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SARCOPENIA IN THE ELDERLY: PATHOGENESIS, DIAGNOSIS AND TREATMENT

A Literature Review

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ABSTRACT

'Sarcopenia' involves a progressive age-related loss of muscle mass and associated muscle weakness that renders frail elders susceptible to serious injury from sudden falls and fractures and losing their functional independence This disease has a complex multifactorial pathogenesis, which involves not only age-related changes in neuromuscular function, muscle protein turnover, and hormone levels and sensitivity, but also a chronic pro-inflammatory state, oxidative stress, and behavioral factors – in particular, nutritional status and degree of physical activity. In the previous definition by the European Working Group on Sarcopenia in Older People (EWGSOP) in 2010, the diagnosis of sarcopenia requires the presence of both low muscle mass and low muscle function. Since the 2010 definition is difficult to be translated to clinical practice, the EWGSOP uses low muscle strength as the primary parameter of sarcopenia in the 2018 definition; sarcopenia is probable when low muscle strength is detected. A sarcopenia diagnosis is confirmed by the presence of low muscle quantity or quality. When low muscle strength, low muscle quantity/quality and low physical performance are all detected, sarcopenia is considered advanced. According to the pathophysiological factors involved in the pathogenesis of sarcopenia, different treatment strategies against sarcopenia are resistance exercise training, increase essential amino acids intake, vitamin D supplementation for those with vitamin D deficiency, polyunsaturated fatty acids (PUFAs) supplementation, testosterone supplementation, angiotensin-converting enzyme inhibitor administration.

Keywords: *Sarcopenia, Older People, Pathogenesis, Diagnosis, Treatment*

ABSTRAK

'Sarcopenia' melibatkan hilangnya massa otot progresif terkait usia dan kelemahan otot terkait yang membuat lansia yang lemah menjadi rentan terhadap cedera serius akibat jatuh dan patah

tulang secara spontan dan kehilangan kemandirian fungsionalnya Penyakit ini memiliki patogenesis multifaktorial yang kompleks, yang tidak hanya melibatkan faktor usia. perubahan fungsi neuromuskular, pergantian protein otot, dan tingkat hormon dan sensitivitas, tetapi juga keadaan pro-inflamasi kronis, stres oksidatif, dan faktor perilaku - khususnya, status gizi dan tingkat aktivitas fisik. Dalam definisi sebelumnya oleh *European Working Group on Sarcopenia in Older People* (EWGSOP) pada tahun 2010, diagnosis sarcopenia ditegakkan berdasarkan adanya massa otot yang rendah dan fungsi otot yang rendah. Karena definisi 2010 sulit diterjemahkan ke dalam praktik klinis, EWGSOP menggunakan kekuatan otot rendah sebagai parameter utama sarkopenia dalam definisi 2018; sarcopenia mungkin terjadi ketika kekuatan otot yang rendah terdeteksi. Diagnosis sarkopenia dikonfirmasi dengan adanya kuantitas atau kualitas otot yang rendah. Ketika kekuatan otot yang rendah, kuantitas/kualitas otot yang rendah dan kinerja fisik yang rendah semuanya terdeteksi, sarcopenia dianggap parah. Menurut faktor patofisiologis yang terlibat dalam patogenesis sarkopenia, strategi pengobatan yang beragam terhadap sarkopenia adalah latihan resistensi, meningkatkan asupan asam amino esensial, suplementasi vitamin D bagi mereka yang kekurangan vitamin D, suplementasi asam lemak tak jenuh ganda (*polyunsaturated fatty acids* =PUFA), suplementasi testosteron, dan pemberian *angiotensin-converting enzyme inhibitor*.

Kata kunci: Sarkopenia, Lansia, Patogenesis, Diagnosis, Pengobatan

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INTRODUCTION

The aging process is often associated with the gradual loss of function of tissues and organs. With age, skeletal muscle mass decreases 0.1-0.5% annually.[1] This decline begins at age 30 and declines rapidly after age 65.[1] This decrease in muscle mass is also accompanied by a decrease in muscle strength. This age-related decline in muscle mass and strength is called "sarcopenia".[1]

Although the use of the term "sarcopenia" began in 1989, a practical clinical definition of sarcopenia was only developed in 2010 by the European Working Group on Sarcopenia in Older People (EWGSOP).[2,3] The EWGSOP defines sarcopenia as a syndrome in which there is progressive and complete loss of muscle mass and strength in which there is the risk of complications, namely physical disability, poor quality of life, and death.[3]

The difficulty in measuring muscle quantity and quality led the EWGSOP to issue a recommendation in 2018 to use low muscle strength as the main parameter of sarcopenia.[4] In this 2018 guide, muscle strength is used as a specific parameter for muscle function. Specifically, sarcopenia is thought to occur when low muscle strength is present. Based on the 2018 guidelines, the diagnosis of sarcopenia is made by the presence of low muscle quality or quantity. If muscle strength and muscle quantity or quality are found to be low with accompanying poor physical performance, the sarcopenia is said to be severe.[4]

Sarcopenia in the elderly has a varying prevalence, that is 1-29% for the elderly living in the community, 14-33% for the elderly living in long-term institutions such as nursing homes, and 10% for those in hospital care.[5] The prevalence of sarcopenia increases with age.[5,6] In addition, sarcopenia has significant health and financial implications. From the health aspect, sarcopenia causes an increased risk of falls and fractures, impaired daily activities, increased occurrence of heart disease, respiratory disease, cognitive impairment, and impaired mobility.[4] Sarcopenia also increases the risk of hospitalization.[4] Further more, a health economic study in the United States in 2000 showed that health costs due to sarcopenia reached US$18.5 million (1.5% of total expenditure per year) or about US$860 for each male patient and US$933 for each female patient.[7] Because of the significant impact of sarcopenia, this literature review will discuss sarcopenia from the pathogenesis, diagnosis, and treatment aspects.

PATHOGENESIS OF SARCOPENIA

Sarcopenia is a complex geriatric syndrome due to multifactorial pathogenesis. Various factors involved in the pathogenesis of sarcopenia include neuromuscular degeneration, changes in muscle protein turnover, changes in hormone levels and sensitivity, chronic inflammation, oxidative stress, behavioral/ lifestyle factors.[1]

Neuromuscular Degeneration

One of the mechanisms involved in the pathogenesis of sarcopenia is neuromuscular degeneration characterized by atrophy of muscle fibers (especially type 2 fibers), decreased number of alpha motor fibers from the spine, and accumulation of fat in the muscles. In addition, due to aging process there is

progressive and irreversible loss of nerve cells which then causes denervation of muscle fibers and results in failure of muscle contraction. Usually, denervated fibers will secrete protein and release chemical compounds to stimulate re-innervation.[1]

But along with the aging process, there is a failure in the cycle of de-innervation and re-innervation in which muscle fiber atrophy (especially type 2) occurs with a gradual decrease in size and accompanied by replacement of muscle with fat and connective tissue.[1] In the aging process, neuromuscular disorders also occur where there is a decrease in the number of presynaptic and postsynaptic cells, resulting in a decrease in the postsynaptic response from the neuromuscular junction (NMJs). Mitochondrial degeneration in NMJs can decrease the amount of neurotransmitter released during repolarization.[1]

Changes in Muscle Protein Turnover

Muscle mass is determined by the balance between protein synthesis and breakdown. Anabolic pathways that support muscle protein synthesis include serine/threonine kinase Akt/Protein Kinase B (PKB), mammalian target of rapamycin (mTOR), exercise, and hormones such as insulin-like growth factor-1 (IGF-1), insulin, and branched amino acids (leucine, valine, and isoleucine).[1]

The mTOR kinase interacts with proteins to form 2 complexes, namely mTOR complex 1 (mTORC1) and mTOR complex 2 (mTORC2). mTORC1 has a role in mediating the effects of mTOR on the protein synthesis process. Although the exact mechanism of control of protein synthesis by mTOR is unknown, mTOR1 is thought to play a role in stimulating protein synthesis by inhibiting eukaryotic translation initiation factor 4-E-binding protein (4E-BP1) and activating p70 S6 kinase 1 (p70s6k). mTOR can be activated by several stimuli such as IGF-1, insulin, amino acids, and exercise. When IGF-1 and insulin bind to the receptor tyrosine kinase, they trigger phosphorylation of the receptor and its various substrates, and activate mTOR through activation of phosphatidylinositol 3-kinase (PI3K) and its effector (Akt/PKB). At the same time, Akt/PKB can trigger apoptosis suppression and protein degradation in skeletal muscle through phosphorylation of the transcription factor FOXO1. As a result, the expression of E3 ubiquitin ligase atrogin01 and muscle RING-finger protein-1 (MuRF-1) was inhibited. The mechanism by which branched amino acids stimulate mTOR is not clearly understood. One hypothesis is that amino

acids can activate mTOR directly or indirectly through stimulation of protein kinases other than PKB. Moreover, amino acids can inhibit protein phosphatase or interact with mTOR-associated proteins. Resistance type exercise can increase skeletal muscle protein synthesis through mTOR activation directly or indirectly through Akt/PKB.[1]

Aging causes a decrease in Akt-PKB-mTOR and changes in protein synthesis and can then lead to sarcopenia. In addition, muscle protein breakdown activates and increases TGFβ and myostatin through activation of the ubiquitin proteasome pathway. TGFβ and myostatin are strong triggers of muscle atrophy. TGF and myostatin stimulate Smad2/3 and TAK1/p38 MAPK. Smad2/3 and TAK1/p38 MAPK induce atrogin-1 and MuRF-1 synthesis in skeletal muscle. Atrogin and MuRF will direct the 26 S proteasome to carry out proteolysis of the polyubiquitinase protein and cause muscle atrophy.[1]

Changes in Hormone Levels and Sensitivity

In sarcopenia there is decrease in several hormones that have metabolic effects on muscle mass such as sex hormones (such as testosterone and dehydroepiandrosterone [DHEA]), growth hormone (Growth Hormone [GH]), and Insulin Growth Hormone – 1 (IGF-1). The decrease in GH and IGF-1 levels in the elderly causes changes in body composition such as an increase in visceral fat and a decrease in lean body mass (LBM) and bone mineral density. [1]

Decreased testosterone levels can reduce muscle mass and bone strength resulting in fractures and other complications. The aging process is also associated with increased levels of the hormone cortisol. Increased exposure to the hormone cortisol and decreased GH will cause an increase in visceral fat and a decrease in LBM and bone mineral density. Furthermore, low levels of vitamin D due to an increase in the hormone cortisol, are also associated with a decrease in muscle strength. The presence of insulin resistance that often occurs in the elderly also increases skeletal muscle loss and will worsen the condition of insulin resistance.[1]

Inflammation and Oxidative Stress

The aging process is characterized by a significant increase in inflammatory markers such as tumor necrosis factor-alpha (TNF-α), interleukin (IL)-6, IL-1, reactive phase protein (CRP). Under conditions of aging in the absence of

infection, a chronic and low-grade (inflammaging) systemic inflammatory process occurs. [1]

This condition will increase the tendency to sarcopenia through activation of the ubiquitin-protease system, decrease in IGF-1-mediated anabolic effects and induction of anabolic resistance. Anabolic resistance is the process of muscle protein resistance to food intake.[1]

Under physiological conditions, oral food intake will increase protein synthesis throughout the body and decrease proteolysis. This increase in protein synthesis and decreased proteolysis is due to the anabolic effect of amino acids and insulin. In sarcopenia there is an increase in catabolic factors such as cortisol, cytokines, and oxidative stress, which have a negative effect (increasing muscle anabolic threshold values) on amino acids or insulin signaling pathways involved in the process of stimulating muscle anabolism after ingestion of food.[1]

The aging process is also characterized by chronic oxidative stress which can trigger the activation of the immune system and cause an inflammatory state that will be exacerbated by chronic oxidative stress. Skeletal muscles will consume large amounts of oxygen and produce reactive species of nitrogen and oxygen (RONS) which will be resisted by the antioxidant system.[1]

Oxidative stress causes sarcopenia through the following mechanisms: mitochondrial dysfunction caused by mutations, deletions, and aging damage; impaired ability of muscle cells to remove damaged mitochondria, and decreased type 2 fiber. RONS can also cause sarcopenia through increased proteolysis and decreased muscle protein synthesis. Both of these will then decrease muscle mass.[1]

Behavioral Factors

Behavioral factors, such as nutritional status and physical inactivity, are common causes of sarcopenia. In the aging process there is decrease in appetite and / or food intake and is called "Anorexia of Aging". This phenomenon occurs due to loss of appetite, sense of smell and taste associated with aging, poor dental health, and gastrointestinal changes, such as delayed gastric emptying and increased cholecystokinin levels, dementia, depression, disability, and social environment.[1]

Furthermore, decreased neuropeptide Y and central nervous system functions such as nitric oxide activity play an important role in anorexia of aging. Decreased food intake and protein consumption causes muscle atrophy and exacerbates sarcopenia. Physical inactivity

can increase loss of muscle mass and strength, and increase the severity of sarcopenia.[1]

SARCOPENIA DIAGNOSIS

Sarcopenia is a progressive and generalized skeletal muscle disease that is associated with an increased tendency for its complications such as falls, fractures, physical disability and mortality. The 2010 EWGSOP definition of sarcopenia suggests that the diagnosis of sarcopenia requires the presence of low muscle mass and function, which is then defined as low muscle strength or low physical performance (Figure 1).[1]

Along with the results of existing studies, muscle strength was found to play a more important role than muscle mass in predicting complications that could occur. Therefore, EWGSOP2 in 2018 recommended low muscle strength as the main parameter of sarcopenia because muscle strength is used as a parameter of muscle function (Figure 2).[4] Specifically, sarcopenia is said to be "probable" in the presence of low muscle strength.[4]

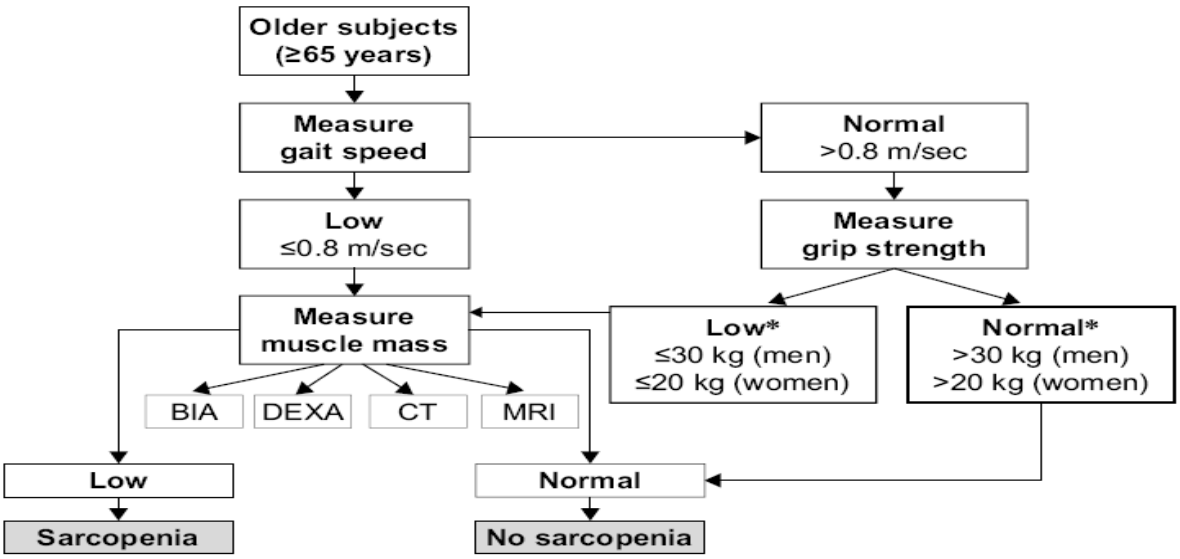

Figure 1. Diagnostic flow of Sarcopenia based on the 2010 EWGSOP.[1]

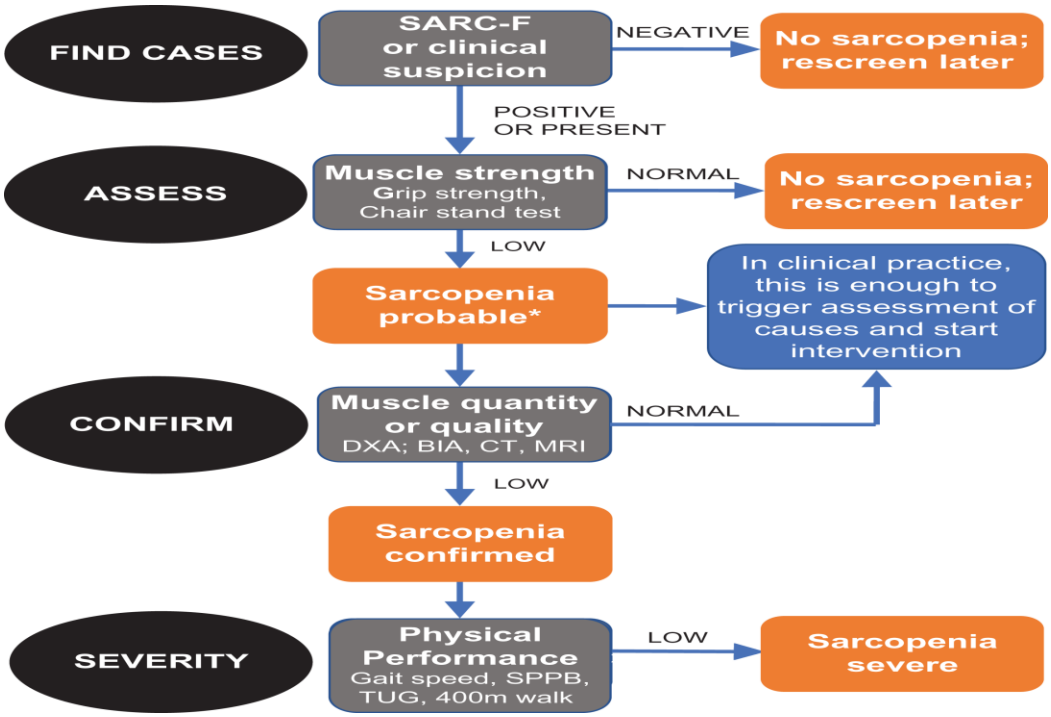

Figure 2. Diagnostic flow of Sarcopenia based on the 2018 EWGSOP2.[4]

The diagnosis of sarcopenia is confirmed in the presence of low muscle quantity or quality.[4] In conditions where muscle strength, muscle quantity/quality and low physical performance are found, sarcopenia is categorized as advanced.[4]

The diagnosis of sarcopenia according to the 2018 EWGSOP2 is divided into four stages: finding cases (Find Cases), assessing cases (Assess), confirming cases (Confirm) and assessing severity (Severity).[4]

Finding Sarcopenia Cases (Find Cases)

In clinical practice, the process of finding a case of sarcopenia begins when a patient reports signs or symptoms of sarcopenia such as falling, feeling weak, slow walking, difficulty standing up from a sitting position, weight or muscle loss.[4]

In patients with suspected sarcopenia, further testing for sarcopenia should be performed. Various follow-up tests include the 2-Phase Algorithm according to Cruz-Jentoft,[4] the SARC-F Questionnaire by Malmstrom and Morley,[8] Screening Grid according to Goodman Goodman, Ghate,[9] Score chart according to Ishii, Tanaka,[10] and Anthropometric Prediction Formulas according to Yu, Khow [11] can be used to screen for sarcopenia.[12] These five screening tests have a high negative predictive value and are similar (87.2 - 100%) when compared to one another.[12]

Since the EWGSOP2 recommends the use of the SARC-F questionnaire, this

article will discuss more regarding this screening questionnaire as a method to rapidly identify individuals requiring diagnostic testing for sarcopenia in the community and in various health facilities.[4,12] Responses to this questionnaire were based on the patient's perception of his or her limited strength, ability to walk, get up from sitting in a chair, climb stairs, and experience falls. Each of these patient perceptions will then be assigned a maximum score of 2 for each component (total score of 10). A score of 4 on the SARF-C questionnaire suggests that sarcopenia is suspected.[8] Further assessment of muscle strength should be performed in patients with suspected sarcopenia.

Assessing Cases (Assess)

In the Assess stage, muscle strength is assessed by measuring grip strength using a calibrated handheld dynamometer. Low grip strength i.e. grip strength <26-30 kg for men or <16-20 kg for women1. Low grip strength is a strong predictor of further complications, such as longer hospital stays, poor health quality, and mortality.[4] Grip strength also correlates moderately with strength in other parts of the body, such as the arms and legs.[4]

In conditions where grip strength could not be measured due to hand disability such as in the case of stroke or severe arthritis, the chair stand test can be used to measure leg muscle strength (quadriceps).[4] This test measures the time it takes for a patient to rise five times from a sitting position without using his arms.[4] In a study conducted by Pinheiro, Carneiro (2016), it was found that the time required was significantly positively correlated with the occurrence of sarcopenia (Odd Ratio [OR] = 1.08; 95% Confidence Index [95%CI]: 1.01- 1.06). For every 1 second increase in the chair stand test, the probability of developing sarcopenia increases by 8% in women over 60 years of age.[13] The time to the chair stand test of more than 13 seconds in women or more than 15 seconds in men and/or low grip strength indicates the possibility of sarcopenia.[4,13]

Confirm Case (Confirm)

The next step is to measure muscle mass. Muscle mass can be estimated by measuring the appendicular skeletal muscle mass (ASM) using the Dual Energy X-Ray Absorptiometry (DEXA) examination; measuring whole body skeletal muscle mass (SMM) using bioelectrical impedance analysis (BIA);

measure the mass of specific muscle groups using computed tomography (CT), and magnetic resonance imaging (MRI).[1,4]

Compared with DEXA and BIA examinations, which are widely used to assess skeletal muscle mass, MRI and CT examination are the gold standard and the most accurate imaging methods that can accurately assess the mass, density, and fat infiltration of a muscle.[1] However, MRI and CT examination cannot be used as the main modality due to the absence of low muscle mass standard, high cost, and the need for trained personnel to operate this examination.[4]

DEXA examination is one of the most widely available tests to determine skeletal muscle mass non-invasively.[4] Fundamentally, muscle mass is correlated with body size.[4] Therefore, muscle mass measured using DEXA can be defined by the skeletal muscle mass index (SMI). SMI is appendicular skeletal muscle mass (ASM) divided by height^2 (kg/m^2).[1]

Low muscle mass according to DEXA is SMI 7.26 kg/m2 for men and SMI 5.5 kg/m2 for women.[1] The advantage of this DEXA check is that it can generate ASM estimates within minutes when used with the same tool and the same threshold value. The weakness of this DEXA examination is that it cannot be implemented in the community yet. In addition, DEXA examination is also influenced by the patient's hydration status.

The BIA examination estimates muscle mass indirectly, namely through the electrical conductivity of the whole body. BIA checks are affordable, widely available, and can be moved more easily. Skeletal muscle mass can be calculated using the Janssen formula.

Skeletal muscle mass (kg) = [height^2 (cm^2) / BIA resistance (ohms) x 0.401] + [gender x 3.825] + [age (years) x (-0.71)] + 5.102.[1]

In this Janssen formula, the gender for male is 1 and for female is 0.[1]

Then the skeletal muscle mass index (SMI) was calculated.

SMI = (skeletal muscle mass / body weight) x100

Low muscle mass according to BIA is SMI 8.87 kg/m2 for men and SMI 6.42 kg/m2 for women.[1]

Assessing Severity (Severity)

After the diagnosis of sarcopenia is confirmed with low muscle mass, the severity of sarcopenia will be assessed by measuring physical performance.[4] In clinical practice, physical performance is evaluated by walking speed, Short Physical Performance Battery (SPPB), the Timed-Up and Go test (TUG).[1,4] This physical performance check cannot be used in

people with dementia, walking disorders, or balance disorders.[4]

Assessment of walking speed is a quick and safe test for patients with sarcopenia. Walking speed can be used to predict complications of sarcopenia, namely disability, cognitive impairment, hospitalization, falls, and mortality.[4] One of the walking speed tests that is often used is to measure the walking speed on a four meters normal walking test. Walking speed ≤ 0.8 m/s indicates severe sarcopenia.[4]

SPPB is a combination test that assesses walking speed, balance test, and chair stand test.[4] With a maximum score of 12 points, SPPB ≤ 8 points indicates poor physical performance.[4]

TUG evaluates physical function. In this test, the patient is asked to stand up from a sitting position in a chair, then walk 3 meters, and turn back towards the chair and sit back down. TUG ≥ 20 seconds indicates poor physical performance.[4]

The 400 meter walking test is used to evaluate walking ability and endurance. In this test, participants are asked to complete 20 laps (1 lap = 20 meters) as quickly as possible. Participants are allowed to rest a maximum of 2 times during the examination. Inability to complete a test or complete ≥ 6 minutes indicates poor physical performance.[4]

Among the three physical performance tests, the EWGSOP2 recommends the use of the walking speed test for the assessment of physical performance.[4] This is due to the ability of this test to predict complications of sarcopenia and the ease with which the test is performed.[4]

DIFFERENTIAL DIAGNOSIS

The diagnosis of sarcopenia is often confused with the diagnosis of dynapenia and frailty. Dynapenia is the loss of muscle strength associated with the aging process.[4] One of the differences between dynapenia and sarcopenia is that in dynapenia, normal muscle mass is often obtained.[14,15] One of the reasons is in dynapenia the decrease in muscle strength is much faster than the decrease in muscle mass.[15]

Frailty is a multidimensional geriatric syndrome characterized by a cumulative decline in bodily functions or systems.[4] Similar to sarcopenia, low grip strength and slow gait are also found in frailty.[4] The difference between frailty and sarcopenia is that frailty is a geriatric syndrome and sarcopenia is a disease.[1,4] Compared to sarcopenia which is a contributor to frailty, frailty is a decrease

in various physiological systems of the body that have negative consequences on physical, cognitive, and social dimensions.[4] Indicators that can be used to assess frailty are the Groningen Frailty Indicator and the Frailty Index of Rockwood.[4]

TREATMENT OF SARCOPENIA

Based on the pathophysiological factors of sarcopenia, various treatment strategies for sarcopenia can be performed and the majority of these treatments aim to improve behavioral and endocrine factors.

Physical training

Physical inactivity and disease in the elderly are the main contributors to the decline in muscle function and mass.[1] Resistance and aerobic exercise have been shown to increase muscle strength and improve physical function.[1,5,16] One that is recommended is progressive resistance type exercise (PRT). At PRT, the elderly train muscles against progressively increased external forces.[1] Studies show that PRT can improve muscle strength and physical performance.[1]

PRT is therefore a first-line therapeutic strategy in the management and prevention of sarcopenia and other complications.[1] However, the implementation of PRT for elderly people in the community still face obstacles because they require trained therapists and certain equipment.[1]

Nutrition

Malnutrition may contribute to poor muscle function in the elderly.[1] Food intake may decrease in the elderly due to various conditions such as inability to chew, medications, physiological anorexia, changes in diet, etc.[1] As a consequence, the prevalence of sarcopenia varies from 5%-20% in the elderly in the community to more than 60% in the elderly in institutions.[1] Various nutritional strategies that can be used in the treatment of sarcopenia are as follows.

1. Increase protein intake

Protein intake of 1 g / kg body weighthas been identified as the minimal amount required to maintain muscle mass in old age.[1] Increasing protein intake may increase muscle mass and function.[1] The composition of amino acids in protein intake affects muscle protein metabolism

Essential amino acids are the main stimulus for protein synthesis.[1,17] The elderly should consume protein containing high essential amino acids.[1] Protein intake and physical exercise together may produce synergistic effects in improving muscle function.[1]

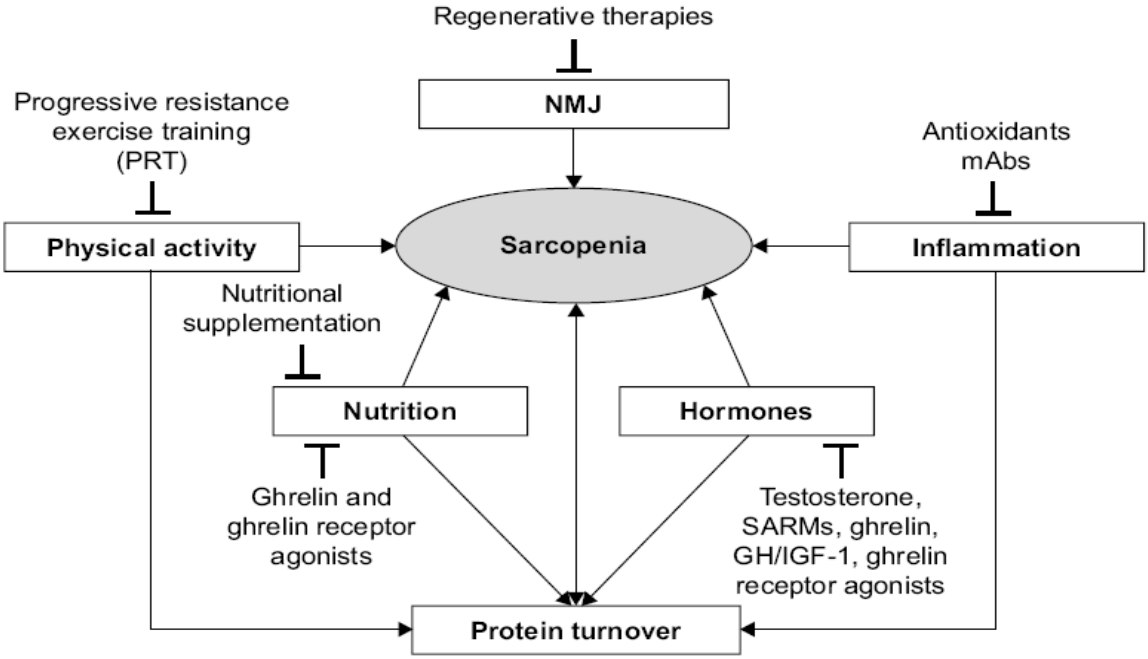

Figure 3. Management of Sarcopenia

SARMs, Modulator reseptor androgen selektif; GH/IGF-1, Growth Hormon/ insulin-like growth factor-1; NMJ, Neuro-muscular Junction.

2. Vitamin D supplementation

Vitamin D levels decrease with aging.[1] Vitamin D is a vital factor because vitamin D affects muscle metabolism and vitamin D deficiency is often associated with sarcopenia.[1,17] Although the provision of calcium and vitamin D supplementation is controversial,a 2019 meta-analysis showed a 19% reduced risk of falls in the elderly who consumed a minimum of 700 IU of vitamin D supplements per day.[1] Based on the results of this meta-analysis, measurement of 25-hydroxy vitamin D levels in all patients with sarcopenia and recommended administration of 800 IU (20 g/day) vitamin D supplementation in patients with serum 25-hydroxy vitamin D levels less than 100 nmol/L (40 ng/ml).[1]

3. Creatinine (Cr) monohydrate

Cr monohydrate is used as nutritional supplementation to increase muscle mass and performance in the elderly when combined with resistance type physical exercise.[1] Therefore, short-term Cr supplementation (5-20 g/day for 2 weeks) may be used in the

elderly undergoing muscle strength training program.[1]

4. Antioxidant

The involvement of oxidative stress in the pathogenesis of sarcopenia led to the hypothesis that antioxidants, (such as selenium, vitamin E, vitamin C) could be administered in the treatment of sarcopenia.[1] An Italian study found that higher plasma antioxidant levels were associated with a lower risk of disability and decreased muscle strength.[1] However, the facts show the opposite where the administration of antioxidants increases the risk of mortality through the pro-oxidant effect.[1]

5. Other nutrition strategies

a. β – hydroxy β – methylbutyrate (HMB). HMB is a metabolite of leucine which is thought to be used as a nutritional supplement to fight sarcopenia.[17] However, it still requires further research.

b. Ornithine -ketoglutarate (OKG)

OKG is a precursor of various amino acids such as glutamate, glutamine, arginine, and proline, which are important modulators of muscle protein metabolism.[1]

c. Omega-3 fatty acids

Omega-3 fatty acids have been shown to increase muscle protein synthesis and muscle strength.[1]

d. Caloric restriction

Caloric restriction and physical exercise have a positive effect on muscle health and homeostasis in old age. However, the long-term restrictive effect on weight loss can be harmful in non-obese elderly because it can accelerate muscle loss and increase the risk of disability and mortality.[1]

Testosterone

The positive effect of testosterone supplementation on bone and muscle tissue is it may increase muscle strength and physical performance, as well as reduce fat mass and the risk of hospitalization in the elderly. Testosterone supplementation at lower levels may increase protein synthesis and cause an increase in muscle mass.[1] At higher levels, testosterone supplementation may activate satellite cell uptake and decrease adipose stem cells, thereby increasing myogenesis and decreasing adipogenesis.[1] Testosterone replacement in the elderly is often associated with

several side effects such as cardiovascular disease, fluid retention, gynecomastia, worsening of sleep apnea, polycythemia, and accelerated benign or malignant prostate disease.[1] Among several drugs that have been investigated for the treatment of sarcopenia, testosterone is the most effective and safest because the side effects are highly dose dependent and associated with very high doses of 300 and 600 mg/week.[1]

Specific Androgen Receptor Modulators (SARMs)

Because the side effects of testosterone are dose-related, the researchers developed a substance with anabolic effects specific for skeletal muscle and bone tissue.[1] Selective androgen receptor modulators (SARMs) are androgen receptor ligands that have androgenic effects on some tissues such as muscle and bone and have no effect on other organs such as the prostate or skin.[1]

SARMs supplementation reduce the side effects of testosterone such as prostatic hyperplasia or androgenization. Although SARMs appear to be safe and effective in increasing lean body mass (LBM) and muscle strength, the effects of SARMs on muscle mass and function are similar to those of high-dose testosterone therapy.[1] Long-term monitoring and research to evaluate more effective and selective SARMs is still needed.

Growth Hormone [GH] / Insulin Growth Hormone – 1 (IGF-1)

GH may cause the release of IGF-1 which will then increase LBM in the elderly and also various other side effects such as muscle and joint pain, edema, Carpal Tunnel syndrome, and hyperglycemia.[1]

Administration of IGF-1 is also associated with some side effects such as orthostatic hypotension, gynecomastia, myositis, edema, and risk of cardiovascular disease.[1]

Ghrelin and ghrelin receptor agonists

Ghrelin is produced by the gastric fundus, and increases food intake and GH1 secretion. Studies show that ghrelin and its receptor agonists (anamorelin and

capromorelin) have positive effects in increasing food intake and muscle mass and function.[1] However, further studies are needed to evaluate the effect in patients with sarcopenia.[1]

Angiotensin-Converting Enzyme (ACE) Inhibitors

ACE inhibitors may be used to maintain skeletal muscle. Among ACE inhibitors, perindopril may improve physical performance and reduce hip fracture in the elderly.[1]

CONCLUSION

Sarcopenia is a disease characterized by progressive loss of muscle mass associated with aging. This disease has a multifactorial pathogenesis such as neuromuscular degeneration, changes in muscle protein turnover, changes in hormone levels and sensitivity, chronic inflammation, oxidative stress, behavioral/lifestyle factors. In the 2010 EWGSOP definition, the diagnosis of sarcopenia requires the presence of low muscle mass and muscle function. This definition was later updated with the 2018 definition where a patient is suspected of having sarcopenia if there is low muscle strength. Furthermore, the diagnosis of sarcopenia is made by the presence of a low quantity or quality of muscle mass. Sarcopenia is said to be severe if there is low muscle strength, low muscle mass, and low physical performance. The management strategy for sarcopenia is resistance-type physical exercise, increasing intake of essential amino acids, vitamin D supplementation in patients with vitamin D deficiency, polyunsaturated fatty acids (PUFAs) supplementation, testosterone supplementation, and administration of angiotensin-converting enzyme inhibitors.

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