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Advances in the diagnosis and treatment of osteoporosis and sarcopenia

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Abstract: With the increase in human life expectancy and the advent of an aging society, the prevalence of osteoporosis and sarcopenia, as age-accelerating diseases, has been increasing year by year, creating a heavy burden on society. Osteoporosis and sarcopenia have multiple etiologies, including genetic, metabolic, lifestyle, and exercise variables. Moreover, poor nutritional status, including insufficient consumption of calcium, vitamin D, and protein, as well as decreased physical activity, are major risk factors for sarcopenia and osteoporosis. Osteoporosis and sarcopenia raise chances of fractures and falls, affects exercise capacity, reduces quality of life, and directly or indirectly affects the life expectancy of the population. Adequate nutritional supplementation and physical activity are the main strategies for preventing and delaying osteoporosis and sarcopenia, in addition to pharmacological interventions that are thought to be potentially beneficial. This review provides the progress of epidemiologic, diagnostic, and therapeutic studies of osteoporosis and sarcopenia, and provides some reference value for further research.

1. Introduction

Osteoporosis and sarcopenia have a high degree of homology, as they belong to the same skeletal-muscular system, are physiologically close to each other, share many common pathophysiological mechanisms and clinical manifestations, and the muscles and bones promote each other developmentally, cooperating with each other to accomplish the daily activities of the human body. Because of population and local differences, the epidemiology and diagnosis of osteoporosis and sarcopenia differ greatly around the world. Adequate nutritional supplementation and physical activity are recognized as the primary strategies for preventing and delaying osteoporosis and sarcopenia, and the relative lack of pharmacological treatment requires early recognition and management by researchers and clinicians.

2. Definition and epidemiology of osteoporosis and sarcopenia

2.1 Osteoporosis

Definition: Osteoporosis is defined by the World Health Organization as a condition affecting the

bones on a systemic level, marked by reduced bone density, deterioration of bone structure, and a higher likelihood of suffering from fractures due to fragility, with hip fractures being the most severe outcome [1]. In osteoporosis can be divided into two main categories: primary and secondary osteoporosis. This article focuses on primary osteoporosis, it is the most frequently occurring metabolic bone disorder [2].

Epidemiology: As a well-defined ageing disease, as human life expectancy rises and the global population ages, osteoporosis is becoming a significant health issue and is now recognized as a major non-communicable disease, impacting the quality of life for individuals. A 2021 study showed that the global prevalence of osteoporosis was estimated to be 18. 3%, 23. 1% in women and 11. 7% in men, and a cross-sectional study in Germany [3] showed that the estimated prevalence of osteoporosis among people over 50 years of age was estimated to be 8.7%, 12.2% in women and 4.7% in men. A survey conducted in the United States [4] revealed that osteoporosis affected 29.9% of women and 16.0% of men aged over 50, with a tendency to increase with age. The epidemiologic survey of osteoporosis in China [5] showed that the prevalence of osteoporosis in people over 50 years of age in China was 19.2%, of which 32.1% were women and 6.9% were men. In summary, the prevalence of osteoporosis in women over 50 years of age in China is much higher than that in Europe and the United States, and with the large population base in China, with the aging society approaching in China, the prevalence of osteoporosis is projected to rise annually, leading to a significant social burden on the country.

2.2 Sarcopenia

Definition: sarcopenia is a relatively new term, referred to as myasthenia gravis, or "Sarcopenia" in English.The concept of sarcopenia first arose in 1989, and was first proposed by Irwin Rosenberg [6].In 2010, the European Working Group on Sarcopenia (EWGSOP) first published the a consensus on sarcopenia, defining sarcopenia as a geriatric syndrome with ageing-associated loss of muscle mass, loss of muscle strength and/or reduced somatic function, which was the first time that an assessment of somatic function was included in the diagnostic entry, along with muscle mass and muscle strength, as a diagnostic criterion for sarcopenia [7].In 2016 sarcopenia was included in the International Diseases List of the World Health Organization (WHO) as one of the most important international diseases.In 2016 sarcopenia was included in the International Diseases List of the World Health Organization (WHO). The inclusion of sarcopenia in the International Classification of Diseases, ICD-10,was a landmark and raised concerns. With the continuous research on sarcopenia and the updating of its understanding, in the sarcopenia expert consensus released in 2019, the Asian Working Group for Sarcopenia (AWGS) proposed the new term "possible sarcopenia" for the first time in the expert consensus published in 2019 [8], and called for earlier intervention before sarcopenia occurs, which means that the importance of sarcopenia has reached a new level.

Epidemiology: the prevalence of myasthenia gravis varies considerably both around the world and in our country due to differences in diagnostic modalities, diagnostic criteria, and study populations. 2017 study by Shafiee et al states that the global prevalence of myasthenia gravis is 10. 00 %. By 2022 the study of Petermann-Rocha et al stated that the global prevalence of sarcopenia is about 10 %-27 %.The occurrence of sarcopenia differs across various countries worldwide. According to a study in Canada,the prevalence of sarcopenia was 38.9% in males and 17.8% in females. Similarly,a study in the United Kingdom reported rates of 4.6% for males and 7.9% for females. As highlighted in another study,the prevalence of sarcopenia in China is closely linked to advancing age, according to a study [9], the prevalence of sarcopenia among Chinese individuals aged 60 and above is reported to be 6.4% , 17.4% in the group of people aged 65 years and above, and the prevalence of sarcopenia in the group of people aged 80 years and above reaches 18.52% to 55.56%. Meanwhile, the prevalence

of sarcopenia in China also has a large geographical difference, with the prevalence in urban areas being much smaller than that in rural areas [10]. In conclusion, the disease rate of sarcopenia in the world is gradually increasing, and there is an obvious correlation between the prevalence of sarcopenia and age in China, which, combined with the national conditions of China, is expected to increase with the development of the aging society.

3. Screening and diagnosis of osteoporosis and sarcopenia

3.1 Osteoporosis

Screening: the more recognized is the main osteoporosis risk assessment tools are (Osteoporosis Self-assessment Tool for Asians,OSTA) [11] and (International Osteoporosis Foundation,IOF) Osteoporosis Risk1 min test questions [12]. It is worth noting that these two screening tools are only suitable for early screening of osteoporosis and are not diagnostic, and BMD or FRAX risk assessment is recommended for those with high-risk screening results.

Diagnosis: The most common diagnosis of osteoporosis is still based on the assessment of bone mass by dual-energy X-ray absorptiometry (DXA). [13] While osteoporosis involves many aspects beyond simply measuring bone mineral density, this assessment is still crucial for quantifying bone tissue as a diagnostic tool and is an indicator of potential fracture risk. Therefore, it is considered the most effective way to assess the rate of bone loss.According to the WHO recommendations, the classification based on the T-value of BMD is as follows: (i) In normal cases, the T-value is -1.0. (ii) In cases of bone loss, the T-value falls between -2.5 and -1.0. (iii) In cases of osteoporosis, the T-value is -2.5.and (iv) Severe or previously diagnosed osteoporosis: T-value $\leq$ -2.5 + fragility fracture. T-value = (measured value of bone mineral density - peak bone mineral density in normal young people of the same race and sex)/standard deviation of peak bone mineral density in normal young people of the same race and sex [14]. Furthermore,alternative techniques exist,such as Quantitative Ultrasound (QUS),which relies on the attenuation of ultrasound signals caused by the interaction of sound waves with structures. However,there is insufficient evidence to support the clinical use of parameters obtained from this test for diagnosing osteoporosis. Another assessment method is Quantitative Computed Tomography (QCT), which measures volumetric Bone Mineral Density (BMD) in both trabecular and cortical bone. Nevertheless,this approach is not recommended due to its high economic cost and the greater ionizing radiation exposure requiblue for patients compablue to DXA scans [15]. Diagnosing osteoporosis can involve a bone tissue biopsy, an invasive technique that entails extracting tissue samples, typically only performed if there is evidence of a tumor [16]. Another commonly utilized test is bone turnover markers (BTM), which are valuable for identifying metabolic bone diseases [17], offering insights into overall health and factors contributing to secondary osteoporosis [18]. These markers can measure amino and carboxy-terminal peptides during bone formation or resorption [19], including formation markers like alkaline phosphatase (ALP), indicative of osteoblast activity [20]. Notably, bone isoenzymes exhibit no gender-based differences or circadian rhythm influences, thus serving as straightforward markers with limited sensitivity and specificity in metabolic bone disorders. Conversely, CTX (collagen type 1 cross-linked carboxy-terminal peptide) and NTX (collagen type 1 cross-linked amino-terminal peptide) are widely used resorption markers reflecting osteoclast activity, being peptides released during bone resorption. CTX and NTX are recognized as clinically valuable markers for bone resorption and are crucial in diagnosing osteoporosis [21].

3.2 Sarcopenia

Screening: There are many screening tools for sarcopenia, the main ones being the Calf Maximum

Circumference Measurement [22], the Sarcopenia-Five (SARC-F) questionnaire, the SARC-CalF scale, the SARC-EBM scale, the MSRA questionnaire [23], the Ishii score [24], the Finger-Circle Test, and the Finger-Circle Test [25]. Test (Finger-circle Test). The simple five-item questionnaire is the most widely used method, the Ishii score has a high screening standard for community-dwelling elderly people [25], and the Finger-circle Test is expected to be the mainstream screening method for sarcopenia at the grassroots level in the future because it does not require the use of any instrumentation.

Diagnosis: diagnostic criteria for sarcopenia were recommended according to our expert consensus on sarcopenia-osteoporosis published in 2022. It is recommended to have any one positive muscle mass test accompanied by any one positive muscle strength test or accompanied by any one positive muscle function test [26].

Muscle mass testing: Instruments for muscle mass testing include dual energy X-ray absorptiometry (DXA) [27], bioelectrical impedance analyzer (BIA), CT, as well as MRI [28], of which DXA and BIA measurements are similar.The gold standard for measuring muscle mass is considered to be MRI [29], but it is not suitable for mass screening at the grassroots level because of its expensive equipment and the contraindications to the test. Another measurement method is D3-creatine dilution, his disadvantage is that it can only assess the whole body muscle mass, and cannot assess specific sites [30], with the result that DXA and BIA are still the mainstay of muscle mass measurement.

Muscle strength and muscle function tests: grip strength test, 6m walking speed, and 5-repetition get-up-and-sit test [31] are currently commonly used methods for assessing muscle strength and muscle function, and the equipment required is simple, suitable for universal use, and is being continuously optimized [32], and it is hoped that in the future, more and more convenient and easy-to-administer methods will be available for testing muscle strength and muscle function.

4. Treatment of osteoporosis and sarcopenia

Osteoporosis and sarcopenia are part of the same skeletal-muscular system and have much in common in terms of treatment, and the combination of the two is reviewed below.

4.1 Non-pharmacologic treatment

Exercise therapy: Randomized controlled trials [33] have demonstrated that progressive resistance exercise [34] is effective in stimulating osteoclastogenesis and muscle protein synthesis, thereby improving bone microarchitecture, muscle mass, strength, and function, and decreasing the risk of falls in people with osteoporosis and sarcopenia. Some researchers recommend that [35]the best approach to preventing falls in older adults who live in the community is a mix of resistance training, balance exercises, and functional workouts.

Nutritional therapy: Increasing protein intake to 1.2/kg/day is recommended and combined with resistance exercise has been shown to increase muscle mass and bone mass [36], with whey protein, a rapidly digested and absorbed protein rich in leucine, being the most effective dietary strategy for increasing muscle protein synthesis [37]. However, increasing protein intake is more effective when vitamin D levels are in the optimal range. Supplementation with at least 1000 IU of vitamin D per day may be required to achieve the goal of protecting bone and muscle [38]. Calcium is the most abundant mineral in bone, and adequate intake of vitamin D and calcium is recommended to delay osteoporosis; these trace minerals may also play a role in muscle metabolism. Finally, creatine has been shown to increase muscle mass and strength, and recent research suggests that this nutrient may also increase bone density[39].

4.2 Pharmacological treatment

At present, there are no medications designed specifically for sarcopenia unlike the various pharmacological treatments commonly used for osteoporosis. These treatments for osteoporosis include antiresorptive medications like denosumab and bisphosphonates, anabolic drugs such as teriparatide and abaparatide, anti-osteosclerotic proteins like romosozumab, and hormonal drugs like hormone replacement therapy and selective estrogen receptor modulators. While there are no approved drugs specifically for sarcopenia, studies have indicated that denosumab[40] can enhance muscle and bone mass, as well as decrease the risk of falls and fractures in older individuals. Further assessment of denosumab's effectiveness in treating sarcopenia will be necessary through future double-blind pilot studies.

5. Conclusion

The research on osteoporosis is relatively mature, while the research on sarcopenia is still in its infancy. In the future, it is necessary to pay more attention to the connection between the two, to look for common diagnostic methods and biomarkers that are easier and have higher diagnostic value, and to strengthen the research on sarcopenia-specific drugs, so as to realize the joint prevention and treatment of osteoporosis and sarcopenia in the future.

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