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Research Progress of Insulin-like Growth Factor-1 in the Diagnosis and Efficacy Prediction of Sarcopenia in the Elderly

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Abstract: Sarcopenia in the elderly is a syndrome characterized by age-related progressive loss of muscle mass, decline in muscle strength, and deterioration of muscle function. Its high incidence significantly increases the risk of falls, fractures, disability, and mortality among the elderly, posing a global public health challenge for geriatric health. Insulin-like growth factor-1 (IGF-1), a key cytokine regulating muscle growth, repair, and metabolism, exhibits a progressive decline in serum levels with aging and is closely associated with the onset and progression of sarcopenia in the elderly. This study reviews the research progress of IGF-1 in the diagnosis and efficacy prediction of sarcopenia in the elderly, providing theoretical references for precise diagnosis, treatment, and prognosis assessment of sarcopenia in the elderly.

Keywords: Insulin-like growth factor-1; Sarcopenia in the elderly; Diagnosis; Efficacy prediction; Research progress

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1. Introduction

Sarcopenia is a syndrome characterized by a decline in skeletal muscle mass, strength, and function that occurs with aging. It is closely associated with a decrease in quality of life, falls, disability, osteoporosis, hospitalization rates, and mortality among the elderly [1]. American scholar Irwin Rosenberg proposed the concept of age-related muscle decline in 1989 and first suggested the use of the term sarcopenia in 1997 [2]. Afterwards, the International Working Group on Sarcopenia (IWGS) and the Asian Working Group for Sarcopenia (AWGS) also introduced new consensus documents that largely adopted this definition. Due to factors such as diagnostic criteria and ethnicity, the reported prevalence of sarcopenia varies significantly both domestically and internationally. According to reports, based on the diagnostic criteria of the European Working Group on Sarcopenia in Older

People (EWGSOP), the prevalence of sarcopenia among community-dwelling elderly individuals ranges from 1% to 29%, among those in elderly care facilities from 14% to 33%, and among hospitalized elderly patients is approximately 10% [3]. In the Asian elderly population, the prevalence of sarcopenia is approximately 4.1% to 11.5%, slightly lower than that in European and American populations. Insulin-like growth factors (IGFs) are a class of polypeptides that not only promote cell differentiation and proliferation but also exhibit insulin-like effects. They can exert systemic effects as hormones or act locally as autocrine/paracrine factors [4]. IGFs function by binding their ligands to receptors on the cell surface. When these receptors are activated, they trigger the activation of tyrosine protein kinases, initiating a series of cascade reactions that ultimately result in different biological effects in various cell types. Research has found that serum IGF-1 levels in the elderly population show a significant declining trend with age, and that serum IGF-1 levels in patients with sarcopenia are significantly lower than those in healthy elderly individuals, suggesting that IGF-1 may be involved in the pathophysiological processes of sarcopenia in the elderly [5]. In recent years, research on IGF-1 as a biomarker for the diagnosis and prognosis prediction of sarcopenia in the elderly has gradually become a focal point. This article aims to systematically review relevant research progress and provide references for clinical practice.

2. The associated mechanisms between IGF-1 and sarcopenia in the elderly

2.1. Regulating the proliferation and differentiation of muscle satellite cells

Muscle satellite cells are stem cells in skeletal muscle with the potential for self-renewal and differentiation, serving as key cells for repairing muscle damage and maintaining muscle mass. IGF-1 can bind to IGF-1 receptors on the surface of muscle satellite cells, triggering the activation of the PI3K/Akt signaling pathway, promoting the activation of muscle satellite cells from a quiescent state, and accelerating their proliferation and differentiation, thereby generating new muscle fibers and repairing damaged muscle tissue [6]. Among the elderly, reduced serum IGF-1 levels can lead to weakened activation capacity and decreased proliferation and differentiation efficiency of muscle satellite cells, resulting in diminished repair after muscle injury. Over time, this can lead to a reduction in muscle mass and deterioration in muscle function.

2.2. Promoting muscle protein synthesis and inhibiting breakdown

Maintaining muscle mass primarily involves achieving a balance between muscle protein synthesis and breakdown. IGF-1 can enhance the expression of genes related to muscle protein synthesis through the PI3K/Akt/mTOR signaling pathway, promoting the synthesis of structural proteins such as actin and myosin. IGF-1 can also inhibit the activation of the ubiquitin-proteasome system, reducing muscle protein breakdown. In old age, a decline in IGF-1 levels leads to decreased anabolic activity and increased catabolic activity in muscle protein metabolism, easily resulting in a net loss of muscle protein and ultimately leading to sarcopenia.

2.3. Anti-inflammatory and antioxidant effects

Chronic low-grade inflammation is a key risk factor for sarcopenia in the elderly. Inflammatory factors such as TNF-α and IL-6 can inhibit the function of muscle satellite cells and promote the breakdown of muscle proteins by activating inflammatory signaling pathways. IGF-1 exhibits certain anti-inflammatory and antioxidant activities, reducing the expression of inflammatory factors and mitigating the damage caused by inflammatory responses to muscle tissue. IGF-1 can enhance the body's antioxidant capacity, reducing oxidative stress damage to muscle

cells induced by reactive oxygen species, thereby protecting muscle function. In the elderly, a decline in IGF-1 levels weakens its anti-inflammatory and antioxidant effects, potentially exacerbating inflammatory damage to muscle tissue and accelerating the progression of sarcopenia [7].

3. Application of IGF-1 in the diagnosis of sarcopenia in the elderly

3.1. Correlation studies on IGF-1 as a diagnostic biomarker

Multiple clinical studies have confirmed that serum IGF-1 levels are significantly lower in elderly patients with sarcopenia compared to healthy elderly individuals, and IGF-1 levels are positively correlated with muscle mass and muscle strength. A cross-sectional study involving 200 elderly individuals aged over 65 found that serum IGF-1 levels were significantly lower in the sarcopenia group compared to the non-sarcopenia group, and serum IGF-1 levels showed a significant positive correlation with the appendicular skeletal muscle mass index (ASMI) and grip strength [8,9]. Another prospective study with a 3-year follow-up period found that elderly individuals with low baseline serum IGF-1 levels (< 100 ng/mL) had a significantly higher incidence of sarcopenia compared to those with normal IGF-1 levels (35.2%/12.8%) [10]. This suggests that a decrease in IGF-1 levels may serve as an early warning marker for sarcopenia in the elderly.

3.2. Research on the diagnostic threshold of IGF-1

Given the variations in population characteristics and detection methods across different studies, a unified threshold standard for diagnosing sarcopenia in the elderly using IGF-1 has not yet been established. Scholars both domestically and internationally have conducted exploratory work on threshold values for different populations. For the European and American populations, research indicates that a serum IGF-1 level below 120 ng/mL can serve as a reference threshold for diagnosing sarcopenia in the elderly, with a sensitivity of 72.3% and a specificity of 68.5% [11]. In studies focusing on Asian populations, a study involving 150 elderly Chinese individuals found that an IGF-1 level below 105 ng/mL demonstrated a sensitivity of 76.2% and a specificity of 73.1% for diagnosing sarcopenia, aligning more closely with the physical characteristics of elderly Chinese individuals [12]. The team led by Yu Kang from Peking Union Medical College Hospital creatively proposed screening indicator cut-off values for sarcopenia in elderly Chinese individuals based on data from a multi-center Chinese population, which included relevant reference ranges for IGF-1, providing significant evidence for the localized diagnosis of sarcopenia in elderly Chinese individuals.

3.3. Diagnostic value of combining IGF-1 with other indicators

The diagnostic efficacy of IGF-1 alone is suboptimal, prompting some scholars to explore the diagnostic significance of combining IGF-1 with other indicators. Combining IGF-1 with indicators such as creatine kinase (CK) and albumin (ALB) can significantly enhance the diagnostic performance for sarcopenia in the elderly. One study indicated that the combined diagnosis using IGF-1 and the SARC-F scale achieved a sensitivity of 82.5% and a specificity of 78.3%, significantly surpassing the diagnostic efficacy of detecting IGF-1 alone or using the SARC-F scale alone [13]. Combining IGF-1 with muscle mass indicators measured by bioelectrical impedance analysis can further enhance diagnostic accuracy, providing a more reliable basis for the early screening and confirmation of sarcopenia.

4. Research progress on IGF-1 in predicting therapeutic efficacy in elderly sarcopenia

4.1. Predicting therapeutic efficacy in nutritional interventions

Nutritional intervention serves as a foundational approach for managing elderly sarcopenia, primarily through the supplementation of nutrients such as protein, vitamin D, and Omega-3 to enhance muscle metabolism. After nutritional intervention, the extent of the increase in serum IGF-1 levels are closely related to improvements in muscle mass and strength. A randomized controlled study involving 80 elderly patients with sarcopenia had patients take 20 g of whey protein and 800 IU of vitamin D daily for a 12-week intervention [14]. Following the intervention, there was a significant increase in serum IGF-1 levels, and patients with an IGF-1 increase of ≥ 20% showed significantly greater improvements in appendicular skeletal muscle mass index and grip strength compared to those with an IGF-1 increase of less than 20%. The precise nutritional intervention program of "whey protein + vitamin D + Omega-3" introduced by Yu Kang's team also confirmed the correlation between the post-intervention increase in IGF-1 levels and improvements in muscle function, indicating that IGF-1 can serve as a metric.

4.2. Predictive indicators for the efficacy of exercise interventions

Exercise interventions, particularly resistance training, are potent means of improving sarcopenia in the elderly, promoting muscle contraction and facilitating muscle protein synthesis. Changes in serum IGF-1 levels following exercise interventions can predict their efficacy. For instance, in a 16-week resistance exercise intervention study, serum IGF-1 levels increased significantly post-intervention, and patients with initially higher IGF-1 levels exhibited more pronounced improvements in muscle strength after the exercise intervention [15]. The combined "nutrition + exercise" intervention yielded even more remarkable results, with a greater increase in IGF-1 levels post-intervention, which positively correlated with improvements in muscle mass and strength. This suggests that IGF-1 can serve as a key predictive indicator for the efficacy of combined intervention strategies.

4.3. Efficacy prediction in pharmacological treatments

Pharmacological treatments for sarcopenia in the elderly are still under exploration, with some medications exerting their effects by regulating IGF-1 levels. Growth hormone-releasing hormone analogs can stimulate the secretion of growth hormone, elevate serum IGF-1 levels, increase muscle mass, and enhance muscle function. The magnitude of the increase in serum IGF-1 levels following pharmacological treatment can predict the efficacy of the treatment. Patients whose IGF-1 levels rise above 120 ng/mL demonstrate significantly better improvements in muscle mass and strength compared to those who do not reach this threshold. Similarly, certain anti-inflammatory and antioxidant medications can also exert their effects by regulating IGF-1 levels, and their efficacy can also be predicted based on changes in IGF-1 levels [16].

5. Conclusions and prospects

In summary, as a key regulatory factor in muscle metabolism, IGF-1 is closely related to the onset and progression of sarcopenia in the elderly. In terms of diagnosis, IGF-1 can serve as an early warning biomarker for sarcopenia in the elderly. When combined with the detection of other indicators, it can significantly enhance diagnostic efficacy. Moreover, the exploration of localized thresholds for the Chinese population provides an important reference for

clinical diagnosis. In terms of therapeutic effect prediction, changes in IGF-1 levels can effectively predict the outcomes of nutritional interventions, exercise interventions, and pharmacological treatments, providing a basis for the formulation and adjustment of individualized intervention plans.

Despite the progress made in research on IGF-1 in the diagnosis and therapeutic effect prediction of sarcopenia in the elderly, numerous controversies remain. Firstly, there is no unified diagnostic threshold for IGF-1. Different populations and detection methods result in significant variations in thresholds, and there is a lack of a widely recognized standardized threshold. Secondly, IGF-1 has relatively low specificity, as various diseases such as chronic kidney disease, liver disease, and diabetes can all lead to a decrease in serum IGF-1 levels, potentially affecting its diagnostic efficacy. Thirdly, the mechanism of action of IGF-1 in therapeutic effect prediction is not yet fully understood, and there are differences in the impact of different interventions on IGF-1 levels, necessitating further in-depth research. Future research directions can focus on the following aspects: firstly, conducting multi-center, large-sample prospective studies to establish standardized IGF-1 diagnostic thresholds for elderly individuals in different regions and age groups, thereby improving the accuracy and applicability of diagnosis; secondly, exploring the combined detection of IGF-1 with other novel biomarkers (such as microRNAs and exosomes) to enhance the specificity and sensitivity of diagnosis.

Disclosure statement

The authors declare no conflict of interest.

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