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Exploration of the Prevention and Treatment Strategies of Traditional Chinese Medicine for Osteosarcopenia Based on the Theory of "Bone-Muscle Disharmony"

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Abstract: ***Osteosarcopenia(OS) , a degenerative disease of the musculoskeletal system, shares similarities with the concepts of "bone atrophy" and "muscle atrophy" in Traditional Chinese Medicine (TCM). Its pathological mechanism is succinctly summarized as the "Bone-Muscle Disharmony." With the accelerating aging of society, the incidence of OS continues to rise, imposing substantial economic burdens on families and society. However, there remains no definitive single therapeutic agent for OS in clinical practice, and treatment efficacy remains uncertain. Given the necessity for long-term or even lifelong management, the development of highly effective, safe, and cost-effective therapeutic strategies is imperative. As a traditional medical system, TCM offers unique advantages in treating musculoskeletal disorders. Based on the theory of "Bone-Muscle Disharmony," this study explores the overlapping etiological and pathological mechanisms of OS from both TCM and modern medical perspectives. It posits that the core pathology of OS lies in the musculoskeletal system, rooted in the deficiency of the spleen and kidneys. Dysfunction of these two organs leads to "Bone-Muscle Disharmony," resulting in musculoskeletal imbalance and disease onset. The therapeutic approach emphasizes replenishing deficiencies, harmonizing the spleen and kidneys, and concurrently treating bone and muscle to nourish both the innate (kidney) and acquired (spleen) foundations. This strategy aims to restore flexibility to tendons and bones, reestablishing harmony between bone and muscle, thereby offering novel insights for the prevention and treatment of OS in clinical TCM practice.***

Keywords: Bone-Muscle Disharmony, Osteosarcopenia, Traditional Chinese Medicine, Spleen-Kidney Deficiency, Prevention and Treatment Strategies**.**

1. Introduction

Sarcopenia, an age-related disease, is characterized by progressive loss of muscle mass, decreased muscle strength, and impaired physiological muscle function [1]. Osteoporosis, a systemic metabolic bone disorder, manifests as reduced bone mass, deteriorated bone microarchitecture, increased bone fragility, and elevated fracture risk [2]. In 2009, the concept of "Osteosarcopenia" (OS) was first proposed, defined as a covert degenerative geriatric syndrome involving the coexistence of sarcopenia and osteoporosis [3-4] With China's deepening population aging, the rising prevalence of sarcopenia and osteoporosis has consequently increased OS incidence [5], imposing heavier socioeconomic burdens on both patients and society [6].

TCM classical texts do not explicitly mention "OS," though sarcopenia is often categorized under "flaccidity syndrome" or "muscle atrophy", while osteoporosis corresponds to "bone desiccation" or "bone atrophy". Given OS as a comorbid syndrome, its pathogenesis and clinical manifestations align with the combined TCM classifications of "muscle atrophy," "bone atrophy," and "Flaccidity Syndrome" [7]. From a TCM perspective, OS presents superficially as bone desiccation and muscle atrophy, with its root cause lying in spleen-kidney deficiency. Guided by the "Bone-Muscle Disharmony" theory, this paper elucidates OS etiology and pathogenesis, proposing spleen-kidney tonification as the cornerstone for restoring musculoskeletal function. These insights aim to offer valuable references for clinical OS prevention and treatment.

2. Connotation of the Theory of "Bone-Muscle Disharmony"

The Classic of Difficult Issues (Nanjing), Chapter 24 states: "When bones and muscles fail to maintain their inseparable relationship, the muscles lose nourishment and atrophy. Consequently, teeth become elongated and brittle, while hair loses its luster. This lack of vitality indicates that the bones perish first." This describes the pathological manifestation of the "Bone-Muscle Disharmony" in TCM, where muscles lose nourishment and weaken, leading to deterioration of teeth and hair [8]. These observations align with the characteristics of OS, which presents with reduced muscle mass, decreased muscle strength, diminished bone mass, increased bone fragility, and reduced bone density. The concept of "Bone-Muscle Disharmony" epitomizes TCM's holistic understanding of musculoskeletal pathology. From the perspective of TCM's "five-zang organ unity theory," the kidney governs bones and marrow production, while the spleen governs the muscles of the limbs. These two organs play pivotal roles in regulating the skeletal and muscular systems. Dysfunction of either organ directly impacts the morphology and function of bones and muscles. As recorded in The Yellow Emperor's Inner Classic: On Atrophy (Suwen: Weilun Pian): "Spleen-heat leads to muscle atrophy... kidney-heat leads to bone atrophy." Thus, spleen deficiency impairs its ability to nourish muscles, causing muscle atrophy, while kidney deficiency weakens its capacity to sustain bones, resulting in bone atrophy. In TCM theory, OS falls under the category of "flaccidity syndrome", characterized by the

co-existence of both “bone atrophy” and “muscle atrophy”. The root pathogenesis lies in kidney deficiency leading to bone desiccation and spleen deficiency causing muscular flaccidity.

3. Modern Medicine’s Understanding of the Etiology and Pathogenesis of OS

3.1 Mechanoregulatory Mechanisms of the Musculoskeletal System: A Biomechanical Perspective

The pathogenesis of OS is closely associated with the musculoskeletal system. As two critical components of the locomotor system, muscles and bones share common genetic regulatory factors originating from the same progenitor cells - mesenchymal stem cells. These two tissues are not merely anatomically adjacent; their mechanical and chemical interactions play vital roles in maintaining musculoskeletal homeostasis [9]. Mechanistically, bones not only provide structural anchors for muscle attachments but also function as biomechanical levers that coordinate effective movement execution. Conversely, muscle contractions exert significant influence on bone morphology through mechanical loading. The mechanical forces generated during muscular contraction stimulate osteoblast activity, promoting bone formation and enhancing bone mass to maintain skeletal homeostasis. Conversely, diminished mechanical stimulation may inhibit osteogenesis, reduce bone density, and potentially contribute to osteoporosis development. This underscores the essential role of mechanical regulation in preserving normal musculoskeletal function. Notably, insufficient mechanical loading predisposes individuals to degenerative disorders such as osteoporosis and sarcopenia [10-11].

3.2 The Biological Mechanisms of Endocrine and Paracrine Regulation Between Muscle and Bone

Bone and muscle tissues possess secretory functions and can produce a variety of biochemical factors, which play pivotal roles in the musculoskeletal system. Irisin, a myokine generated after skeletal muscle contraction [12], regulates bone homeostasis and muscle regeneration [13]. Studies have revealed that physical exercise increases irisin secretion in muscles. Irisin modulates osteoblasts and osteoclasts by enhancing osteoblast activity and suppressing osteoclast formation, thereby promoting bone mass accumulation [14]. A castration-induced rat model of kidney-yang deficiency osteoporosis (OS) demonstrated a positive correlation between decreased irisin levels and OS pathogenesis, suggesting that irisin concentration influences skeletal muscle and bone function. This may occur through endocrine pathways that alter musculoskeletal morphology, though the precise mechanisms remain unclear. These findings provide evidence for the role of muscle-bone energy metabolism in OS development [15]. Research indicates that osteoporosis often coexists with sarcopenia [16], and skeletal muscle-derived myostatin (MSTN) not only regulates muscle growth [17], but also impacts bone metabolism [18]. The Wnt/β-catenin signaling pathway serves as a key regulator of the musculoskeletal system, while shared pathways like Ras-Raf-MAPK/ERK signaling influence the proliferation and differentiation of bone metabolic cells [19]. Bone marrow mesenchymal stem cells (BMSCs), stromal cells critical for bone marrow formation and human development, align closely with the physiological functions of “kidney essence” in TCM [20]. BMSCs can differentiate into myoblasts for sarcopenia treatment. Originating from bone marrow [21], BMSCs’ myogenic differentiation potential correlates with TCM theories of “kidney governing bones” and “spleen governing muscles,” reflecting the spleen-kidney functional interrelationship.

4. Traditional Chinese Medicine’s Understanding of the Etiology and Pathogenesis of OS

4.1 The Theory of Congenital and Acquired Foundations in Traditional Chinese Medicine

In Yizong Bidu·On Kidney as Innate Foundation and Spleen as Acquired Foundation (1637), Li Zhongzi of the Ming Dynasty stated: “A skilled physician must trace the root of disease, distinguishing between innate and acquired foundations. The innate foundation resides in the kidney... while the acquired foundation lies in the spleen.” This emphasizes that the kidney stores primordial qi and essence-blood, which constitute the indispensable basis for human growth and development. The spleen, as the acquired foundation, governs the transportation and transformation of water-grain essence to nourish the whole body and sustain vital activities [22]. Fu Qingzhu’s Gynecology·Pregnancy further elucidates: “The spleen represents the acquired foundation while the kidney embodies the innate foundation. The spleen cannot transform without the support of innate qi, nor can the kidney thrive without acquired qi.” This highlights the physiological interdependence between the spleen and kidney. Their mutual nourishment of innate and acquired essences forms a ceaseless yin-yang cycle that sustains human vitality [23]. As the “acquired foundation” and “source of qi-blood production,” the spleen-stomach system ensures systemic nourishment through its transformative functions. Normal spleen function guarantees adequate nourishment to muscles, manifesting as robust and well-developed musculature. Spleen dysfunction disrupts nutrient distribution, leading to malnourishment of bones and muscles – presenting as bone desiccation, muscle atrophy, and limb flaccidity. This “disconnection between bones and muscles” mirrors pathological manifestations of OS: qi-blood deficiency causing muscle wasting and weakness, coupled with kidney essence depletion resulting in decreased bone mass, reduced bone strength, skeletal deformation, and pain. The perpetual mutual transformation between innate and acquired qi depends on normal spleen-kidney coordination. Robust bones and well-nourished muscles epitomize their synergistic roles in sustaining human vitality, underscoring the spleen and kidney’s pivotal contribution to life’s cyclical processes.

4.2 The theory of Visceral Manifestation in TCM

The term “zangxiang” (visceral manifestations) was first introduced in Su Wen·Liu Jie Zang Xiang Lun (Basic Questions·Treatise on Visceral Manifestations of Six Seasonal Divisions). “Zang” refers to internal organs, while “xiang” den-otes their external manifestations encompassing both physiological and pathological presentations. TCM posits that refined subst-ances such as essence, qi, blood, and

body fluids are generated and stored by the five zang organs, with their essence serving as the material basis for huma-n mental activities. Both the spleen and kidney, as two of the five zang orga-ns, function to transform and store human essence. The spleen governs muscle tissues and dominates transportation and transformation. Spleen dysfunction in transportation leads to insufficient production of qi and blood, resulting in malnutrition of muscles and subsequent "muscle wilting". As stated in Su Wen·Bi Lun (Basic Questions·Treatise on Impediment): "Persistent muscle impediment with recurrent pathogenic invasion will affect the spleen," indicating that muscular disorders under external pathogenic influence may impair spleen function, thus demonstrating the bidirectional relationship between muscle activity and splenic physiology [24]. The kidney governs bone tissues and dominates essence storage. As the structural framework of the body, bones provide support and protection. Renal functional status directly determines bone integrity. The concept of "kidney governing bones" emphasizes that bone growth and development rely on kidney essence, with bone conditions reflecting the sufficiency of renal essence [25]. TCM theory holds that the kidney stores essence to generate marrow (including bone marrow and spinal marrow), which nourishes bones. Ling Shu·Jing Mai (Spiritual Pivot·Meridians) states: "Human life begins with the formation of essence," highlighting that renal essence originates from congenital essence inherited from parents. Similarly, bone marrow mesenchymal stem cells (BMSCs), derived from fertilized eggs as progenitor cells in bone marrow, differentiate into osteoblasts under specific conditions. Age-related decline in their differentiation capacity contributes to reduced bone mass and osteoporosis [26]. Both renal essence and BMSCs share developmental origins from parental reproductive essence, serving as fundamental materials for human growth and closely associating with bone marrow formation. The hypothesis of "marrow transformation preceding bone changes" proposes that bone diseases should be treated by addressing marrow first, as sufficient marrow ensures strong bones [27]. Renal essence deficiency leads to marrow depletion and bone malnutrition, manifesting clinically as osteoporosis with symptoms including lumbar/knee weakness, muscular atrophy, and walking disability—termed "bone atrophy" in TCM. In elderly populations, this increases bone fragility and fracture risk. Additionally, spleen and kidney dysfunction may synergistically contribute to bone disorders and osteoporosis pathogenesis [28]. According to the theory of "spleen and kidney - Ying Wei - collaterals", we should pay attention to regulating spleen and kidney function, regulating Ying Wei Qi, unblocking meridians and activating collaterals in the treatment of OS, so as to achieve the effect of treating both symptoms and signs [29]. As stated in Ling Shu·Ben Zang (Spiritual Pivot·Root Organs): "Observe external manifestations to understand internal organ pathologies," emphasizing that external abnormalities reflect visceral disorders, guiding identification of disease etiology. Collectively, spleen-kidney functional abnormalities disrupt the musculoskeletal system, ultimately leading to osteoporosis development.

4.3 The Theory of Five Elements (Wu Xing) in TCM

The theory of Five Elements (Wu Xing), a fundamental doctrine in TCM, elucidates the interdependent relationships among universal elements. As one of the regulatory mechanisms governing zang-fu organs, the generative and restrictive cycles of the Five Phases manifest through visceral interactions [30]. The spleen, recognized as the source of biochemical activities in life processes, shares functional homology with earth's capacity to nurture all living beings. This vital organ governs the cultivation and distribution of life-sustaining energies, thereby being categorized under the Earth phase in Five-Phase theory, symbolizing life's gestation and nourishment. Conversely, the kidney demonstrates water-like attributes through its essential functions of essence storage and qi regulation. Its characteristic of preserving fundamental substances aligns with water's subtle yet pervasive nourishing properties, warranting its classification under the Water phase, representing the conservation of vital essence and perpetual flow of life-sustaining fluids. Anatomically, "the spleen governs flesh while the kidney dominates bones", establishing flesh as Earth-element and bones as Water-element. According to Five-Phase generation principles (Earth - Metal - Water), Earth indirectly nourishes Water through Metal mediation, forming an endless generative cycle. This interconnection facilitates mutual nourishment between osseous and muscular systems. The spleen's transformative processing of nutritional essence not only sustains muscular tissue but also replenishes renal essence, achieving a harmonious state of "bone and flesh in mutual affinity". The restrictive cycle simultaneously maintains physiological balance: Earth controls Water, where excessive spleen-Earth energy may pathologically constrain kidney-Water (Earth over-restricting Water), while hyperactive kidney-Water might reversely overwhelm spleen-Earth (Water counter-restricting Earth). The spleen-kidney interdependence manifests through two physiological axes: The spleen-derived postnatal essence constitutes the primary source for kidney's acquired essence storage; Renal water regulation fundamentally relies on splenic fluid metabolism. Consequently, clinical strategies often employ spleen-tonifying methods to enhance renal essence production and utilize dampness-resolving therapies to alleviate water retention [31]. Pathological discordance between spleen-Earth and kidney-Water frequently manifests as osseous-muscular disharmony, clinically presenting as "disrupted bone-flesh affinity". This paradigm exemplifies the Five-Phase theory's clinical relevance in diagnosing and managing viscera-related disorders through elemental interaction analysis.

5. Syndrome Differentiation-Based Prevention and Treatment of OS in TCM

In TCM, OS is considered a comprehensive age-related geriatric disease characterized by the coexistence of "muscle atrophy" and "bone atrophy." The disease primarily affects the muscles and bones. According to TCM theory, the kidney serves as the "congenital foundation" of life, while the spleen represents the "acquired foundation." The spleen governs muscle function and nutrient metabolism, whereas the kidney governs bone development and marrow production. The relationship between muscles and bones fundamentally reflects the interplay between the spleen and kidney. Normal physiological functions of the spleen and kidney ensure harmonious interactions between bones and muscles. Furthermore, essence (Jing) and qi are foundational

substances for human life. Their production relies on the spleen's transformation of nutrients from food (acquired essence) and the kidney's storage of innate essence (congenital essence). Thus, the "deficiency due to depletion of essence and qi" is fundamentally attributed to spleen-kidney dual deficiency [32]. Consequently, the therapeutic strategy for OS should focus on regulating the spleen and kidney through integrated approaches of fortifying the spleen and tonifying the kidney.

Acupuncture, a distinctive external therapy in TCM, regulates meridians, balances yin-yang, promotes qi-blood circulation (via needling), and warms meridians to dispel cold and activate blood flow (via moxibustion). As OS falls under the category of "atrophy syndrome" in TCM, manifesting as "withered bones" and "sunken muscles," acupuncture has demonstrated clinical efficacy in treating atrophy-related disorders [33]. Experimental studies indicate that needling spleen- and kidney-tonifying acupoints (e.g., Shenshu (BL23) and Pishu (BL20)) can significantly increase muscle mass in rats [34]. Guided by the TCM principle of "treating atrophy by focusing on the Yangming Meridian," acupuncture protocols often select Yangming Meridian acupoints combined with Kidney Meridian acupoints. Electroacupuncture is applied to stimulate muscle contraction, enhance local blood circulation, and improve muscle strength. Improved muscle function further stabilizes bone structure and biomechanics. Moxibustion, with its warming properties, activates qi-blood circulation and addresses deficiency-cold patterns. Postmenopausal osteoporosis, characterized by kidney qi deficiency and impaired Governor Vessel (Du Mai) function, leads to yang deficiency, blood stasis, and pain. Governor Vessel moxibustion can invigorate yang qi, strengthen bones, increase bone mineral density, and alleviate pain [35]. Experimental studies reveal that spleen-kidney tonifying herbs regulate the SDF-1/CXCR4 signaling pathway to promote bone marrow mesenchymal stem cell (BMSC) myogenic differentiation, validating the TCM "spleen-kidney correlation theory" in OS prevention and treatment [36]. Numerous studies confirm that herbal monomers and formulas exert anti-OS effects by modulating the Wnt/β-catenin signaling pathway [37]. Herbal formulas holistically restore muscle-bone balance, ameliorating pathological states of the musculoskeletal system [38]. Astragalus membranaceus (Huangqi), through its multi-target mechanisms involving key bioactive components, demonstrates therapeutic potential against OS [39]. Panax ginseng (Renshen) contains saponins that enhance muscle growth (via Akt/mTOR pathway activation) and bone formation (via Wnt/β-catenin signaling), improving skeletal quality [40-41]. Angelica sinensis (Danggui) derivatives, such as isocoumarins, regulate myocyte and osteocyte differentiation through similar pathways [37], influencing musculoskeletal development [42-43]. Clinical trials show that Modified Bazhen Decoction combined with nutritional support improves muscle strength, mass, and quality of life in elderly sarcopenia patients [44]. Drynariae Rhizoma (Gusuibu) decoction activates Wnt/β-catenin signaling in ovariectomized rats, promotes osteogenesis, inhibits BMSC adipogenic differentiation, and enhances muscle strength [45-46]. Zhuanggu Formula, a herbal compound, modulates osteoblast, osteoclast, and myoblast differentiation while regulating lipid metabolism, demonstrating therapeutic efficacy against OS [47].

6. Summary and Prospect

OS, a degenerative disease prevalent in the elderly, has garnered increasing attention due to its substantial societal burden. However, current research on OS remains relatively limited, with its pathogenesis not yet fully elucidated. Particularly, there is a lack of drugs targeting common pathways of muscle and bone. Clinical management primarily focuses on symptom relief to alleviate suffering and improve quality of life. Modern medicine attributes OS pathogenesis to muscle-bone interactions, mainly through biomechanical regulation and endocrine-paracrine signaling mechanisms. TCM similarly emphasizes the intrinsic relationship between muscles and bones in OS development, attributing its essence to insufficient nourishment from the spleen and kidney – the "foundation of innate and acquired constitutions" – leading to symptoms such as lumbar and knee weakness, back pain, and fractures. Exploring the mechanistic role of spleen and kidney in OS pathogenesis through TCM theories including "Congenital and Acquired Foundations" "Visceral Manifestation Theory," and "Five-elements theory," it becomes evident that deficiency of these organs progressively impairs musculoskeletal function. The TCM concept of "disconnection between bone and muscle" aptly summarizes the pathological manifestations. The fundamental therapeutic principle of "fortifying the spleen and tonifying the kidney," implemented through syndrome differentiation and treatment, aims to restore organ function at its root. This approach facilitates bone-muscle synergy, tendon flexibility, and smooth qi-blood circulation, ultimately achieving dynamic balance in the musculoskeletal system. This paradigm embodies TCM's holistic view of the five zang organs and exemplifies the principle of "treating disease by addressing its root cause." Such theoretical framework may provide novel research directions for OS prevention and treatment, potentially enhancing our understanding of the disease while showcasing the unique advantages of TCM therapeutics.

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