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RESPIRATORY SARCOPENIA AND SARCOPENIC RESPIRATORY DISABILITY: CONCEPTS, DIAGNOSIS, AND TREATMENT

A. NAGANO[1], H. WAKABAYASHI[2], K. MAEDA[3], Y. KOKURA[4], S. MIYAZAKI[5], T. MORI[6], D. FUJIWARA[7]

1. Department of Nursing, Nishinomiya Kyoritsu Neurosurgical Hospital, Hyogo, Japan; 2. Department of Rehabilitation Medicine, Tokyo Women's Medical University Hospital, Tokyo, Japan; 3. Department of Geriatric Medicine, National Center for Geriatrics and Gerontology, Aichi, Japan; 4. Department of Clinical Nutrition, Keiju Medical Center, Ishikawa, Japan; 5. Rehabilitation Center, KKR Takamatsu Hospital, Takamatsu, Japan; 6. Department of Oral and Maxillofacial Surgery, Southern Tohoku General Hospital, Koriyama, Japan; 7. Department of Rehabilitation Medicine, Saka General Hospital, Miyagi, Japan. Corresponding author: Hidetaka Wakabayashi, MD, PhD, Department of Rehabilitation Medicine, Tokyo Women's Medical University Hospital, 8-1, Kawada-cho, Shinjuku-ku, Tokyo, Japan. Code; 162-0054, Tel: +81-3-3353-8111, Fax: +81-3-5269-7639, E-mail: noventurenoglory@gmail.com

Abstract: The condition of muscle fiber atrophy and weakness that occurs in respiratory muscles along with systemic skeletal muscle with age is known as respiratory sarcopenia. The Japanese Working Group of Respiratory Sarcopenia of the Japanese Association of Rehabilitation Nutrition narratively reviews these areas, and proposes the concept and diagnostic criteria. We have defined respiratory sarcopenia as "whole-body sarcopenia and low respiratory muscle mass followed by low respiratory muscle strength and/or low respiratory function." Respiratory sarcopenia can be caused by various factors such as aging, decreased activity, undernutrition, disease, cachexia, and iatrogenic causes. We have also created an algorithm for diagnosing respiratory sarcopenia. Respiratory function decreases with age in healthy older people, along with low respiratory muscle mass and strength. We have created a new term, "Presbypnea," meaning a decline in respiratory function with aging. Minor functional respiratory disability due to aging, such as that indicated by a modified Medical Research Council level 1 (troubled by shortness of breath when hurrying or walking straight up hill), is an indicator of presbypnea. We also define sarcopenic respiratory disability as "a disability with deteriorated respiratory function that results from respiratory sarcopenia." Sarcopenic respiratory disability is diagnosed if respiratory sarcopenia is present with functional disability. Cases of respiratory sarcopenia without functional disability are diagnosed as "at risk of sarcopenic respiratory disability." Functional disability is defined as a modified Medical Research Council grade of 2 or more. Rehabilitation nutrition, treatment that combines rehabilitation and nutritional management, may be adequate to prevent and treat respiratory sarcopenia and sarcopenic respiratory disability.

Key words: Rehabilitation nutrition, secondary sarcopenia, muscle wasting, aging, respiration.

Introduction

The condition of muscle fiber atrophy and weakness that occurs in respiratory muscles along with systemic skeletal muscle with aging is known as respiratory sarcopenia (1-4). Respiratory sarcopenia causes deterioration of respiratory force generation (5) and pulmonary function (3, 6), which then adversely affect activities of daily living and quality of life (3, 5-7). Therefore, it is important that medical professionals become aware of respiratory sarcopenia. However, the concept of and diagnostic criteria for respiratory sarcopenia have not been discussed before. Therefore, the Japanese Working Group of Respiratory Sarcopenia of the Japanese Association of Rehabilitation Nutrition has developed a narrative review of these areas.

Aging causes a decrease in respiratory muscle mass, weakness in respiratory muscle strength, and a decline in respiratory function. However, there has been no definition or term for a decline in respiratory function due to aging. Therefore, we termed a decline in respiratory function with aging as "presbypnea", which is created by combining "presby-" meaning geriatric and "-pnea" meaning respiratory (Table1). Minor respiratory function disability, such as that represented by a modified Medical Research Council (Modified MRC) (8) level of 1, is an indicator of presbypnea.

Respiratory sarcopenia is caused by various factors such as aging, decreased activity, undernutrition, hypoxic stress, disease, and cachexia (6). Diaphragm and intercostal muscles are the main respiratory muscles (9) and respiratory muscle mass can be measured by computed tomography (CT) (10, 11) or ultrasonography (12-14). Low respiratory muscle strength is commonly evaluated using peak expiratory rate (15) or maximum respiratory pressure (16). Kera et al. (1) have given a definition of respiratory sarcopenia using peak expiratory flow rate (PEFR) and have adopted a PEFR value 1 standard deviation below the mean as the cut-off value for the diagnosis. However, considering that whole-body sarcopenia in Asia is defined as ˋage-related loss of skeletal muscle mass plus loss of muscle strength and/or reduced physical performance˝, (17) the criteria for respiratory sarcopenia should include not only loss of respiratory muscle strength but also loss of respiratory muscle mass. Thus, in this article, we define respiratory sarcopenia as "whole-body sarcopenia and low respiratory muscle mass followed by low respiratory muscle strength and/or deteriorated respiratory function." Moreover, we propose an algorithm for the diagnosis of respiratory sarcopenia.

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Table 1
Terms and definitions

Terms	Definitions
Presbypnea	A decline in respiratory function with aging.
	Minor functional respiratory disability, such as that represented by a modified Medical Research Council level of 1, is an indicator of presbypnea.
Respiratory sarcopenia	Whole-body sarcopenia and low respiratory muscle mass followed by low respiratory muscle strength and/or deteriorated respiratory function.
	Cases where other criteria are met without the measurement of respiratory muscle mass are diagnosed as "probable respiratory sarcopenia." Cases with the possibility of diseases that are causative of respiratory dysfunction are diagnosed as "possible respiratory sarcopenia."
Sarcopenic respiratory disability	Disability with deteriorated respiratory function due to respiratory sarcopenia.
	Cases of respiratory sarcopenia without functional disability are diagnosed as "at risk of sarcopenic respiratory disability." When functional disability is present in the absence of respiratory sarcopenia, the cause is considered to be another respiratory disease.

Discussions of respiratory disability have focused on oxygen consumption or its impact on disability in terms of work rather than its impact on daily living (18-20). However, other conditions such as functional disability and limitations in activity participation caused by respiratory sarcopenia deserve focus and should be defined. We define "sarcopenic respiratory disability" as a disability with deteriorated respiratory function due to respiratory sarcopenia.

This article describes age-related respiratory decline, the diagnostic criteria for respiratory sarcopenia and sarcopenic respiratory disability, and rehabilitation nutrition management as a treatment.

Age-related respiratory sarcopenia

Respiratory function decreases with age in healthy older people (21, 22). Furthermore, the risk of respiratory infections and complications also increases with age (23-25). Age-related respiratory sarcopenia may cause respiratory infections and complications.

Aging and respiratory muscles

Respiratory muscle strength and muscle mass decrease with age, resulting in the development of diaphragm muscle sarcopenia. Age and sex are related to respiratory muscle strength (26), and respiratory muscle strength also decreases with age (27, 28). Intercostal muscle mass also decreases with age (29). The diaphragm is the most important muscle used for breathing and it is also affected by aging and sarcopenia (30). In an elderly population, transdiaphragmatic pressure, an indicator of diaphragmatic muscle activity, decreases by 20-41%, with a decline in overall respiratory muscle strength of 30% (30). Older mice have been shown to suffer a loss of maximal diaphragm muscle force and decreased muscle fiber type IIx and/or IIb size and develop diaphragm muscle sarcopenia (6). In human autopsy cases, advancing age has been associated with histopathologically abnormal findings in diaphragm structure, including small diaphragm size or shape and loss of cytoplasmic integrity (31).

Whole-body muscle, respiratory muscle, and function

Respiratory muscle strength and respiratory function are related to whole-body muscle mass and strength. The skeletal muscle mass index correlates with maximal inspiratory pressure (MIP) and maximal expiratory pressure (MEP) in older people (32). Diaphragm weight in autopsy cases with a mean age of 70.8 ± 16.8 years has shown a significantly positive correlation with lean body mass measured during life (33). For whole-body muscle mass and respiratory function, appendicular skeletal muscle mass (34) and skeletal muscle area of the third lumbar vertebrae level (35) are associated with forced vital capacity (FVC) and one-second forced expiratory volume (FEV1), respectively. Hand-grip strength is independently associated with MIP and MEP in older people (32). In community-dwelling older women without chronic diseases or pulmonary diseases, higher hand-grip strength is associated with higher FVC and FEV1. Additionally, the adjusted odds ratio of impaired pulmonary function is greater for participants in the first quartile of hand-grip strength than for those in the fourth quartile (36). Furthermore, hand-grip strength has been associated with MIP and peak cough flow in male nursing home residents (37). MIP also correlates with knee extensor strength and hand-grip strength in both males and females, including young adults (38).

Physical performance, respiratory muscles, and function

Low physical performance is related to low respiratory muscle strength and respiratory function. In older people, low inspiratory muscle endurance is associated with the low walking performance (27). The time taken to perform a task in

chair stand tests shows a positive correlation with FVC, FEV1, and peak expiratory flow (PEF) (39). Physical performance, balance, and gait scores in low PEF group were significantly lower compared to a normal PEF group (40). Moreover, higher levels of respiratory muscle strength are associated with a slower rate of decline in mobility (7).

Sarcopenia, frailty, respiratory muscles, and function

Respiratory muscle strength, diaphragmatic thickness, and respiratory function are impaired in older adults with sarcopenia or frailty. MIP, MEP (5), and PEFR (41) have been used to discriminate sarcopenia in community-dwelling elderly. Sarcopenic patients have a thinner diaphragm and lower PEFR compared to non-sarcopenic patients (42). Frail and pre-frail older adults present with significantly lower MIP and MEP compared to non-frail older people. Therefore, respiratory muscle strength may be useful for discriminating frailty (43). Besides, decreased PEFR is a risk for frailty and can be a marker of general robustness in older people (44). These suggest that sarcopenia and/or frailty in older people are associated with respiratory sarcopenia.

Disease-related respiratory sarcopenia

Relationship between respiratory sarcopenia and inflammation

Skeletal muscle is impaired by systemic inflammation. Increased production of inflammatory cytokines such as TNF-α, IL-1, IL-6, IFN-γ is one of the causes of catabolism in skeletal muscle (45, 46). In cases of influenza, inflammatory endocrine signals caused by damaged lungs activate the signaling pathway of muscles, inducing dysfunction (47). Since these mediators of inflammation are related, the same phenomenon could occur with bacterial infections and viral infections, including coronavirus disease 2019 (COVID-19).

The inflammatory response due to infection also causes a decrease in the function of the diaphragm, as one of the skeletal muscles. Endotoxin induces weakening of the diaphragm through the activation of caspase 3 in the diaphragm (48). Also, in the process promoting protein catalysis, the oxidative stress of mitochondria is associated with diaphragm atrophy and induced dysfunction in patients with severe infection (49). Inflammation of the respiratory muscles becomes a promoter of respiratory sarcopenia, which can then be one of the factors causing respiratory dysfunction.

Factors promoting disease-related respiratory sarcopenia

Factors promoting sarcopenia, such as disease, cachexia, and undernutrition, may cause dysfunction of the respiratory muscles. Aspiration pneumonia is an acute inflammatory disease that induces muscle atrophy of the respiratory and swallowing systems (50). The cycle of inflammation and sarcopenia has been proposed as follows: Okazaki et al. reported that inflammation caused by aspiration pneumonia can cause undernutrition and sarcopenia, which can be a risk for aspiration pneumonia (51). Chronic obstructive pulmonary disease (COPD) is also a chronic inflammatory disease. In COPD patients, fibers degenerated not only in the diaphragm but also in appendicular skeletal muscle (52). Cachexia caused by cancer is associated with atrophy of the appendicular skeletal muscle and respiratory muscles (53). The function of the diaphragm has also been reportedly reduced by undernutrition (54).

Ventilators also impair respiratory muscles. Muscle strength and muscle mass of the diaphragm have been reported to decrease with mechanically ventilated conditions (55-57). In addition, Goligher et al. (14) evaluated patients whose diaphragm was atrophied by ventilator mounting. The reported condition of the diaphragm was associated with clinical outcomes such as days on mechanical ventilation and hospitalization periods in intensive care units. Acute and chronic inflammation, undernutrition, cachexia, and inactivity may become promoting factors for respiratory sarcopenia and respiratory dysfunction.

The vicious cycle of respiratory sarcopenia and sarcopenic respiratory disability

Respiratory sarcopenia, like whole-body sarcopenia, is caused by aging, low activity, undernutrition, and inflammation from disease. In age-related diaphragmatic sarcopenia, the selective atrophy of type IIx and/or IIb muscle fibers results in a reduction in forced ventilation and coughing ability mainly related to airway clearance (3). These functional changes may contribute to an increased risk of respiratory infections and complications in older adults (58). Acute inflammation associated with acute diseases such as infections (50) and chronic inflammation associated with chronic diseases such as cancer (59) cause respiratory muscle sarcopenia. Loss of appetite and reduced nutritional intake associated with aging or inflammation can cause respiratory muscle sarcopenia due to undernutrition (54). Age-related decline of physical activity may cause respiratory muscle sarcopenia due to low activity (60). The combination of these multiple factors causes and worsens respiratory sarcopenia.

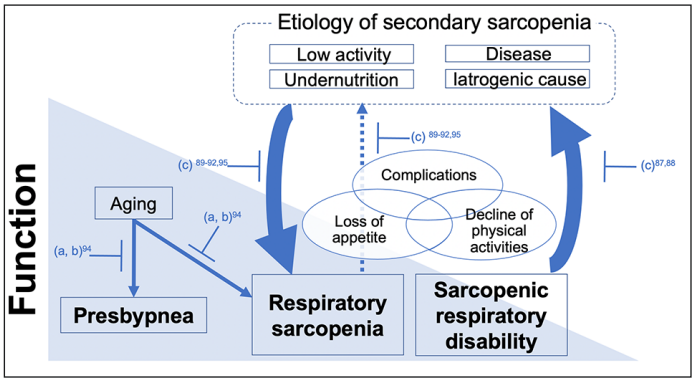
Sarcopenic respiratory disability occurs as a result of a vicious cycle of respiratory sarcopenia (Figure 1). Respiratory sarcopenia promotes low activity, undernutrition, and inflammation. These etiologies of sarcopenia exacerbate respiratory sarcopenia, causing functional disability. In sarcopenic respiratory disability, shortness of breath becomes apparent. Shortness of breath further contributes to the risk of respiratory infections and complications, decreased appetite and nutritional intake (61), and low physical activity (62). These factors, in turn, exacerbate respiratory sarcopenia and sarcopenic respiratory disability.

In patients under ventilator management, the difficulty of weaning from a ventilator may occur as a result of a vicious

cycle of respiratory sarcopenia. Low diaphragm function caused by mechanical ventilation is known as ventilator-induced diaphragmatic dysfunction (63). Diaphragm inactivity with ventilator management leads to diaphragm atrophy (55). Acute inflammation associated with acute diseases such as respiratory infections leads to systemic and diaphragmatic muscle atrophy (50). Undernutrition is caused by increased energy demand associated with acute inflammation and reduced energy supply associated inadequate nutritional management. Undernutrition can also lead to systemic and diaphragmatic muscle atrophy. Neuromuscular blockers (64) and corticosteroids (65) used during ventilator management can lead to contractile dysfunction of the diaphragm. Diaphragm atrophy and reduced contractile function increase the risk of reintubation and tracheostomy, prolong ventilation, and increase hospital mortality (66). Prolonged ventilation promotes low activity, undernutrition, and inflammation, and exacerbates diaphragm atrophy and contractile dysfunction.

Figure 1

Vicious cycle of respiratory sarcopenia and sarcopenic respiratory disability and intervention of combined exercise and nutrition



Aging, low activity, undernutrition, inflammation, and iatrogenic causes are etiologies of whole-body sarcopenia and respiratory sarcopenia. Whole-body sarcopenia and respiratory sarcopenia further exacerbate low activity, undernutrition, and inflammation. The vicious cycle results in sarcopenic respiratory disability. Rehabilitation nutrition is presumed to be effective for treating respiratory sarcopenia and sarcopenic respiratory disability, and may break the vicious cycle of respiratory sarcopenia and sarcopenic respiratory disability. a) Exercise, b) Nutrition, c) Exercise + Nutrition (Rehabilitation Nutrition)

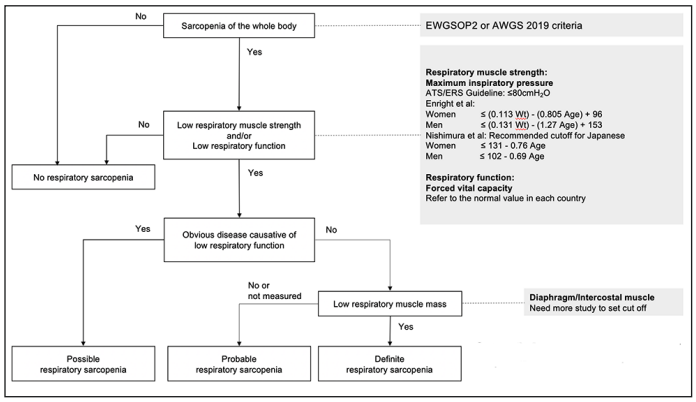
Diagnosis of respiratory sarcopenia and sarcopenic respiratory disability

Diagnosis of respiratory sarcopenia

Respiratory sarcopenia is defined as "whole-body sarcopenia and low respiratory muscle mass followed by low respiratory muscle strength and/or deteriorated respiratory function" (Table 1). The algorithm for diagnosing respiratory sarcopenia is shown in Figure 2. The criteria reported by the Asian Working Group of Sarcopenia 2019 (17) and the position paper for sarcopenic dysphagia (67) may be adopted for diagnosing whole-body sarcopenia in our algorithm. "Definite sarcopenia" is diagnosed when whole-body sarcopenia with low respiratory muscle mass is identified followed by low respiratory muscle strength and/or deteriorated respiratory function with the exclusion of obvious disease causative of low respiratory muscle mass: lung tumors, pulmonary edema, bronchiectasis, diaphragmatic paralysis, neuromuscular diseases, and congenital morphological abnormalities. CT (10, 11) and ultrasonography (12-14) are common methods used to assess respiratory muscle mass. Since, at this point, quantitative measurement of respiratory muscle mass is difficult in clinical settings, it is hard to diagnose a decrease in respiratory muscle mass. Cases where other criteria are met alone (respiratory muscle mass measurement is excluded) are diagnosed as "probable respiratory sarcopenia." Besides, respiratory diseases such as COPD may also be accompanied by generalized sarcopenia and low respiratory muscle mass. However, it is difficult to determine whether the decline in respiratory function is due to disease or a decline in respiratory muscle strength and volume. Thus, cases with possible diseases causative of respiratory dysfunction are diagnosed as "possible respiratory sarcopenia."

Figure 2

A flow-chart for diagnosing respiratory sarcopenia



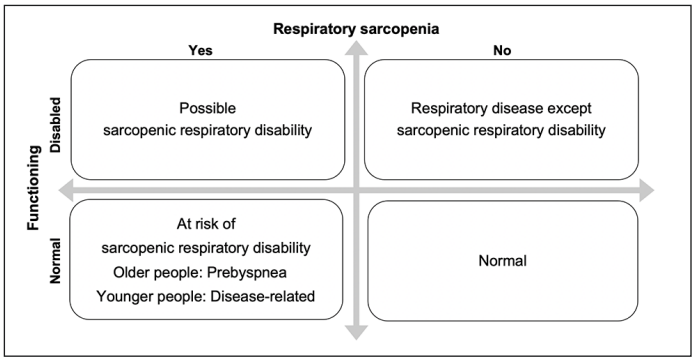
"Definite sarcopenia" is diagnosed when whole-body sarcopenia with low respiratory muscle mass is identified followed by low respiratory muscle strength and/or deteriorated respiratory function with the exclusion of obvious disease causative of low respiratory muscle mass. Cases where other criteria are met alone (respiratory muscle mass measurement is excluded) are diagnosed as "probable respiratory sarcopenia." Cases with possible diseases causative of respiratory dysfunction are diagnosed as "possible respiratory sarcopenia." Abbreviations: EWGSOP, European Working Group on Sarcopenia in Older People; AWGS, Asian Working Group of Sarcopenia; ATS/ERS, American Thoracic Society/European Respiratory Society; Wt, weight

As for respiratory muscle strength, MIP value may be adopted as a diagnostic criterion in the algorithm of respiratory sarcopenia. Indicators of respiratory muscle strength include MIP/MEP, maximum cough strength, and maximum sniff pressures (16). MIP and MEP are useful measurement methods of respiratory muscle strength in clinical settings (9, 68). In particular, MIP has a stronger association with skeletal muscle mass and muscle strength than to MEP (32), and also MIP is used to indicate ventilation failure. Thus, MIP may be adopted as a diagnostic criterion for respiratory sarcopenia. Guidelines

from the American Thoracic Society/European Respiratory Society (ATS/ERS) (16) give a cut-off value for low respiratory muscle strength of < PImax 80cmH_2O. Enright et al. (28) also presented an equation for estimating a reference value for MIP. In Japan, a reference value estimated using an equation by Nishimura et al. (69) is preferred, as an equation used for a western population may lead to overestimation in an Asian population due to differences in body size.

FVC may be adopted as a respiratory function in our algorithm. Vital capacity and FVC are common measurement methods for respiratory function. We adopted FVC as a measure of respiratory function, as FVC is associated with sarcopenia (39, 70). As with MIP, FVC varies by body size, so it is considered adaptable to local standards (21). In Japan, the reference value estimated using the LMS method is recommended for assessing respiratory function (22). Peak flow rate is another measure of respiratory function, and it is adopted as a definition of respiratory sarcopenia as reported by Kera et al. (1) However, as PFR is strongly affected by respiratory diseases such as COPD and asthma, we did not adopt it as a measure of respiratory sarcopenia.

Figure 3
Diagnosis of sarcopenic respiratory disability



Sarcopenic respiratory disability is diagnosed as respiratory sarcopenia with functional disability. Functional disability is assessed using a modified Medical Research Council of grade 2 or more. Cases of respiratory sarcopenia without functional disability are diagnosed as "at risk of sarcopenic respiratory disability." Presbypnea is a possible cause of sarcopenic respiratory disability in older people. On the other hand, respiratory diseases may be possible causes of sarcopenic respiratory disability in the young. When functional disability is present in the absence of respiratory sarcopenia, the cause is considered to be other respiratory diseases.

We have proposed the algorithm for diagnosing respiratory sarcopenia and presented some measures and cut-off values. However, there is a lack of evidence in specificity of the measures and its cut-off values. Further research is required to validate the algorithm in clinical settings.

Diagnosis of sarcopenic respiratory disability

Sarcopenic respiratory disability is defined as "disability with deteriorated respiratory function due to respiratory sarcopenia" (Table 1). Sarcopenic respiratory disability is specified as respiratory sarcopenia with functional disability (Figure 3). Cases of respiratory sarcopenia without functional disability are diagnosed as "at risk of sarcopenic respiratory disability," since the vicious cycle of respiratory sarcopenia may aggravate respiratory sarcopenia. Presbypnea is a possible cause of sarcopenic respiratory disability in older people. On the other hand, respiratory disease may be a possible cause of sarcopenic respiratory disability in the young. Moreover, when functional disability occurs in the absence of respiratory sarcopenia, functional disability may be caused by another respiratory disease.

Functional disability due to respiratory sarcopenia is assessed using a modified Medical Research Council (modified MRC) (8) score. The modified MRC is a globally standardized scale used to evaluate function related to dyspnea. The modified MRC is a five-level scale: Grade 0, not troubled with breathlessness except with strenuous exercise; Grade 1, troubled by shortness of breath when hurrying or walking straight up hill; Grade 2, walks slower than people of the same age due to breathlessness or has to stop for breath when walking at own pace on a level surface; Grade 3, stops for breath after walking 100m or after a few minutes on a level surface; Grade 4, too breathless to leave the house or breathless when dressing or undressing (8). For the diagnosis of sarcopenic respiratory disability, functional disability was assessed using a modified MRC of grade 2 or more. Dyspnea due to neuromuscular disease is not included in the criteria for sarcopenic respiratory disability, because it is associated with respiratory tract palsy rather than sarcopenia. Moreover, acute aggravation of respiratory diseases is not included as sarcopenic respiratory disability. However, the difficulty of weaning from a respirator after acute respiratory failure is considered a criteria for sarcopenic respiratory disability, since diaphragm inactivity with ventilator management leads to diaphragm atrophy (55) and causes respiratory dysfunction (63).

Rehabilitation nutrition as a therapeutic strategy

There are no previous studies that have investigated the effect of a therapeutic approach for respiratory sarcopenia and sarcopenic respiratory disability. Here, we propose a rehabilitation nutrition treatment (novel nutritional management using a combination of nutritional therapy and exercise) for respiratory sarcopenia and sarcopenic respiratory disability. This is based on the results of interventional studies in older adults with sarcopenia and patients with respiratory disease.

Exercise intervention including respiratory rehabilitation

Exercise intervention is presumed to be useful for respiratory sarcopenia and sarcopenic respiratory disability.

Strength training of respiratory muscles

Strength training of respiratory muscles may be effective in improving physical function, respiratory function, and muscle strength. Inspiratory muscle training improved dyspnea (Baseline Dyspnea Index), exercise capacity (6 min walk test

(6MWT)) in COPD (71), maximum expiratory pressure in the adult population (72), and skeletal muscle strength in older adults with sarcopenia (73). In addition, in patients with COVID-19, FEV1, FVC, FEV1 / FVC%, DLCO%, and 6MWT also improved with respiratory rehabilitation (74).

Strength training of the lower limb

Strength training of the lower limb increases muscle mass, muscle strength, and motor performance. In severely dyspneic individuals with COPD, lower-limb muscle training improves quadriceps muscle endurance, exercise performance, lower-limb fat-free mass, exercise-induced symptoms of dyspnea, and fatigue compared to baseline (75). Lower limb resistance training improves muscle strength (isometric/isokinetic muscle evaluation) and motor endurance (6MWT) in patients with COPD (76). It also improves performance in a five-repetition sit-to-stand test compared to respiratory rehabilitation (76). In addition, after a squat exercise program, grip strength, knee extensor strength, and 3-min walk distance increased in patients with sarcopenia (77).

Resistance training of the whole body

Resistance training of the whole body is effective in improving physical function and increasing muscle strength and muscle mass. Resistance training of the whole body can increase the 6MWT, upper extremity endurance capacity, knee endurance, and knee strength more than the control group in patients with moderate-to-severe COPD (78). In geriatric people with sarcopenia, resistance training of the whole body resulted in higher appendicular skeletal muscle mass compared to baseline. Also, their high-sensitivity C-reactive protein levels were lower than they were at baseline. At follow-up, handgrip strength, back strength, and PEF were higher than in a control group (79).

Combined aerobic and resistance training

Aerobic and resistance exercise training is effective in improving exercise capacity, muscle mass, and muscle strength. Aerobic and resistance exercise training improved the 6MWT in lung transplant candidates (80). Combined aerobic and resistance exercise training increases rectus femoris thickness (81) and quadriceps muscle strength (82) in COPD patients. Exercise intervention may be useful for respiratory sarcopenia and sarcopenic respiratory disability.

Nutritional intervention

Nutritional intervention beneficially affects muscle mass, performance status, physical activity, respiratory muscle strength, and respiratory muscle function. In stable COPD patients, nutritional supplementation improves lean body mass (83) and the 6MWT (83, 84). In addition, there were improvements in MIP and MEP (84). In lung cancer patients, oral nutritional supplement intervention showed a higher Karnofsky Performance Status and physical activity than a control (85). In older individuals with sarcopenia, nutritional intervention improves functional performance measured by walking time and maximum static expiratory force compared to placebo (86).

Combined exercise and nutritional intervention

Exercise and nutritional intervention may be useful for respiratory sarcopenia and sarcopenic respiratory disability. As interventions, high-intensity exercise training and nutritional supplementation had additional effects on skeletal muscle mass, quadriceps muscle strength, and cycle endurance time. Inspiratory muscle strength only improved in the intervention group (87). Uptake of nutritional supplementation during pulmonary rehabilitation improved quadriceps muscle strength, and inspiratory muscle function (88). Respiratory muscle rehabilitation, exercise, and enteral nutrition support increased MIP, MEP, and FVC (89).

Rehabilitation Nutrition

Rehabilitation nutrition is presumed to be effective for treating respiratory sarcopenia and sarcopenic respiratory disability. Rehabilitation nutrition is defined as that which is evaluated holistically by the International Classification of Functioning, Disability and Health, and the presence and cause of nutritional disorders, sarcopenia, and excessive or deficient nutritional intake. In several case reports, rehabilitation nutrition combined with adequate nutrition and aggressive rehabilitation contributed to increased muscle mass (90-92) and muscle strength (91, 92), and improved physical function (93) and sarcopenia (90). Rehabilitation nutrition can be practiced more effectively and comprehensively by using the rehabilitation nutrition care process, which is a systematic problem-solving method (94). In clinical practice guidelines for sarcopenia (95), regular exercise and proper nutritional intake may be effective in preventing the development of sarcopenia and is therefore recommended. In addition, compared with singular interventions, combined interventions, including comprehensive exercise-based treatment, such as resistance training and nutritional intervention, are more effective for improving sarcopenia and are recommended (96). Therefore, rehabilitation nutrition may break the vicious cycle of respiratory sarcopenia and sarcopenic respiratory disability (Figure 1). However, the ability of this approach to improve long term outcomes is not yet clear (96). Further research is required to verify the efficacy of rehabilitation nutrition for preventing or improving respiratory sarcopenia and sarcopenic respiratory disability.

Conclusion

Respiratory function decreases with age in healthy older people, for which we have created a new term, “presbypnea.” Respiratory sarcopenia is characterized as whole-body sarcopenia with low respiratory muscle mass followed by low

respiratory muscle strength and/or deteriorated respiratory function. Respiratory sarcopenia is caused by various factors such as aging, inactivity, undernutrition, disease, inflammation, and cachexia. Moreover, a vicious cycle of these factors worsens respiratory sarcopenia and causes sarcopenic respiratory disability. Respiratory muscle sarcopenia is not recognized in clinical practice due to a lack of concept and diagnostic criteria, but it may in fact be present in a number of cases. We have proposed an algorithm for diagnosing respiratory sarcopenia. Clinical diagnosis and rehabilitation nutrition interventions may improve function. It is important to increase clinical interest in respiratory sarcopenia and sarcopenic respiratory disability through research and clinical practice. Further research is required to validate the algorithm for diagnosing respiratory sarcopenia and the efficacy of rehabilitation nutrition for preventing and treating respiratory sarcopenia and sarcopenic respiratory disability.

Conflict of interest: Ayano Nagano, Hidetaka Wakabayashi, Keisuke Maeda, Yoji Kokura, Shinjiro Miyazaki, Takashi Mori, Dai Fujiwara have nothing to disclose.

Ethical Standards: This study has been performed in accordance with the ethical standards established in the 1964 Declaration of Helsinki and later amendments.

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