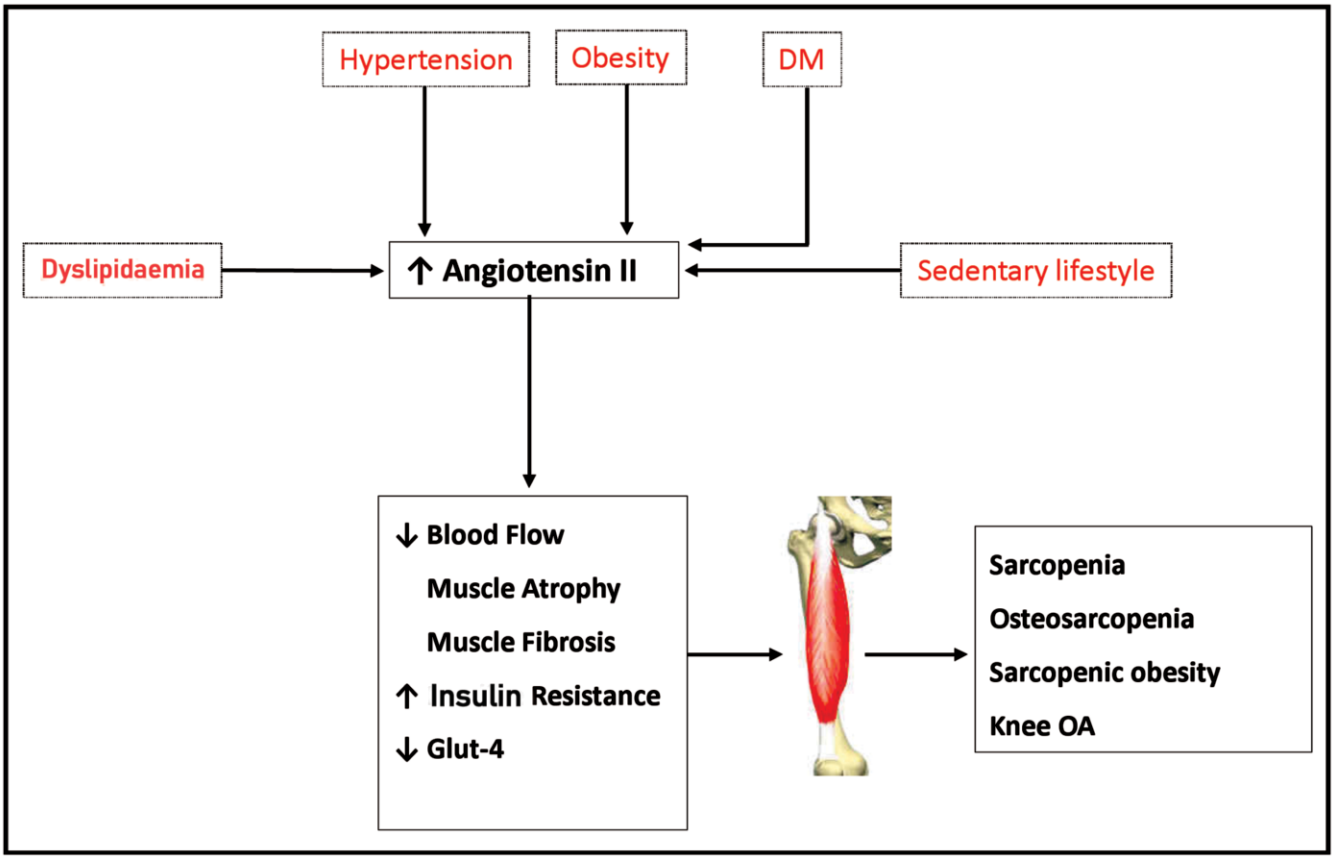

DM: Diabetes mellitus.

Figure-1: Overactivation of the renin angiotensin system is strongly related with all components of the metabolic syndrome, and its main effector angiotensin II plays a central role in age-related metabolic and degenerative disorders such as sarcopenia, osteosarcopenia, sarcopenic obesity and knee osteoarthritis (OA).

processes by acting on the protein turnover, cellular apoptosis, and collagen metabolism. The classical axis induces protein degradation through accumulation of intracellular reactive oxygen species (ROS), and negatively influences the pro-synthetic pathway of the insulin-like growth factor receptor (IGF-R).[6] On the other hand, with an opposite mechanism, the non-classical axis inhibits the ROS mediated effects, myonuclear apoptosis, and stimulates the anabolic processes of the muscle protein synthesis. In this sense, the balance between these two pathways also defines the quality/quantity of the muscle. The counteracting effects of these two axes on the intracellular pathway of the IGF-R deeply influence the expression of Glut-4 receptors over the cellular membrane — modulating the muscle insulin resistance (Figure-1).[6]

On the other hand, ageing with comorbid diseases (chronic inflammatory conditions, osteoarthritis, metabolic disorders), inactivity and malnutrition leads to declined muscle mass and function. Evidence suggests that genetic predisposition, loss of motor units/neurons, dysregulation of cell-signaling pathways, mitochondrial dysfunction, and endocrine dysfunction (e.g. estrogens, androgens, growth hormone, and vitamin D) all contribute to the pathophysiology of sarcopenia.[7] These pathophysiological processes are affected by multiple factors including persistent low-grade inflammation, metabolic disorders, insulin resistance and lipodystrophy.[8]

Assessment and Diagnostic Evaluation

The diagnostic evaluation of sarcopenia is still a focus of ongoing discussion in various working groups globally. To diagnose sarcopenia in the elderly, the core component of muscle quantity (i.e., muscle mass) is measured along with the clinical assessment of muscle quality (i.e., power/strength).

The European Working Group on Sarcopenia in Older People, recommends using appendicular muscle mass and grip strength or CST with specific cut-off-points for each test.[9] However, a recent guideline by ISarcoPRM

recommends the measurement of anterior thigh muscle mass instead of appendicular muscle mass.[1] ISarcoPRM also suggests screening of all older adults and adults with RAS-related disorders to detect and treat sarcopenia earlier. To identify low muscle function, it proposes the use of ≥12 s for CST, and grip strength (cut-off values <32 kg for males, <19 kg for females). Once low muscle function (assessed by CST or grip strength) is detected, with a diagnosis of "probable sarcopenia", it is suggested to use gender and BMI-adjusted Sonographic Thigh Adjustment Ratio (STAR) values (i.e. <1.0 for females and <1.4 for males) to explore significant loss of muscle mass.[1,3] If the subject has both loss of muscle function and mass, the condition is termed as sarcopenia. If the subject has normal STAR values (i.e. loss of muscle function alone), the scenario can be defined as 'dynapenia' and other causes affecting the neuromotor control (e.g. cognitive impairment, polyneuropathy, movement/balance disorder, depression) should also be investigated. If there is mobility limitation i.e. gait speed ≤0.8 m/s and/or inability to rise from a chair without support, then it is categorized as severe sarcopenia.[1]

Interventions in Sarcopenia

Chronic disorders can increase activation of the classical RAS axis, which causes sarcopenia (Figure-1).[2] Therefore, treatments targeting the inhibition of the classical RAS overactivity can be important in the management of several age-related pathologies, such as sarcopenia, sarcopenic obesity, osteosarcopenia and knee osteoarthritis.[10] Therefore, RAS blockers, vitamin D, exercise, and a balanced diet rich in protein can be beneficial for the modulation of RAS overactivity and prevention of sarcopenia.[2] A 3-year longitudinal study demonstrated that continuous use of angiotensin-converting enzyme inhibitors plays a role in the decline of knee extension strength and gait speed.[11] In a cross-sectional study, including 2431 community-dwelling older adults, it has been found that ACEI users had larger lower extremity muscle mass than non-drug users.[12]

Clinicians may also consider a protein-rich diet for older adults with sarcopenia along with exercise interventions. There is insufficient evidence to support vitamin D supplementation in older adults with sarcopenia.[2] Different types of exercise (e.g. aerobic, strengthening, power, balance, coordination, flexibility) can improve blood pressure, muscle mass, strength, and physical function, and seem to be crucial for the management of both hypertension and sarcopenia.[2] A meta-analysis of 391 randomized controlled trials concluded that aerobic or resistance exercises were equally effective as most antihypertensive medications for lowering baseline systolic blood pressure in hypertensive patients.[13]

Future Research

There are still many knowledge gaps about sarcopenia and its coexistence with some metabolic/degenerative disorders such as obesity, osteoporosis and knee osteoarthritis. Although anterior thigh muscle mass is correlated with body mass index (BMI) up to a certain level/age, the increase in BMI with aging can also induce age- and obesity-related metabolic disorders including insulin resistance, hypertension, dyslipidaemia (Figure-1).[10] Therefore, age- and obesity-induced RAS overactivity can cause loss of muscle mass and function especially in the anterior thigh. For instance, sarcopenic obesity (sarcopenia together with obesity) has more adverse effects on body composition and cardiovascular morbidity and mortalities as well. In this sense, it has been shown that sarcopenia and obesity act synergistically to increase the disability risk.[14]

On the other hand, osteosarcopenia has been defined as the concomitant occurrence of sarcopenia and osteoporosis/osteopenia. A recent pooled analysis has demonstrated that osteosarcopenia significantly increased the risk of fracture (odds ratio (OR)=2.46), falls (OR=1.62) and mortality (OR=1.66).[15] Although increased BMI was shown to be protective both for osteoporosis and muscle mass, obesity-induced metabolic problems (hypertension, diabetes mellitus, hyperlipidaemia) may accelerate loss of muscle mass and function in the anterior thigh (i.e. sarcopenia) which may also increase the risk of knee osteoarthritis.[10]

High quality longitudinal randomized control trials are recommended for future research to test and refine well designed algorithms for applicability as a tool. Further research areas include the interventions to prevent/manage sarcopenia before it causes considerable activity/mobility limitation in older adults.

Conclusion

Sarcopenia is a global public health problem, and there is a need for global consensus on the definition, diagnosis, evaluation techniques and interventions to promptly prevent and treat sarcopenia. Adequate treatment should comprise multi-system approach containing vitamin D, exercise, and possibly RAS blockers as well.[2] It is also important that early detection of sarcopenia and its treatment efficacy should be evaluated using more commonly affected muscle measurements (i.e., anterior thigh muscle mass/strength).[1]

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