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Article

# Research Progress on the Relationship between Sarcopenia and Pain

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**Abstract:** With the global population aging rapidly, the prevalence of age-related conditions such as sarcopenia and chronic pain is increasing. Sarcopenia is a progressive skeletal muscle disorder characterized by loss of muscle mass and function, while pain, particularly musculoskeletal pain, is a common geriatric syndrome. Although both conditions are associated with reduced physical activity and functional decline, their direct relationship remains unclear. This review synthesizes current evidence on the correlation between pain and sarcopenia. Epidemiological studies reveal a complex and often bidirectional association influenced by demographic factors such as age, gender, and living environment. Pain may contribute to the development of sarcopenia by limiting mobility and physical activity, while sarcopenia-related muscle degeneration and fat infiltration may exacerbate pain symptoms. Potential underlying mechanisms include chronic inflammation driven by pro-inflammatory cytokines (e.g., TNF-α, IL-6), malnutrition, and reduced anabolic hormone levels. However, findings are inconsistent across studies due to differing diagnostic criteria and population characteristics. While a direct causal link has not been established, the indirect correlation between pain and sarcopenia suggests that integrated assessment and management of both conditions could improve outcomes in elderly populations. Further longitudinal research is needed to clarify their pathophysiological relationship.

**Keywords:** sarcopenia; pain; elderly

## 1. Background

The main part of the annual increase in the world's population is the elderly, and according to researchers, by the mid-20th century, the elderly population will grow by about one-fifth [1]. With the increasing aging of the population, more and more people are suffering from age-related diseases, such as sarcopenia, which is more common in the elderly. This age-related disease has attracted widespread attention. According to research, muscle mass decreases at a rate of about 1% per year with age after the age of 40 [2]. Sarcopenia is a systemic and progressive skeletal muscle disease characterized by muscle loss, often accompanied by adverse consequences such as falls, weakness, decreased body function, and poor prognosis [3]. Skeletal muscle pain, as a common disease in the elderly and sarcopenia, belongs to the geriatric syndrome. Prolonged skeletal muscle pain can lead to decreased physical function. Although both pain and sarcopenia can reduce physical activity and function, a causal relationship between pain and sarcopenia has not been found yet. This article will discuss the correlation between pain and sarcopenia.

## 2. Definition and Fashion Trends

The term “sarcopenia” first appeared in the 1990s and is defined as the non-physiological decline in muscle mass and function associated with aging [4]. Although definitions of sarcopenia vary considerably, defining it solely by the reduction in muscle mass is somewhat insufficient. The diagnostic criteria for sarcopenia are divided into European and Asian versions. The European Working Group on Sarcopenia in Older People (EWGSOP2) considers it a syndrome characterized by the generalized and progressive loss of skeletal muscle strength and mass. The minimum grip strength values are 20 kg for women and 30 kg for men. Male muscle mass <7.40 kg/m$^2$ or female muscle mass <5.14 kg/m$^2$ is considered low skeletal muscle mass [5], and meeting both conditions constitutes sarcopenia. The consensus of the Asian Working Group for Sarcopenia holds that sarcopenia should include all of the following outcomes: low muscle mass (male <7.0 kg/m$^2$, female <5.7 kg/m$^2$), low muscle strength (male <26 kg, female <18 kg), and slow gait speed (<1.0 m/s) [6]. However, neither of these diagnostic criteria systematically analyzes pain. The relationship between sarcopenia and pain remains unclear, and analyzing the link between the two may be helpful for the diagnosis and treatment of sarcopenia. The incidence of sarcopenia varies depending on factors such as age, gender, ethnicity, living conditions, residential environment, and assessment methods of the surveyed population. Currently, the total number of people with sarcopenia worldwide is 50 million, and it is expected to exceed 200 million in the next 40 years [1]. The prevalence of sarcopenia among the elderly population aged over 60 but under 70 is 5–13%, while the prevalence among those over 80 years old is 11–50% [7]. Studies have shown that female patients are more likely to develop sarcopenia than males [8], especially postmenopausal women aged 60–70, which may be related to a decrease in sex hormones [9].

Pain is a painful sensation and emotional experience associated with actual or potential tissue damage [10]. A systematic review of a UK study reported an overall prevalence of chronic pain of 43.5%, with an incidence of moderate to severe disabling pain ranging from 10.4% to 14.3% [11]. A 4-year study also conducted in the UK found that the annual incidence rate of chronic pain was 8.3%, and the cure rate was 5.4% [12]. According to the research, demographic factors (elderly, female), clinical factors (pre-existing pain, diabetes, hyperlipidemia), psychosocial factors (depression, anxiety, smoking, alcohol, overweight, sleep disorders) and genetic factors are all related to pain [10,13]. However, there are no clinical parameters related to sarcopenia in these reports. Studying the relationship between pain and sarcopenia can help improve and prevent sarcopenia status, and reduce adverse consequences.

## 3. The Relationship between Pain and Sarcopenia

### *3.1. The Relationship between Pain and Sarcopenia in Different Demographic Factors*

A South Korean study showed that pain is associated with sarcopenia, which leads to muscle atrophy and fat infiltration, and that muscle atrophy and fat infiltration are linked to pain [14]. A Brazilian study on lower back pain in 322 elderly women found that pain intensity was associated with poor mobility and balance in sarcopenia [15]. Scott et al. studied pain in 1452 Australian elderly men aged ≥70 years and found that elderly men with occasional and persistent pain had an increased risk of developing sarcopenia and disability within five years, and the association between pain and sarcopenia appeared to be mediated by gait speed [16]. A study on elderly people living in Japanese communities revealed that the prevalence of chronic pain with sarcopenia was about one-tenth, and elderly people with chronic pain were more likely to develop sarcopenia [6]. Whoan et al. indicated that there is only a weak correlation between sarcopenia and the severity of back pain, and the severity of pain is more strongly related to back muscle degeneration than to sarcopenia [17]. A study conducted in Africa found that sarcopenia is not a direct cause of low back pain; rather, low back pain reduces activity levels, and reduced activity levels contribute to the development of sarcopenia [18]. A study on the relationship among low back pain, sarcopenia, and frailty in 730 Japanese community-dwelling elderly found that low back pain was closely related to frailty but not to sarcopenia [19]. The relationship between pain and sarcopenia is controversial and complex.

In the EWGSOP2, the definition of sarcopenia includes muscle mass, whereas the definition of sarcopenia in the Sarcopenia Diagnosis and Outcomes Consortium (SDOC) includes only measurements of handgrip strength and gait speed [16]. Removing the condition of low muscle mass may lead to an increased prevalence of sarcopenia. In a Japanese study, according to the SDOC, 21% of men had sarcopenia, but according to the EWGSOP2, only 6% of patients presented with sarcopenia. The authors also found that among all factors contributing to sarcopenia, gait speed was most consistently associated with pain, and elderly men with persistent pain were more likely to develop SDOC-defined sarcopenia [16,20]. The small sample size may have contributed to the lack of correlation between pain and EWGSOP2-defined sarcopenia, and the EWGSOP2 does not require gait speed to diagnose sarcopenia. Therefore, this might be one of the reasons for the controversy regarding the relationship between sarcopenia and pain. This complex relationship is also bidirectional. If it is a direct causal relationship between sarcopenia and pain, there is currently no definitive clinical evidence. However, if pain is sufficiently persistent

and intrusive, it can limit daily activities and lead to the development of sarcopenia and disability. Conversely, sarcopenia causes muscle atrophy and fat infiltration, which in turn are causes of pain.

Sarcopenia is more common in women. Men have greater muscle mass than women, and estrogen levels in menopausal women decrease significantly. This decline in estrogen levels has been proven to accelerate muscle atrophy in postmenopausal women. Postmenopausal women with chronic low back pain should increase physical activity and exercise to reduce the risk of sarcopenia [21,22].

Sarcopenia is related to the living environment of the elderly. Community-dwelling residents engage in more physical activity and have better eating habits. Elderly individuals with sarcopenia living in nursing homes report more sedentary behavior and are more likely to be malnourished. In addition, hospitalized patients have other risk factors for sarcopenia and functional decline, such as reduced energy intake, decreased physical activity or prolonged bed rest, low mood, and social isolation. Furthermore, decreased physical activity, malnutrition, and mood are also closely related to pain [13,23,24]

### *3.2. The Relationship between Pain and Sarcopenia in Different Diseases*

Sarcopenia is associated with musculoskeletal disorders, including chronic low back pain, osteoporosis, and lumbar spinal stenosis [17]. These three conditions are major components of musculoskeletal diseases and can directly or indirectly cause pain. The mechanism by which sarcopenia affects the occurrence of pain and reduced quality of life in elderly patients with musculoskeletal diseases remains unclear. However, research findings have shown that patients with osteoporosis and sarcopenia have higher pain scores after osteoporotic fracture surgery compared to general patients [25]. A study from Taiwan indicated that sarcopenia causes muscle weakness and incoordination, and can also lead to tendon injury pain due to joint instability. For patients already experiencing pain, this may result in physical inactivity, further exacerbating the state of sarcopenia [5]. This creates a vicious cycle of sarcopenia-pain-inactivity-sarcopenia. Recently, an association has been found between sarcopenia and fibromyalgia syndrome as well as joint pain [4]. In studies on degenerative lumbar spine diseases, it was found that 74% of the variation in gait speed was related to pain intensity, but it is currently impossible to determine whether the gait speed is caused by the degenerative lumbar spine disease or by sarcopenia [8].

The correlation between sarcopenia and low back pain may be related to lumbar spinal stenosis and degenerative lumbar scoliosis in patients [26,27]. Sarcopenia may lead to lumbar scoliosis and spinal curvature, which causes pelvic retroversion. Both sarcopenia and pelvic retroversion are associated with low back pain [28]. It is currently unclear whether sarcopenia induces spinal disorders, but spinal disorders are correlated with aging and sarcopenia. In studies investigating the prognosis of patients after pancreatic cancer surgery, nutritional damage caused by insufficient pancreatic exocrine and endocrine function, other metabolic factors, pain, and infection can all promote the development of sarcopenia [29,30]. In patients with rheumatoid foot, sarcopenia may exacerbate pain and the progression of joint destruction [31].

Sarcopenia has been shown to be associated with pain in various diseases, but there is a lack of clinical evidence proving a direct causal relationship between the two. Based on a review of current research findings, it appears that pain and sarcopenia have a complex indirect correlation, and the direct correlation between them requires further in-depth investigation.

## 4. The Mechanism of Pain Induced Muscle Atrophy

The etiology of sarcopenia is complex and diverse, with identified factors including decreased nutrient intake, low-level physical activity, progressive increase in muscle fibrosis, chronic inflammatory status, oxidative stress, changes in muscle metabolism and neuromuscular junction degeneration, specific comorbidities (elevated blood sugar, cardiovascular and cerebrovascular diseases, and tumors), and neuro psychological disorders (cognitive impairment, depression, etc.) [21,32–34]. Recently, research has reported that muscle atrophy may be secondary to some medications commonly used in the elderly, such as statins [35]. According to existing research findings, there may be several mechanisms by which pain induces sarcopenia.

### *4.1. Pro-Inflammatory Factor*

The association between muscle loss and pain mechanisms is not yet clear, but inflammation may promote pain. As age increases, the number of immune cells decreases, while tumor necrosis factor-α (TNF-α), interleukin-6 (IL-6), interleukin-1 (IL-1), and C-reactive protein (CRP) increase. It has been suggested that these cytokines trigger the ubiquitin proteasome system and increase susceptibility to muscle atrophy. The activation of this cellular signaling pathway can promote inflammatory states and lead to synthetic metabolic resistance, which is one of the main factors in muscle atrophy [23,32]. Therefore, it can be considered that inflammation may lead to

sarcopenia and may also cause pain. Pain and sarcopenia often occur simultaneously, but there is currently no evidence to prove a direct correlation between the two.

### *4.2. Malnutrition*

Insufficient nutrient intake and low protein synthesis are common among the elderly, with a 25% reduction in food intake and a significant impact on the quality of food intake [23]. The decrease in muscle strength is associated with low levels of vitamin D in the blood and decreased protein intake. Pain may also be related to low vitamin D levels, as reduced bone mass makes it easier to cause osteoporotic fractures [36]. In addition, vitamin D not only has the effect of preventing bone loss and muscle loss, but also can inhibit the production of several pro-inflammatory cytokines in the serum, including IL-6 and TNF-α. The pathogenesis of these inflammatory factors may be correlated with the pain process and the pathology of sarcopenia [37]. In addition, dietary magnesium can also reduce the circulation of inflammatory cytokines and prevent muscle mass and function decline in the elderly [38]. For patients with muscle atrophy, specific nutrition and nutritional supplements interventions may play a relevant role in long-term pain management plans.

### *4.3. Reduction of Synthetic Metabolic Hormones*

Insulin like growth factor-1 can mediate the proliferation of muscle satellite cells, and one of the reasons for muscle atrophy is the failure of satellite cell activation in muscles. Therefore, a decrease in related hormones may also lead to muscle mass loss [32]. Postmenopausal estrogen deficiency leads to decreased bone mass, which can easily cause osteoporotic fractures and muscle loss, which may be the cause of persistent lower back pain during the aging process [38,39].

## 5. Conclusions

Currently, many studies have found a correlation between pain and sarcopenia, but the direct causal relationship between sarcopenia and pain is not yet clear and further longitudinal research is needed. At present, there are no drugs used in clinical practice to improve sarcopenia. Nutritional supplementation and exercise can delay the progression of sarcopenia. Studying the relationship and specific mechanisms between the two not only benefits the improvement and early prevention of sarcopenia, reduces the adverse consequences of sarcopenia, and improves the quality of life of patients, but also provides some directions for finding drugs and methods to treat sarcopenia.

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The authors declare no conflict of interest.

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