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Rehabilitation Nutrition and Exercise Therapy for Sarcopenia

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Sarcopenia is an age-related loss of skeletal muscle associated with adverse outcomes such as falls, fractures, disability, and increased mortality in older people and hospitalized patients. About half of older male nursing home residents have sarcopenia. The diagnostic criteria by the European Working Group on Sarcopenia in Older People (EWGSOP) and the Asian Working Group for Sarcopenia (AWGS) have led to increased interest in sarcopenia. Exercise and nutritional management are crucial for the prevention and treatment of sarcopenia. Nutritional therapy for sarcopenia that includes 20 g of whey protein and 800 IU of vitamin D twice a day improves lower limb strength. Exercise therapy for sarcopenia, such as resistance training and 6 months of home exercises, improves muscle strength and physical function. Combination therapy that includes both nutritional and exercise therapy improves gait speed and knee extension strength more than either exercise alone or nutrition therapy alone. Excessive bedrest and mismanagement of nutrition in medical facilities can lead to iatrogenic sarcopenia. Iatrogenic sarcopenia is sarcopenia caused by the activities of health care workers in health care facilities. Appropriate nutritional management and exercise programs through rehabilitation nutrition are important for prevention and treatment of iatrogenic sarcopenia. Nutritional and exercise therapy should be started very early after admission and adjusted to the level of inflammation and disease status. Repeated assessment, diagnosis, goal setting, interventions, and monitoring using the rehabilitation nutrition care process is important to maximize treatment effectiveness and improve patients' functional recovery and quality of life.

Keywords: Frail elderly; Iatrogenic disease; Muscles; Proteins; Residence characteristics

INTRODUCTION

Sarcopenia refers to the loss of muscle strength and physical function due to the loss of skeletal muscle caused by aging or disease. Skeletal muscle volume and muscle strength in patients in their 70s is reduced by about 30%–35% compared to that in their 40s [1]. Muscle mass is reduced by about 1%–2% every year after age 50 [2,3]. Gait speed decreases with age, lowering quality of life and increasing the risk of falls [4]. Sarcopenia causes dysphagia and respiratory dysfunction, which prolongs the disease treatment period [5-7]. Sarcopenia is also one of the factors related to the severity of cardiovascular disease and cancer, and sarcopenia

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affects survival rates for patients [8]. Therefore, sarcopenia is an important topic in men's health and aging.

Sarcopenia received an ICD-10-CM (M62.84) code in 2016 and has received further attention since new criteria were announced at meetings of the European Working Group on Sarcopenia in Older People 2 (EWGSOP2) [8] and the Asian Working Group for Sarcopenia 2019 (AWGS2019) [9]. The new EWGSOP2 criteria aimed to reflect the many studies completed since the publication of the EWGSOP in 2010. The criteria changed the diagnostic algorithm to focus on muscle strength and recommended early detection and treatment. The update from the AWGS2019 recommends early intervention in the community and primary care settings. The new standards from the AWGS2019 include two flowcharts, one for communities and one for hospitals. Treatments for sarcopenia include nutritional therapy and exercise therapy [8-10]. An intervention combining nutritional therapy with a comprehensive exercise program that includes resistance training is more effective than a single intervention in improving sarcopenia [9].

Rehabilitation nutrition is an effective way to prevent and treat iatrogenic sarcopenia. Iatrogenic sarcopenia is more likely to occur in acute care hospitals due to function-related disorders and medical treatment. It has been reported that 14.7% of older patients who did not have sarcopenia before hospitalization had new onset sarcopenia at the time of discharge [11]. Rehabilitation nutrition is used to maximize the patient's function, activity, and participation through both rehabilitation and nutrition care management. A multidisciplinary team approach is important when evaluating the patient, identifying the cause of iatrogenic sarcopenia, and setting up a plan that meets the goals of rehabilitation nutrition [12].

The number of patients with comorbid sarcopenia is expected to increase as the population ages, and effective prevention and treatment strategies are necessary. In this review, we discuss the following: diagnosis, epidemiology, and prognosis of sarcopenia; nutritional and exercise therapy for sarcopenia in community-dwelling older people; as well as rehabilitation nutrition and exercise therapy for iatrogenic sarcopenia.

SARCOPENIA

1. Definition

EWGSOP2 defines sarcopenia as a progressive and generalized skeletal muscle disorder that is associated with an increased likelihood of adverse outcomes including falls, fractures, physical disability, and mortality [8]. AWGS2019 defines sarcopenia as "age-related loss of muscle mass, plus low muscle strength, and/or low physical performance" [9].

2. Diagnostic criteria

Two setting-specific diagnostic criteria were created for AWGS2019. The first, in either a hospital or research setting is as follows: sarcopenia is diagnosed using low muscle mass plus low muscle strength or low physical performance. If all three are present at the same time, severe sarcopenia is diagnosed. The second, in a primary health care or preventive services setting is as follows: screening of either calf circumference, SARC-F, or SARC-CalF, introduces "possible sarcopenia," defined by low muscle strength or reduced physical performance [9].

3. Epidemiology

The prevalence of sarcopenia by setting among community-dwelling, nursing home, or hospitalized older people aged over 60 years was 11% among male and 9% among female [13]. The prevalence of sarcopenia in nursing homes was 51% in male and 31% in female, and the prevalence of sarcopenia in those hospitalized was 23% in male and 24% in female [13]. The prevalence of sarcopenia by disease was 31.4% in individuals with cardiovascular disease, 26.4% in individuals with dementia, 31.1% in individuals with diabetes mellitus, and 26.8% in individuals with respiratory diseases [14].

4. Causes of sarcopenia

Sarcopenia can be classified into two categories: primary sarcopenia, which is age-related, and secondary sarcopenia, for which other causes such as decreased activity, disease, and poor nutrition can be identified [15]. Conditions underlying primary sarcopenia include the following: a decrease in muscle satellite cells and motor neurons; decreased secretion of growth hormone, testosterone, and ghrelin; increased proinflammatory cytokines; impaired mitochondrial function; abnormal myokine production; and weight loss associated with food insecurity [16,17]. At the molecular level there is a decrease in skeletal muscle protein synthesis and/or an increase in skeletal muscle protein breakdown [16].

Secondary sarcopenia results from inactivity, disease, and under-nutrition. Inactivity-related sarcopenia is caused by prolonged bed rest, weightlessness, and anorexia [15]. This includes hospital-associated deconditioning and disuse muscle atrophy. Inactivity and other forms of disuse result in a reduction in skeletal muscle mass of approximately 0.5% per day, with losses from 0.3% to 4.2% in muscle strength [18]. Disease-related sarcopenia is associated with inflammatory diseases such as organ failure, malignancies, and endocrine disorders [15]. Cachexia, a complex metabolic syndrome and predominantly a loss of skeletal muscle [19] is one of the causes of disease-related sarcopenia. Cancer cachexia is characterized by a negative protein-energy balance with concomitant anorexia and metabolic abnormalities [20]. Nutrition-related sarcopenia results from inappropriate energy and protein intake [15]. This includes starvation, where energy intake is consistently lower than energy expenditure, leading to a decline in muscle mass and strength.

5. Prognosis of sarcopenia

Sarcopenia worsens the physical functional and prognosis of patients with a wide variety of diseases (Fig. 1). In cardiovascular disease, high mortality, peripheral arterial disease, and critical limb ischemia were associated with sarcopenia [21]. Low skeletal muscle mass is associated with mortality in patients after abdominal aortic aneurysm repair surgery [22]. Hand grip strength and frailty are predictors of poor functional outcome and mortality in patients with hip fractures [23]. In patients with cirrhosis, sarcopenia was associated with an increased incidence of hepatic encephalopathy, complications such as sepsis and serious infections after transplantation, and increased mortality [24,25].

Sarcopenia is associated with poor survival in cancer patients. In patients with gastric cancer, sarcopenia was associated with mortality, postoperative complications, hospital costs, and postoperative hospital stay [26]. In renal cell carcinoma and urogenital tumors, patients with sarcopenia showed reduced overall survival and cancer-specific survival compared to patients without sarcopenia [27,28]. Sarcopenia is associated with a reduction in overall and recurrence-free survival in head and neck cancer [29].

Sarcopenia is associated with cognitive and mental decline. Sarcopenia is independently associated with cognitive impairment [30] and also has a significantly positive association with depression [31].

NUTRITION AND EXERCISE THERAPY FOR SARCOPENIA IN COMMUNITY-DWELLING OLDER PEOPLE

1. Nutritional therapy for sarcopenia

Protein intake is an important part of nutritional

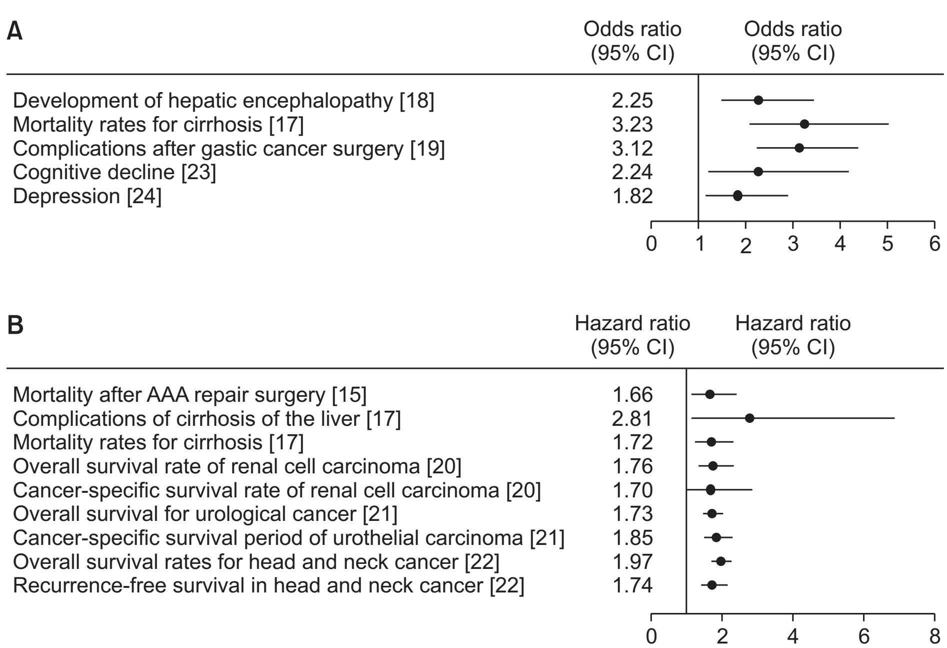

Fig. 1. Association between sarcopenia and disease prognosis. The figure shows the association between sarcopenia and disease outcomes such as increased mortality and complication rates of various diseases. (A) shows the odds ratios indicating the association between sarcopenia and hepatic encephalopathy, cirrhosis, gastric cancer, cognitive decline, and depression. (B) shows hazard ratios indicating the association with thoracic aortic aneurysm, liver cirrhosis, renal cell carcinoma, urological cancer, and head and neck cancer. Sarcopenia was shown to be associated with a worse prognosis for most diseases. CI: confidence interval.

therapy for sarcopenia. The EWGSOP2 states that treatment should include provisions of optimal protein intake and physical exercise [8]. Clinical practice guidelines developed by the Japanese Society for Sarcopenia and Frailty reported that intervention with 3 g of essential amino acids twice daily may improve knee extensor strength in sarcopenic patients [32]. However, no statistically significant effect of nutrition intervention alone on muscle mass, muscle strength, or walking speed has been reported [32]. Therefore, recommendations for nutritional therapy for sarcopenia are scarce, and the certainty of the evidence is low [33].

Adequate energy and protein intake are important elements of nutritional therapy for sarcopenia. There are many studies using nutritional supplements for sarcopenia, however the usefulness of nutritional supplements is still unclear [34]. For example, in the PROVIDE study [35], a nutritional supplement (containing 20 g whey protein, 3 g total leucine, 9 g carbohydrates, 3 g fat, and 800 IU vitamin D per serving along with a mixture of vitamins, minerals, and fibers) was administered to sarcopenic patients after breakfast and lunch in addition to their normal diet. Results showed that nutritional supplements did not increase skeletal muscle mass in patients with serum concentrations of vitamin D of 50 nmoL/L 25-hydroxyvitamin D and dietary protein intake of less than 1.0 g/kg/dL. Breakfast for older people is often insufficient in protein [36]. If energy and protein intake are insufficient, improvement of sarcopenia is difficult. Texture modification, using snacks and nutritional supplements, and adjusting medications may be helpful to achieve sufficient energy and protein intake [37].

2. Exercise therapy for sarcopenia

Exercise interventions for community-dwelling older people with sarcopenia have been recommended because of their effectiveness in improving skeletal muscle mass, knee extension strength, and normal maximum walking speed [32]. The types of exercise intervention that have shown beneficial results include resistance training, aerobic exercise, weight training, and balance training [38]. Resistance training using low/moderate intensity and low weight-bearing exercises significantly increases lean mass, skeletal muscle mass, skeletal muscle mass index, leg strength, and grip strength [39]. However, reports of exercise interventions for patients with sarcopenia are highly heterogenous across trials, and there are currently few studies comparing each outcome, so further evidence needs to be developed.

Exercise habits and an abundance of physical activity prevent sarcopenia [40]. Physical exercise, particularly resistance training, has been recognized as effective in improving skeletal muscle mass, knee extension strength, normal walking speed, and maximum walking speed in community-dwelling older people [41]. Programs of combined exercise interventions yield greater improvements than single exercises [42,43]. Many exercise interventions that require special equipment or routine monitoring such as weightlifting devices, have been reported [44,45]. Similarly, some reports have also shown superior improvements in muscle strength and physical function after 6 months of relatively simple daily exercises such as squats, one-legged stands, heel raises, and 20–30 minutes of walking [46]. Thus, habitual exercise is beneficial for preventing sarcopenia in older people, and it is important to find ways to practice it in daily life.

3. A combination of nutritional and exercise therapy for sarcopenia

The combination of nutrition and exercise therapy for sarcopenia may be more effective than either intervention alone. The AWGS2019 showed that a combination of nutrition and exercise therapy can improve muscle strength and function [9]. The EWGSOP2 states that it is important to consider a combination of protein intake and exercise as well as an active lifestyle [8]. The International Conference on Frailty and Sarcopenia Research (ICFSR) has reported improved gait speed and knee extension strength using a combination of nutrition and exercise therapy compared to one or the other intervention alone, although the level of evidence was low [10].

The combination of nutritional therapy and exercise therapy for sarcopenia patients is important to continue in order to maintain their therapeutic effect. The EWGSOP2 states that cessation of exercise decreases the effectiveness of exercise. Toward the continuation of treatment, it may be helpful to devise ways to reinforce the effects. For example, have patients start with simple tasks that fit their lifestyle and gradually increase the load, have them keep a diary, or have them share their progress with others.

REHABILITATION NUTRITION AND EXERCISE THERAPY FOR IATROGENIC SARCOPENIA

1. Iatrogenic sarcopenia

Iatrogenic sarcopenia is defined as sarcopenia caused by the activities of doctors, nurses, and other health care workers in a health care facility [12]. There are three causes of iatrogenic sarcopenia. The first is low activity levels. Activity-related iatrogenic sarcopenia is mainly caused by muscle atrophy due to extended bed rest and immobilization. Muscle atrophy associated with inactivity results in a decrease in muscle protein synthesis and an increase in muscle protein degradation [12]. Tentative *nil per os* (nothing by mouth) due to aspiration pneumonia upon admission has a negative impact on the patient, including prolonged treatment time and disuse muscle atrophy of swallowing-related muscles [47]. The second cause of iatrogenic sarcopenia is inappropriate nutritional management, primarily in a hospital setting. Nutrition-related iatrogenic sarcopenia occurs as a result of starvation due to insufficient energy and protein intake [12]. In acute care hospitals, recovery from dysphagia is significantly worse in cases where proper nutritional management is not in place [48]. The third cause is iatrogenic illness (a morbidity caused by medical treatment). This can be caused by medical devices, drugs and materials, physician misdiagnosis, medical errors (*e.g.*, inappropriate drug selection, inappropriate or premature surgery and testing), and nosocomial infections [12].

2. Rehabilitation nutrition

Rehabilitation nutrition is defined as that which 1) evaluates the patient holistically using the International Classification of Functioning, Disability and Health (ICF), as well as evaluates the presence and cause of nutritional disorders, sarcopenia, and excessive or deficient nutritional intake; 2) conducts rehabilitation nutrition diagnosis and rehabilitation nutrition goal setting; 3) uses "nutrition care management with rehabilitation in mind" and "nutritionally conscious rehabilitation" for the disabled and frail elderly; 4) improves nutritional status, sarcopenia, and frailty; and 5) elicits the best physical function, activity, participation, and quality of life [12]. However, in clinical practice, nutritional management often remains inadequate. Patients with malnutrition are more likely to be discharged to an acute hospital or recuperation hospital than nourished patients [49,50]. Moreover, 49%–67% of older people in recovery care are underfed to some degree [51].

The Global Leadership Initiative on Malnutrition published in 2018 offers a common definition of malnutrition worldwide. It was established by the American Society for Parenteral and Enteral Nutrition (ASPEN), European Society for Clinical Nutrition and Metabolism (ESPEN), Federación Latino Americana de Terapia Nutricional, Nutrición Clínica y Metabolismo (Latin American Federation of Nutritional Therapy, Clinical Nutrition and Metabolism: FELANPE), and Parenteral and Enteral Nutrition Society of Asia (PENSA). Their criteria allow for the diagnosis and severity classification of malnutrition. In addition to the Subjective Global Assessment (SGA) and Mini Nutritional Assessment-Short Form (MNA®-SF) assessments, inflammation is also evaluated. Determination of the causes of malnutrition can lead to early intervention.

When goal setting, we can evaluate the effectiveness of an intervention by considering the acronym SMART. SMART stands for S: Specific, M: Measurable, A: Achievable, R: Related, and T: Time-bound. In patients with nutritional deficits, rehabilitation and nutritional management can be expected to help improve activities of daily living (ADLs) and quality of life. High quality rehabilitation nutrition can be performed by the rehabilitation nutrition care process (Fig. 2). The rehabilitation nutrition care process consists of 5 steps including 1) rehabilitation nutrition assessment and diagnostic reasoning, 2) rehabilitation nutrition diagnosis, 3) rehabilitation nutrition goal setting, 4) rehabilitation nutrition intervention, and 5) rehabilitation nutrition monitoring.

3. Nutritional therapy for iatrogenic sarcopenia

When an organism is exposed to an invasion or acute inflammation, an acute biological reaction develops that affects neuroendocrine, immune mechanisms, and metabolism. The insulin resistance effect of catecholamines and cytokines increases blood glucose levels, resulting in increased protein catabolism and lipolysis. This is classified by Moore into four stages, in the following order, 1) a period of high catecholamine, 2) a period when muscle protein synthesis begins, 3) a period when muscle recovery begins to occur, and 4) a period

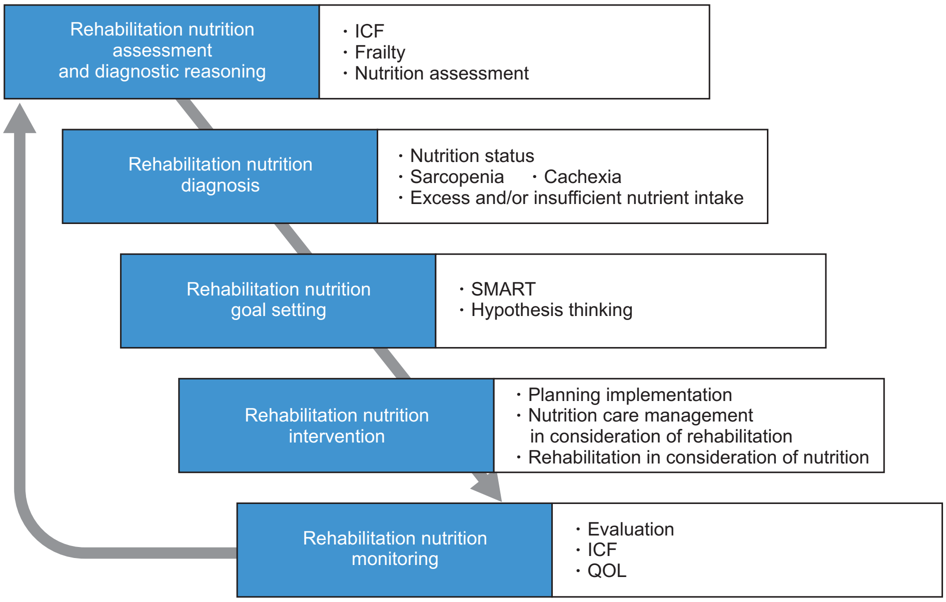

Fig. 2. The cycle of the rehabilitation nutrition care process. This cycle is continued from rehabilitation nutrition monitoring to rehabilitation nutrition assessment and diagnostic reasoning. To repeat this management cycle several times is important for high quality rehabilitation nutrition. ICF: International Classification of Functioning, Disability and Health, SMART: Specific, Measurable, Attainable, Relevant, and Time-bound, QOL: quality of life.

Table 1. Nutrition and exercise in different the stages of care

Stage	Nutritional therapy	Exercise therapy	
		Objective	Interventions
Hyperacute care[a]	Intake: less than 70% of the target energy goal Protein: 1.3 g/kg/day for protein	To minimize the loss of muscle strength, muscle mass and physical function	Early mobilization or neuromuscular electrical stimulation or bedside ergometer
Acute care[b]	Intake: not to exceed 20–25 kcal/kg/day	To maintain muscle strength, muscle mass and physical function	Gait training: increasing the steps per day Using a pedometer and setting a target step count
Subacute care[c]	Intake: 25–35 kcal/kg/day Protein: 1.2–1.5 g/kg/day	To increase muscle strength, muscle mass and physical function	Resistance training and aerobic exercise Patients have muscle weakness and loss of motor function, so an exercise program needs to be structured to avoid injury[e]
Convalescent care[d]	Intake: more than the target energy to match the activity level	To increase muscle strength, muscle mass and physical function	Resistance training and aerobic exercise

[a]Hyperacute care: within 48 hours of admission or onset disease. [b]Acute care: within 2 weeks after admission or onset disease. [c]Subacute care: 2 to 4 weeks after admission or onset disease. [d]Convalescent care: more than 4 weeks after admission or onset disease. [e]This is an example. Its duration depends on the level of invasion, inflammation, and severity of the disease.

of weight gain [52]. The timing of these vary according to the degree of invasion, inflammation, and severity of the disease. Examples of the timing of each stage are given as follows: Hyperacute care, given within 48 hours of admission or disease onset; acute care, given within 2 weeks after admission or disease onset; subacute care, given 2 to 4 weeks after admission or disease onset; and convalescent care, given more than 4 weeks after admission or disease onset (Table 1). In order to prevent iatrogenic sarcopenia, appropriate nutritional therapy is needed during each stage.

Nutritional management and adequate oral intake early in the hospitalization process will shorten the hospitalization period [53]. Early initiation of increased oral intake in hospitalized older people with pneumonia reduces hospital stay [54], and it improves the function and ADLs of stroke patients [55]. For surgical patients, preoperative nutritional status affects the postoperative period. Nutritional therapy should be started during the hyperacute stage of new disease onset, surgery, or acute exacerbation of a condition within 48 hours. Oral rather than continuous enteral feeding is recommended for administration. Doses should be given at less than 70% of the target energy level and at 1.3 g/kg/day for protein [56].

The acute care stage is a period of hyper-catabolism, and energy supplementation exceeding 20–25 kcal/kg/day may result in excessive energy administration and poor prognosis [56]. The subacute care stage moves into a period of anabolism. During this period, energy supply is increased to about 25–35 kcal/kg/day. Protein is recommended at about 1.2–1.5 g/kg/day and fat within 20%–30% of total energy content [56]. The convalescent stage has expanded ADLs and increased physical activity. This stage requires a nutritional level that considers the rehabilitation programs and increases in physical activity. Low nutrition has a negative effect on physical function and rehabilitation [57]. Patients in the convalescent stage should take in more than their target energy in order to match their activity level. Using target energy alone results in decreased muscle mass and worsened nutritional status. Similarly, sarcopenia requires an additional 200–750 kcal/day to aim for weight gain [58].

Aggressive nutrition therapy is a method of nutrition management that uses the patient's daily energy expenditure and daily energy accumulation to establish a daily energy requirement that will increase the body weight and muscle mass of the patient [12]. Approximately 7,500 kcal are required to increase body weight by 1 kg. Therefore, if the goal is to gain 1 kg of weight per month, the target energy intake per day must equal the total energy expenditure +250 kcal. An energy intake of ≥30 kcal/kg/day and a protein intake of ≥1.2 g/kg/day based on ideal body weight has a marked impact on the increase in tongue strength in older adults with sarcopenia [59]. In cases presenting with sarcopenia, aggressive nutrition therapy can improve nutritional status and promote rehabilitation, resulting in treatment of sarcopenia.

4. Exercise therapy for iatrogenic sarcopenia

Exercise to prevent iatrogenic sarcopenia requires a program tailored to the stage of disease and nutritional status of each patient. In the acute care stage, energy consumption increases and the patient is likely to be malnourished [60]. In addition, there are few well-nourished patients (15.7%) in the convalescent rehabilitation ward [61]. Therefore, the degree of inflammation and invasion and the nutritional status of the patient must be assessed, and overwork must be considered when developing an exercise program.

The objective of exercise therapy in the hyperacute care stage is to minimize the loss of muscle strength, muscle mass, and physical function. Exercise therapy is contraindicated under the following conditions: the presence of a significant dose of vasopressors for hemodynamic stability (maintain mean arterial pressure >60 mmHg), an acute neurological event (cerebrovascular accident), an active bleeding process, and bed rest orders [62]. If these exclusion criteria are not met, exercise begins with early mobilization and progresses to gait training. If the patient is unable to get out of bed early or participate in gait training, exercise therapy may be achieved using neuromuscular electrical stimulation [63] or a bedside ergometer [64]. Both these therapies induce muscle activity and can prevent muscle atrophy.

The objective of exercise therapy in the acute care stage is to maintain muscle strength, muscle mass, and physical function. Fewer steps per day and moderate activity levels (>3 metabolic equivalents [METs]) are more likely to result in sarcopenia in community-dwelling older people [65]. Because acute care patients may have difficulty doing moderate activities (>3 METs), exercise therapy during this period should start by increasing steps per day. In addition, use of a pedometer and setting a target step count have the effect of increasing physical activity [66]. Therefore, patients are instructed to meet a target step count and use a pedometer during this stage. Because fewer than 900 steps per day are significantly associated with hospitalization-associated functional decline, the minimum goal for daily steps is set at 900 steps [67]. Then, the patient increases the number of steps progressively.

The objective of exercise therapy in the subacute care stage is to increase muscle strength, muscle mass, and physical function. Therefore, resistance training and aerobic exercise is suitable for this period. Patients in the post-acute phase have muscle weakness and loss of motor function, so an exercise program needs to be structured to avoid injury. Hence exercise therapy begins with a low load and progressively increases in load. Because the combination of exercise and nutritional therapy during this stage is beneficial for muscle mass gain and strength building, nutritional therapy should be used in addition to exercise therapy [68].

CONCLUSIONS

We presented the background on sarcopenia and nutritional and exercise therapy for sarcopenia in community-dwelling older adults and hospitalized patients. The treatment for sarcopenia involves assessing the cause and nutritional status and combining nutritional and exercise therapy as appropriate. It is important for men's health to prescribe nutritional and exercise therapy that is tailored to older people and considers patient characteristics including disease severity and inflammation.

Prevention is key with iatrogenic sarcopenia. Iatrogenic sarcopenia should be evaluated and the cause should be eliminated in health care facilities. Rehabilitation nutrition and proper exercise therapy for preventing and treating iatrogenic sarcopenia should be performed.

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Conflict of Interest

The authors have nothing to disclose.

Author Contribution

Conceptualization: SK, HW, HI, TI, MS, YA, TH, KU, KT, MO, MY, SY, HS. Writing – original draft: SK, HI, TI, MS, YA, TH, KU, KT, MO, MY, SY. Writing – review & editing: SK, HW, HS.

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