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REVIEW

Non-Pharmacological Strategies for Managing Sarcopenia in Chronic Diseases

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Abstract: This article focuses on a range of non-pharmacological strategies for managing sarcopenia in chronic diseases, including exercise, dietary supplements, traditional Chinese exercise, intestinal microecology, and rehabilitation therapies for individuals with limited limb movement. By analyzing multiple studies, the article aims to summarize the available evidence to manage sarcopenia in individuals with chronic diseases. The results strongly emphasize the role of resistance training in addressing chronic diseases and secondary sarcopenia. Maintaining the appropriate frequency and intensity of resistance training can help prevent muscle atrophy and effectively reduce inflammation. Although aerobic exercise has limited ability to improve skeletal muscle mass, it does have some positive effects on physical function. Building upon this, the article explores the potential benefits of combined training approaches, highlighting their helpfulness for overall quality of life. Additionally, the article also highlights the importance of dietary supplements in combating muscle atrophy in chronic diseases. It focuses on the importance of protein intake, supplements rich in essential amino acids and omega-3, as well as sufficient vitamin D to prevent muscle atrophy. Combining exercise with dietary supplements appears to be an effective strategy for preventing sarcopenia, although the optimal dosage and type of supplement remain unclear. Furthermore, the article explores the potential benefits of intestinal microecology in sarcopenia. Probiotics, prebiotics, and bacterial products are suggested as new treatment options for sarcopenia. Additionally, emerging therapies such as whole body vibration training, blood flow restriction, and electrical stimulation show promise in treating sarcopenia with limited limb movement. Overall, this article provides valuable insights into non-pharmacological strategies for managing sarcopenia in individuals with chronic diseases. It emphasizes the importance of a holistic and integrated approach that incorporates exercise, nutrition, and multidisciplinary interventions, which have the potential to promote health in the elderly population. Future research should prioritize high-quality randomized controlled trials and utilize wearable devices, smartphone applications, and other advanced surveillance methods to investigate the most effective intervention strategies for sarcopenia associated with different chronic diseases.

Keywords: sarcopenia, resistance training, nutrition, chronic disease, inflammation

Introduction

Sarcopenia, a progressive skeletal muscle disease characterized by a decline in muscle mass, muscle strength, and physical function, was first proposed by Rosenberg in 1989. However, it was not until 2010 that the European Working Group on Sarcopenia (EWGSOP) published a consensus[1] defining it as a progressive, systemic loss of muscle mass and/or decreased muscle strength or decreased physiological muscle function associated with aging. As the global population ages, the prevalence of sarcopenia has also increased, leading to reduced mobility, increased frailty, a higher risk of falls and fractures, and placing a heavy burden on families and society.[2] According to the EWGSOP estimation, the global prevalence of sarcopenia is projected to reach 1.2 billion by 2025 and 2 billion by 2050. Even with conservative estimates, it is expected that the affected population will exceed 200 million in the next four decades.

Nowadays, the pathogenesis of sarcopenia is not fully understood. The natural loss of muscle mass in the elderly is classified as primary sarcopenia, while muscle loss resulting from other causes, such as reduced hormone levels involved in maintaining muscle mass, decreased physical activity, anabolic resistance, nutritional status, inflammation, mitochondrial

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dysfunction, and chronic diseases, is classified as secondary sarcopenia.[3] The EWGSOP also emphasized the importance of recognizing subclasses of sarcopenia in the consensus revision, such as acute sarcopenia due to acute disease or injury, and chronic sarcopenia due to inflammatory diseases. Managing these subclasses requires additional attention.[4] To prevent and manage sarcopenia, experts recommend resistance training (RT) along with dietary supplements. Chinese experts also advocate for the same approach when it comes to domestic patients.[5] Additionally, incorporating aerobic, stretching, and balance exercises can improve physical function. For elderly individuals with chronic diseases, an individualized approach is necessary to address their specific needs.[6]

Numerous studies have emphasized the significant role of inflammation in the development of sarcopenia and have begun to investigate its characteristics and potential interventions.[7–11] However, it is important to consider the distinct pathological mechanisms of different chronic diseases, as they require specific considerations. For example, in patients with chronic kidney disease, dietary supplements should be administered cautiously to limit protein intake and prevent additional strain on the kidneys.[12] Similarly, when providing exercise guidance to patients with rheumatoid arthritis (RA), the presence of glucocorticoid-induced osteoporosis should be taken into account to avoid fractures caused by inappropriate exercise.[13]

Therefore, this review aims to propose non-pharmacological management strategies, including exercise interventions, dietary supplements, combined exercise and dietary supplements, and other interventions, to guide the management of secondary sarcopenia in patients with chronic diseases.

Exercise

Secondary sarcopenia is often associated with chronic diseases, and non-pharmacological strategies play a crucial role in managing it. By adopting a healthy lifestyle, individuals can not only control chronic inflammation but also slow down the progression of muscle atrophy simultaneously.[14–16] The Chinese expert consensus on prevention and intervention for the elderly with sarcopenia[5] recommends a combination of aerobic, stretching, balance exercises, and resistance training to improve physical function. Numerous researchers have focused on this approach and conducted exercise rehabilitation studies in patients with various chronic diseases, such as RA, pancreatitis and chronic kidney disease to investigate the impact of different exercise prescriptions on sarcopenia.[17–22]

Resistance Training

The International Clinical Practice Guidelines for Sarcopenia (ICFSR) recommend RT to manage sarcopenia.[23] The effects of RT on changing muscle mass have been verified not only in animal models but also in clinical practice, where it is now being promoted. A significant amount of researches support the effective intervention of RT for sarcopenia associated with chronic diseases.[24–28]

For patients with metabolic disease, RT can improve their physical function. In the study conducted by Stoever et al, 28 patients with sarcopenic obesity underwent progressive RT for 16 weeks.[29] After the intervention, the grip strength of these patients increased by 9%, the walking speed increased by 5%, and the quality of life score increased by 13% compared to the control group. Although there were no significant changes in skeletal muscle mass index (SMI), improvements in muscle and physical function still helped patients live independently and reduce the risk of disability and death. Besides, Cunha et al found that RT could not only improve physical function but also increase the skeletal muscle mass (SMM).[30] They analyzed the effects of different intensity of RT in 62 elderly women with sarcopenic obesity. Although there was no striking difference in SMM between the two groups of patients and the control group after 12 weeks, they found all patients in the two groups had a notable better improvement in SMM compared to the control group (Group with 1 set per exercise: +5.3 kg vs Group with 3 sets per exercise: +6.5 kg vs Control group: +1.2 kg).

Exercise is considered as one of the fundamental treatments for type 2 diabetes, and RT is particularly recommended. The intensity, frequency, repetitions, and groups of exercise do not differ significantly between the prevention and treatment of sarcopenia. However, in patients with diabetes who also have retinopathy or kidney disease, the way of exercise should be strictly adjusted to control blood pressure.[31] In the review conducted by Lim et al,[32] it was concluded that RT is good not only in addressing the loss of muscle mass and deterioration of physical function in elderly patients with type 2 diabetes, but also to blood glucose and insulin sensitivity. Additionally, Chien et al conducted a randomized study dividing 40 patients with type 2 diabetes combined with sarcopenia into a sandbag-assisted RT group and a control group.[33] After 12 weeks, the

RT group showed significant improvements in glycated hemoglobin, sitting and standing times, SMM, calf circumference, and quality of life questionnaire scores, indicating the positive effects of RT intervention.

There have also been relevant studies on RT for the treatment of sarcopenia in autoimmune diseases. Hishikawa et al conducted a home-based RT program for a patient with sarcopenia associated with RA.[19] The patient did not engage in habitual exercise and led a relatively inactive lifestyle. Moreover, she had concerns about experiencing joint pain after exercise, which was taken into account by the researchers during the planning of the exercise program. The researchers helped the patient understand that minor muscle pain caused by exercise is not an adverse event and developed a low-intensity RT program that could be adjusted according to her physical condition, aiming to maintain long-term compliance. After 3 months, although there was no significant change in the patient's SMM, her disease activity remained in remission. Additionally, the patient's fear of exercise decreased, allowing her to safely perform the exercise program with high compliance. These findings demonstrate the feasibility of a home-based RT program and its potential effect on preventing sarcopenia. Liao et al conducted RT for postoperative patients with knee osteoarthritis and obesity for 12 weeks.[34] Compared with the control group, the RT group patients significantly improved lean body mass and gait speed, suggesting that RT is a suitable and effective postoperative rehabilitation strategy.

With the development of medical technology, the number of cancer survivors is increasing, along with the probability of sarcopenia, which could significantly affect the quality of life.[35] While RT is considered a safe way for sarcopenia, it is uncertain whether the experience learned from healthy individuals could be generalized to cancer patients.[36] Generally, the recommended exercise regimen for inducing hypertrophy in healthy adults consists of 6–12 repetition maximum and 3–6 sets, with a frequency of 2–3 days per week.[37] However, it is uncertain whether this model is suitable for cancer patients. In a meta-analysis of RT intervention in prostate cancer patients, Lopez et al demonstrated that resistance-based exercise programs have significant effects on body and limb lean mass as well as SMI, with even more significant effects in specific subgroups that are younger and have lower baseline physical function.[38] Koeppel et al included 34 trials in their meta-analysis and found that the lean body mass of limbs in the RT intervention group increased 0.85 kg compared to control individuals.[39] Adams et al compared the effects of RT and aerobic exercise on sarcopenia in breast cancer patients receiving adjuvant chemotherapy and found that SMI increased by 0.32 kg/m^2 compared to the control group. Additionally, RT had a significant effect in reversing sarcopenia.[40] These findings demonstrate that RT plays an important role in improving the overall health of cancer patients, but strict supervision and personalized targeted training are still required.

Aerobic Exercise

In addition to RT, the contribution of aerobic exercise alone for sarcopenia is limited and modest. However, it could led toa visible improvement in strength and physical function to a certain extent. Huffman et al conducted a study using a mouse model for RA, where the mice engaged in three months of wheel running. The results showed significant improvements in joint swelling, Interleukin-6 levels, muscle mass, and function.[41] This suggests that aerobic exercise holds potential as a therapeutic intervention. Furthermore, Cao et al conducted a meta-analysis involving cancer patients and found that aerobic exercise did not lead to significant changes in muscle cross-sectional area and limb lean body mass in breast cancer patients.[35] However, it did result in a 7% improvement in the 6-minute walking distance and a 22% improvement in quadriceps strength, highlighting its role in enhancing physical function and muscle strength.

Overall, these findings emphasize the importance of incorporating aerobic exercise into the management of various conditions, as it can contribute to improvements in muscle mass, function, and overall physical well-being.

Combinatorial Exercise

The effect of exercise on muscles depends on the type of exercise.[42] Shen et al compared the effectiveness of different exercise interventions for elderly patients with sarcopenia and found that RT and RT combined with aerobic and balance training were the most effective interventions in improving the quality of life.[43] Jeon et al conducted a study on postmenopausal women with diabetes and found that the SMM in the exercise group increased compared to the control group when RT was combined with aerobic exercise for 12 weeks.[44] Kobayashi et al randomly divided type 2 diabetes patients into three groups: strength training alone, aerobic training alone and a combination of this two training methods. The results of the study showed that strength training was more effective than aerobic exercise in improving blood glucose and body composition. However, there was no significant difference between strength training and combined training in reducing glycosylated hemoglobin.[45] Park et al conducted a 15-week compound exercise program for female sarcopenia patients who were older than 60, and the compound exercise group showed improvements in inflammation and anabolic effects of secondary sarcopenia.[46]

Other Exercises

In addition to conventional RT and aerobic exercise, researchers have explored specialized exercise interventions for various diseases. Kimura et al conducted a study to examine the impact of broadcast gymnastics exercise on muscle mass in patients with type 2 diabetes.[47] The study revealed that both the group participating in broadcast gymnastics exercise and the control group experienced weight loss during hospitalization. However, the decrease in SMI was significantly smaller in the broadcast gymnastics exercise group compared to the control group.

Yoga has been found to improve protein utilization and help maintain the balance between protein breakdown and synthesis, which may be beneficial for individuals with sarcopenia.[48] Denham-Jones et al conducted a systematic review to evaluate the effectiveness of yoga in improving pain, physical function, and quality of life in older adults with chronic musculoskeletal disorders.[49] The review identified four studies that demonstrated the positive effects of yoga on lower limb osteoarthritis and sarcopenia, providing evidence of its safety and effectiveness.

Furthermore, high-intensity training is another form of exercise that is effective for preventing sarcopenia.[50] However, it remains uncertain whether it is suitable for individuals with chronic diseases due to the limited availability of related studies. The scarcity of references in this area may be attributed to the challenges and potential risks associated with conducting high-intensity training research in patients with chronic diseases.

Dietary Supplements

The role of dietary patterns in regulating immune system is important and complex, and the Mediterranean diet is the most accepted anti-inflammatory dietary pattern.[51,52] Isanejad et al found that women who adhered to the Baltic and Mediterranean diets experienced less relative loss of SMI and total body muscle mass, as well as better physical function.[53] Current research has also found that dietary intake of protein, leucine, vitamin D, and omega-3 supplements could play a key role in preventing sarcopenia. However, the optimal dosage and type of supplements remain unclear.[54–60]

Protein

There are currently many studies exploring the improvement of protein supplements for sarcopenia. Nasimi et al found that supplementation of whey protein alone significantly improved lean body mass and physical function in elderly individuals with sarcopenia.[61] However, Bjorkman et al found that combining whey protein supplement with low-intensity physical exercise at home did not reduce the deterioration of muscle and physical function in community-living elderly people with sarcopenia through a 12-month randomized controlled double-blind trial.[62] In the context of sarcopenia related to chronic kidney disease, Silva et al conducted a literature review and concluded that a protein restriction diet with adequate energy intake could effectively reduce uremic toxicity and decrease the risk of sarcopenia and disease progression.[63] However, if the potential risks associated with sarcopenia outweigh the risks of reaching end-stage renal disease, a modest protein liberalization is recommend, while still avoiding excessive intakes above 1.3 g/kg per day. Prado et al also believe that daily energy requirement should be maintained at 25–30 kcal/kg, with 1.0–1.5 g/kg protein, 2–4 g leucine, 3 g β-hydroxy-β-methylbutyrate (HMB), 0.3 g/kg glutamine, 4–6 g carnitine, 5 g creatine, 2.0–2.2 g fish oil or 1.5 g eicosapentaenoic acid and 600–800 IU vitamin D to combat low muscle mass in cancer patients.[64] Furthermore, Mazzuca et al found that whey protein supplementation for 12 weeks in colorectal cancer patients reduced the prevalence of sarcopenia from 84% to 54%.[65]

Amino Acids

Many studies have concluded that supplementation of essential amino acids is a safe and effective way to combat muscular atrophy, but the conclusions are inconsistent between different studies.[66–68] Martinez-Arnau et al reviewed the literature and found that supplementation with leucine or leucine-rich protein (1.2–6 g/day) significantly reduced the prevalence of sarcopenia in older individuals by improving lean body mass.[69] According to Leenders et al, although a large number of studies have shown that leucine is an effective nutrient for the prevention and treatment of sarcopenia and type 2 diabetes, there is still a lack of long-term nutritional intervention studies.[70] On the other hand, Herrera-Martinez et al compared studies using high-calorie, high-protein, and leucine-rich oral supplements and vitamin D interventions in cancer patients with sarcopenia and found that the muscle mass of patients in the two groups remained stable, with no distinct advantage of leucine observed.[71] Additionally, studies on citrulline supplementation did not show any significant improvement in sarcopenia.[72]

Teixeira et al conducted a dietary supplement intervention study on a patient with type 1 diabetes and sarcopenia.[73] After 120 days of α-hydroxyisocaproic acid supplementation, the patient's body weight increased by 2 kg and grip strength increased by 58.84 N. HMB is a metabolite derived from leucine and is widely used in energy supplements by athletes and bodybuilders due to its ability to regulate muscle protein degradation. Several studies have explored the role of HMB in sarcopenia associated with chronic diseases. Cruz-Jentoft et al found that HMB can increase lean body mass, muscle function, and physical function regardless of exercise intervention in the elderly.[74] Coleman et al found that in the context of obesity, HMB has muscle-protective and anti-tumor activities in animal models of pancreatic cancer.[75] Kitajima et al found that supplementation of branched chain amino acid for 48 weeks could improve hypoproteinemia in patients with cirrhosis and prevent sarcopenia (SMM remained unchanged), reduce fat accumulation in skeletal muscle and improve prognosis in cirrhosis patients.[76] Moreover, Massini et al suggested that low protein and very low protein diets supplemented with essential amino acids and ketoacids showed beneficial effects in maintaining muscle mass and slowing the progression of chronic kidney disease.[12]

Omega-3

Omega-3 is a group of polyunsaturated fatty acids commonly found in deep-sea fish. A number of nutritional studies have focused on them in recent years, most have shown that they can prevent and improve sarcopenia. Okamura et al believed that omega-3 intake is negatively related to the existence of sarcopenia in elderly patients with type 2 diabetes.[77] Giorgio et al had confirmed that omega-3 supplements can indirectly improve protein metabolism and counteract anabolism to prevent sarcopenia.[78,79] Gray et al also found that omega-3 could enhance the effect of RT.[80] Witard found compelling evidence that omega-3 intake rapidly and effectively increases anabolic sensitivity of skeletal muscle in older adults, as well as long-term data on beneficial effects on muscle mass and function. Given the health benefits of omega-3, Rondanelli et al recommend that older adults with sarcopenia consume fish as a "functional food" at least 3 times a week to ensure a minimum of 4–4.59 g of omega-3 per day to prevent sarcopenia.[81]

In addition, in chronic diseases, the role of omega-3 in improving secondary sarcopenia has also been validated. Lanchais et al concluded that omega-3 can prevent the progression of RA, improve muscle metabolism, and limit muscle atrophy in obese and insulin-resistant individuals.[82] While Bird et al found that supplementation with omega-3 had a positive effect on muscle mass and strength in people with diseases like cancer or chronic obstructive pulmonary disease.[83] However, Rolland found that supplementation with omega-3 supplements alone or in combination with multimodal interventions (physical activity, cognitive training, and nutritional advice) did not had a significant effect on muscle strength in older people for more than three years.[84] Therefore, long-term, large-scale clinical studies are still needed to confirm these findings.

Vitamin D

The effects of vitamin D supplementation on muscle in patients with sarcopenia has long been a point of controversy.[85] Okubo et al discovered that vitamin D supplementation (2000 IU once daily for 12 months) may lead to a significant increase in muscle mass and grip strength in patients with decompensated cirrhosis.[86] On the other hand, Bode et al conducted a review of the available evidence and proposed that providing routine cholecalciferol supplementation of 800–1000 IU per day may be a reasonable approach to improve sarcopenia in patients over the age of 65, as long as there are no contraindications.[87] In contrast, Cheng et al found that vitamin D intervention only shortened standing time and did not have a significant effect on walking speed or muscle mass. However, combining vitamin D supplementation with protein supplementation and exercise showed a significant increase in grip strength and a trend towards increasing muscle mass.[88] In a study by Prokopidis et al, which included 10 randomized controlled trials, no significant improvement in muscle strength or muscle mass was observed in the vitamin D supplement group.[89]

Combination of Multiple Dietary Supplements

In addition to the use of dietary supplements alone, numerous studies have started to investigate the impact of compound dietary supplement interventions on the prevention and treatment of sarcopenia. However, there are notable variations in the intervention factors across different studies.

Negro et al designed a randomized controlled double-blind study that lasted for 12 weeks. Thirty-eight healthy elderly individuals were supplemented twice a day with multi-component dietary supplements mainly containing essential amino acids, creatine, and vitamin D. The results revealed that the lean body mass of the limbs in the supplement group increased by 0.34 kg compared with baseline.[90] Cereda et al found that oral dietary supplements rich in whey protein, leucine, and vitamin D could be used to treat sarcopenia.[91] Cochet et al demonstrated that branched-chain amino acids combined with vitamin D can be used to treat sarcopenia and improve mitochondrial activity.[92] Lin et al conducted a study and found that a daily intake of sufficient protein, ranging from 1.2 g/kg to 1.5 g/kg, can effectively enhance SMM in the limbs of elderly individuals.[93] And the quality of protein is considered important according to dietary guidelines and recommendations from the European Society for Clinical Nutrition and Metabolism. Furthermore, supplementation of whey protein and vitamin D on this basis can further improve the walking speed of older individuals. Rondanelli et al found that consuming whey protein-based nutritional formulations rich in leucine and vitamin D can enhance physical performance and function, as well as improve muscle mass in hospitalized elderly patients undergoing rehabilitation.[94] Martin-Cantero et al observed that a combination of amino acids, creatine, HMB, and protein significantly improved muscle mass, whereas supplementation of protein or other components alone did not yield similar effects.[95] Bo et al demonstrated that high whey protein, vitamin D, and vitamin E supplements could protect muscle mass, strength, and quality of life in elderly individuals with sarcopenia. They observed improvements in Relative SMI, muscle strength, and two anabolic markers, Insulin-like Growth Factor-I (IGF-1) and Interleukin-2.[96] Nasimi et al evaluated the effects of daily consumption of a supplement-rich fortified yogurt (3 g HMB, 1000 IU vitamin D, and 500 mg vitamin C) on elderly individuals with sarcotrophic disorders.[97] They found that after 12 weeks of intervention, consumption of fortified yogurt was associated with improvements in grip strength and walking speed. Furthermore, vitamin D and IGF-1 levels were significantly increased in the intervention group, while high-sensitivity C-reactive protein (hs-CRP) levels did not increase at all. Chang et al reported that supplementation with whey protein, leucine, and vitamin D increased limb muscle mass in patients with sarcopenia, regardless of whether they were accompanied by a physical exercise program.[98] Kang et al discovered that twice-daily oral leucine-rich protein supplementation (20 g protein comprising, 50% casein, 40% whey, and 10% soy, with a total leucine content of 3000 mg), along with vitamin D (800 IU or 20 µg), calcium (300 mg), fat (1.1 g), and carbohydrate (2.5 g), increased lean body mass by 0.3 kg after 12 weeks in healthy Korean adults aged 50 and older.[99]

There is limited research on dietary supplements for sarcopenia associated with chronic diseases. Cruz-Jentoft et al suggest that inadequate intake of protein, vitamin D, antioxidant nutrients and long-chain polyunsaturated fatty acids is associated with sarcopenia in immune-mediated rheumatic diseases. Dietary supplements may have a significant improvement effect on RA, ankylosing spondylitis, and systemic sclerosis. However, further clinical validation is needed.[100]

Other Dietary Supplements

In addition to the common dietary supplements mentioned earlier, some scholars have focused their research on more unique dietary supplements. Luk believed that green tea as an antioxidant could maintain a dynamic balance between protein synthesis and degradation. It also promotes the synthesis of mitochondrial energy metabolism, thereby maintaining muscle homeostasis and reducing muscle atrophy with age.[101] Karim conducted a 16-week probiotic intervention in patients with chronic obstructive pulmonary disease and sarcopenia.[102] The study observed reductions in CRP, improved walking speed, and enhanced somatic function scores. However, they did not find a reduction in the prevalence of sarcopenia. According to Ali et al, bee products, including royal jelly, propolis, and bee pollen, are abundant in powerful antioxidants and have the potential to enhance inflammation and oxidative damage.[103] Additionally, they have been found to regulate metabolism, boost satellite stem cell reactivity, enhance muscle blood flow, suppress catabolic genes, and facilitate peripheral neuronal regeneration. Consequently, these products exhibit promising effects in ameliorating muscle mass, muscle strength, and physical function among individuals with sarcopenia. Besora-Moreno et al conducted a study and observed that the consumption of antioxidant-rich foods or the use of antioxidant supplements could enhance muscle strength and function in individuals with sarcopenia.[104] Hamstra et al conducted studies suggesting that low-dose lithium supplements may potentially mitigate the development of primary sarcopenia. However, it is important to note that these findings are based on animal studies and further clinical validation is needed to confirm their efficacy in humans.[105]

Combining Exercise with Dietary Supplements

Interventions that combine a protein-rich diet with RT seem to be an effective strategy for the prevention and treatment of sarcopenia.[106,107] However, compliance with such interventions is generally low,[108,109] and the results of different studies are quite controversial and contradictory.[110–116] For example, Song et al conducted a meta-analysis and found that RT combined with complex dietary supplements containing protein and vitamin D may enhance grip strength in elderly individuals with sarcopenia. However, it was found to have no significant effect on muscle mass.[117] On the other hand, Hernandez-Lepe et al discovered that regular RT combined with daily essential amino acids or whey protein and vitamin D supplements not only helped maintain or increase limb and total SMM in elderly individuals with sarcopenia, but also had synergistic effects on strength, speed, stability, and overall quality of life.[118] In the case of female patients with sarcopenia, Fairfield et al found that a combined intervention of 3 g HMB and 2000 IU vitamin D per day for 12 weeks resulted in increased thigh muscle volume and reduced intermuscular adipose tissue volume. However, it did not show any significant improvement in muscle strength, even when combined with RT.[119] In contrast, Orsatti et al discovered that 16 weeks of RT combined with daily consumption of 25 g soy-based oral milk led to a significant increase in muscle strength in postmenopausal women.[120] For male patients, Nilsson et al conducted a 12-week home-based unsupervised resistance band training (3 days/week) along with daily supplementation of five nutrients including whey protein, micellar casein, creatine, vitamin D, and omega-3. The intervention group showed a 3% increase in limb lean body mass and a 2% increase in total lean body mass. Grip strength increased by 8%, while sitting and standing time for 5 sessions decreased by 9%. Additionally, the cross-sectional area of the quadriceps femoris muscle significantly increased in the intervention group.[121] Overall, these studies highlight the potential benefits of combining RT with specific dietary supplements in improving muscle strength, mass, and overall quality of life in elderly individuals with sarcopenia. However, further research is needed to determine the optimal combination and dosage of supplements for different populations.

In addition to the intervention methods, researchers also investigated whether the timing of the intervention had an impact on the ultimate outcome. Chang et al carried out a two-stage intervention program for patients with sarcopenia, where the first stage involved hospital-based RT and nutritional support (amino acids, calcium, and vitamin D3), and the second stage only involved home-based exercise.[122] In a study comparing different intervention approaches, the early intervention group underwent supervised exercise and dietary supplements initially, followed by home exercise. On the other hand, the delayed intervention group followed the reverse order. The findings indicated that early intervention may contribute to the early recovery of lower limb muscle mass. Nabuco et al found that supplementation of whey protein either before or after RT could effectively increase muscle mass, muscle strength, and physical function in elderly female patients with sarcopenia.[123] Additionally, Hernandez-Lepe et al found that exercise and dietary supplements intervention may have a synergistic effect on reducing chronic inflammation in the elderly. Therefore, it is necessary to further evaluate the effect of different combinations of exercise and dietary supplements on the sarcopenia associated with chronic diseases.

For elderly patients with sarcopenia associated with diabetes, a combination of nutrition and exercise intervention can be performed simultaneously.[124–126] Argyropoulou et al suggest that a combined exercise regimen (aerobic and resistance) while maintaining a protein intake of over 1 g/kg per day is the safest strategy for managing sarcopenia and type 2 diabetes.[127] Yamamoto et al found that neither elastic RT in combination with 6 g of leucine-rich amino acids per day, nor RT alone, had a significant effect on muscle mass or strength after 48 weeks in type 2 diabetes.[128] Saitoh et al proposed that engaging in regular and appropriate physical activity and/or exercise training, along with ensuring adequate nutrient intake or incorporating special dietary supplements, may serve as the most effective strategies for preventing sarcopenia and mitigating the decline of physical function in patients with heart failure.[129]

Liao et al found that protein supplementation combined with exercise training could significantly increase muscle mass and strength in elderly people with knee osteoarthritis.[130] Liao et al used RT combined with protein supplementation to intervene in patients with knee osteoarthritis and sarcopenia, and 12 weeks of RT intervention alone had a significant impact on restoring normal walking speed (≥ 1.0 m/s). Additional dietary supplements could restore the patients to normal walking speed 3 months earlier.[131] Zhao et al found that a whey protein supplement of 10 g/day combined with RT can effectively improve the SMM of the limbs of inflammatory bowel disease patients.[132] Kemmler et al conducted high-intensity dynamic RT combined with whey protein supplement intervention on 43 male patients with osteoporosis who were older than 72, and the lumbar bone density and SMI of the intervention group were significantly improved after 18 months.[50] These results all confirm the effect of combined interventions on sarcopenia associated with autoimmune diseases.

Ispoglou et al conducted a 24-week intervention on a 57-year-old female patient with multiple sclerosis. The intervention included exercise interventions twice a week and the administration of dietary supplements containing 7.5 g of essential amino acids and 500 IU of cholecalciferol twice a day.[133] At week 24, the total lean body mass of the patient increased by 1.0%, and the lean body mass of the arms and legs increased by 6.9% and 6.3%, respectively. In a cross-sectional study, Rivadeneyra et al found that female Parkinson's patients with low physical activity and low energy intake were more likely to develop sarcopenia. Therefore, physical exercise combined with dietary supplements is recommended to prevent and treat sarcopenia.[134]

Targeted exercise and dietary supplements have shown some resistance to cancer-related muscle and bone loss.[135] While advancements are being made in the field, it is important to note that there is currently no definitive consensus on the development of optimal exercise and nutrition prescriptions for managing sarcopenia. Further research is required to address the existing barriers, including determining the ideal composition of dietary supplements, identifying the appropriate intensity of physical exercise, and exploring the potential use of medications.

Other Non-Pharmacological Strategies

Exercise training and dietary supplements are considered the primary treatment approaches for sarcopenia, as there are currently no approved medications specifically targeting this condition. However, there have been significant advancements in the development of new treatment options for sarcopenia, offering potential alternatives to complement non-pharmacological strategies.[136]

Traditional Chinese Exercise

Exercises based on traditional Chinese medicine have been widely used in the prevention and treatment of balance, cardiopulmonary and other related diseases in the elderly.[137–140] Compared to general sports, traditional Chinese exerciseare more like gymnastics, consisting of various components such as endurance, resistance, balance, flexibility, breathing and meditation, which emphasize the proper form and intensity to produce better results. Although traditional Chinese exercise do not specifically target a particular disease, they have shown some feasibility in improving sarcopenia.

Through the inclusion of 21 studies, Guo et al found that traditional Qigong had a positive impact on the muscle strength and physical function of patients with sarcopenia.[141] However, the evidence regarding the impact on muscle mass was inconsistent. In another review, Niu et al included 13 randomized controlled trials and found that traditional Chinese exercise did have significant effects on muscle strength and physical function.[142] Various types of Qigong have shown different effects in improving sarcopenia. Yuen et al conducted an 8-week supervised Baduanjin training on patients with chronic stroke and observed significant improvements in balance ability, lower limb strength, and mobility. This study provides evidence that Baduanjin is a safe and sustainable home exercise option for individuals with sarcopenia.[143] Huang et al conducted a meta-analysis of 11 randomized controlled trials investigating the influence of Tai Chi on elderly patients with sarcopenia. The researchers found that Tai Chi primarily improved physical function, while there was no difference in muscle mass, grip strength, gait speed, or short-term physical fitness test.[144] According to a meta-analysis of 27 studies conducted by Wang et al, Tai Chi was shown to be more effective than Baduanjin and

Qigong in improving physical function and grip strength. On the other hand, Qigong had a greater effect on balance ability.[145] Furthermore, Wei et al conducted a study in which they combined RT with Yijin Jing exercises in elderly patients with sarcopenia.[146] Their findings indicated that this combined exercise regimen resulted in improved muscle area compared to RT alone and the control group.

These studies have provided evidence that traditional Chinese exercise can effectively improve physical fitness, balance, and muscle strength in the elderly. However, it is important to note that the evidence is currently limited and conflicting, highlighting the need for more high-quality clinical trials to further investigate the potential benefits of traditional Chinese exercise in this population.

Intestinal Microecology

In addition to dietary interventions, gut microbes and their metabolites have also been found to potentially influence sarcopenia. Liu et al discovered that the levels of prevotella in the intestinal tract of multi-ethnic patients with sarcopenia in western China were significantly reduced compared to the control group.[147] Furthermore, mice given prevotella gavage showed higher grip strength and a larger gastrocnemius and rectus femoris area than the control group, suggesting that prevotella may have a potential therapeutic role in managing sarcopenia. Liu conducted a systematic review including 10 clinical investigation studies and found that lactobacillus and bifid bacterium may help restore age-related muscle atrophy.[148] Chen et al found that Lactobacillus casei may regulate the occurrence and progression of age-related sarcopenia through the gut-muscle axis.[149] Therefore, probiotics, prebiotics, and bacterial products could be considered as new therapies for sarcopenia.

Other Emerging Non-Pharmacologic Therapies

Furthermore, researchers are focusing their attention on conducting device-assisted intervention studies targeting sarcopenia in patients with significant physical activity limitations.

Whole body vibration training is a method aimed at improving musculoskeletal function by stimulating the body through mechanical vibrations and external resistance loads. Meta-analyses based on systematic reviews have confirmed the significant impact of whole body vibration training on knee extension muscle strength and lower limb motor functions such as jumping height, standing up, and walking tests in the elderly.[150] Blood flow restriction involves the application of a pneumatic cuff on the proximal end of the moving limb and can serve as an alternative to traditional exercise for patients with significant physical activity limitations.[151] In a study conducted by Scarpelli et al, it was implemented on a 99-year-old patient with knee osteoarthritis and secondary sarcopenia.[152] After 24 sessions of treatment, the lateral femoris muscle exhibited a 12% increase in cross-sectional area, an 8% increase in thickness, and an improvement in quality of life based on a questionnaire score. The utilization of electrical stimulation to enhance muscle function and facilitate weight has gained popularity in recent years.[153] In a study conducted by Venugobal et al, 101 participants underwent low-energy pulsed electromagnetic stimulation for 10 minutes once a week.[154] The results indicated significant improvements in mobility (timed to stand and walk, 5 sit-stand, and 4-meter walk) and body composition (increased SMM, decreased total fat mass, and reduction in visceral fat mass).

Overall, these emerging therapies have been regarded as promising interventions in rehabilitation. However, high-quality studies on this topic are limited, and considering the positive effects of exercise training on cardiopulmonary and cognitive function, as well as muscle mass development, further research and exploration of its potential applications are needed.

Summary and Outlook

In conclusion, this review incorporates perspectives from various disciplines to provide a comprehensive overview of the non-pharmacological strategies for managing sarcopenia in individuals with chronic diseases. The findings strongly suggest that RT plays a crucial role in managing chronic diseases and secondary sarcopenia, and it is widely recommended by experts due to its significant impact on overall health. While aerobic exercise has limited ability to improve muscle mass, it can enhance overall quality of life when combined with multi-modal compound training. Current research emphasizes the importance of protein intake, supplements rich in essential amino acids and omega-3 fatty acids, and adequate vitamin D to prevent muscle atrophy. However, the optimal dosage and type of supplement remain unclear, especially for chronic diseases. Combining exercise with dietary supplements appears to be an effective strategy for preventing sarcopenia, but implementing these interventions to achieve desired outcomes is still challenging. The article also suggests other strategies such as traditional Chinese exercise, intestinal microecology, and rehabilitation therapies for individuals with limited limb movement as new treatment options for sarcopenia. These emerging therapies have potential implications for promoting health in the elderly population with chronic diseases.

Sarcopenia has a higher prevalence than previously believed, resulting in a significant burden on both families and society. Therefore, timely and effective interventions are necessary. For elderly individuals with chronic diseases, it is crucial to implement personalized approaches that cater to specific needs based on the characteristics of their chronic conditions. As emphasized in various guidelines for sarcopenia, RT should be the primary intervention strategy. Multimodal therapy, incorporating dietary supplements and other potentially effective measures, plays a vital role in breaking the vicious cycle of chronic diseases and sarcopenia. Numerous clinical studies have demonstrated the effectiveness of this approach. However, it is important to acknowledge the limitations of the literature search, which may have resulted in the omission of relevant studies. Additionally, it is worth noting that the results of different studies could be controversial and contradictory. Therefore, future research should prioritize high-quality randomized controlled trials utilizing advanced monitoring methods such as wearable devices and smartphone applications to enhance the effectiveness of integrated non-pharmacological strategies. The ultimate objective is to improve the health status and quality of life for individuals with secondary sarcopenia caused by chronic diseases.

Disclosure

The authors report no conflicts of interest in this work.

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