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Editorial

Addressing musculoskeletal disorders through new treatment strategies

To date, billions of people have suffered from abnormal musculoskeletal conditions, making them a leading contributor to disability worldwide. A variety of treatment strategies for musculoskeletal disorders have been presented. Still, the clinical outcomes of some strategies are debatable, and the mechanisms for the disease progression and treatment remain to be fully elucidated. In this issue, we have included a number of publications on the latest advances in musculoskeletal disorders in clinical diagnosis, surgical and pharmacological treatments, bench-side explorations on stem cell and biomaterial-based therapies, as well as the mechanisms of those approaches.

Disease diagnosis and treatment is the major work of clinical practice. However, for some particular diseases such as anterior cruciate ligament (ACL) injury, the diagnosis and treatment approach are still unsettled. Therefore, the Chinese Association of Orthopaedic Surgeons (CAOS) and the Chinese Society of Sports Medicine (CSSM) collaboratively developed an expert consensus on diagnosing and treating this disease, aiming to enhance medical quality through refining professional standards [1]. The management of the meniscus is also a critical issue during the ACL reconstruction process. Currently, the recommendation is to perform meniscal repair instead of meniscectomy in certain cases of primary ACL reconstruction, but there is no strong evidence to support this. Hence, Szocs et al. compared the effectiveness of these two methods in addition to ACL reconstruction [2]. Besides the treatment strategy, infection is a critical factor that must be considered in surgery. Simon et al. assessed the prevalence, microbiological spectrum, risk factors, and clinical outcomes of unexpected-positive-intraoperative-cultures (UPIC) in unclear and presumed aseptic hip and knee revision arthroplasties, providing new information on revision rates for UPIC and potential risk factors for UPIC and its treatment failure [3].

Drugs play a central role in pharmacotherapy, and evaluation of the novel drug is essential for their long-term clinical applications. Wong et al. performed a systematic review and meta-analysis on treatment effects and safety of Romosozumab, a novel monoclonal antibody that binds to sclerostin for osteoporosis treatment [4]. Additionally, exploring new functions of the existing medicines or their ingredients is a practical strategy for drug development. Zhang et al. investigated the effect and mechanism of Phillygenin, an active ingredient from Forsythia, on ameliorating spinal cord injury-induced neuroinflammation [5]. Cheng et al. found that Memantine, an N-methyl--D-aspartate (NMDA) receptor antagonist that was approved by the FDA in 2013 for Alzheimer's Disease (AD) management, attenuated the development of osteoarthritis (OA) [6].

In the last few decades, new therapeutic methods such as biotherapy and tissue engineering have made significant progress. As a representative, stem cell therapy has been applied to clinical practice, and it is interesting to see how it goes with musculoskeletal disorders. Tabet analyzed the treatment effects of mesenchymal stromal cell (MSC) therapy for knee OA and chondral lesions [7]. Wu et al. reviewed the therapeutic potential of various types of MSC-derived extracellular vesicles in joint diseases including OA, tendon and ligament injuries, femoral head osteonecrosis, and rheumatoid arthritis [8]. Lv's group focused on exosomes derived from bone marrow mesenchymal stem cells (BMSCs) and found that the exosomes preconditioned by low-intensity pulsed ultrasound stimulation could promote bone-tendon interface fibrocartilage regeneration and ameliorate rotator cuff fatty infiltration [9]. Bone-tendon interface healing is critical for tissue integration, and Dong et al. addressed this challenge with biomimetic scaffolds [10]. Tan et al. prepared another 3D-printed scaffold composed of alginate, hydroxyapatite, and small intestine submucosa for diabetic bone defect treatment [11]. These studies demonstrate promising new strategies for musculoskeletal disorder treatment.

Mechanism studies are the basis of clinical applications, providing precise targets and proper strategies for the treatment. In recent years, scientists have noticed that the organ or tissue crosstalk contributes to disease development. Zou et al. reviewed the roles of the nervous and immune systems in OA progression, especially pain [12], while Gao et al. paid attention to the liver–bone axis in osteoporosis [13]. Mechanics could also lead to crosstalk between bone and adipose tissue, as it reported that mechanical loading on osteocytes regulates thermogenesis homeostasis of brown adipose tissue by influencing osteocyte-derived exosomes [14]. Piezo1 is one of the mechanosensors in cells, which plays an important role in bone homeostasis. Zhou et al. found that hyperbaric oxygen promotes bone regeneration by activating the Piezo1 pathway in osteogenic progenitors [15], and Huang et al. found that strontium zinc silicate bioceramic extract alleviates osteoporosis and sarcopenia via Piezo1 signaling [16]. Osteoporosis could also be regulated by epigenetic modification, as Tang et al. reported that METTL14-mediated HOXA5 N^6-methyladenosine (m^6A) modification alleviates osteoporosis via promoting WNK1 transcription and subsequent macrophage pyroptosis [17]. Endochondral ossification is one of the two ways by which bone is formed, and Wolfgart et al. found that this process occurs in OA cartilage based on their study on the biomarkers for hypertrophic chondrocyte differentiation [18]. These studies provide new insights and ideas for musculoskeletal diseases including OA, osteoporosis, and bone defects.

We anticipate that this issue will provide researchers and clinicians valuable insights into the challenges that musculoskeletal diseases pose, as well as novel strategies to investigate and treat these diseases.

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