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THE USE OF MESENCHYMAL STEM CELLS IN THE RESTORATION OF SOFT TISSUE STRUCTURES AFTER INJURIES: MUSCLES, TENDONS, LIGAMENTS

Abstract. Traumatic injuries of soft tissue structures, including muscles, tendons, and ligaments, represent a serious medical and social problem, as they are among the most common in both sports practice and everyday life. Their incidence is increasing due to the growing involvement of the population in physical activity, professional sports, and the high level of injuries resulting from accidents and occupational hazards. Restoration of the functional capacity of these structures is often prolonged and incomplete, which reduces patients' quality of life and limits their working capacity. Modern therapeutic approaches are frequently insufficiently effective, which stimulates the search for new treatment strategies. Mesenchymal stem cells (MSCs) have proven to be a promising tool in the regeneration of various tissues and organs, and their application in soft tissue repair has attracted significant interest. Objective. To summarize current data on the use of mesenchymal stem cells in the regeneration of muscles, tendons, and ligaments after trauma. Materials and methods. The article is based on data obtained through a systematic search in scientometric

databases including Google Scholar, Scopus, PubMed, and Web of Science. Publications from the last 10 years concerning the application of mesenchymal stem cells in regenerative medicine were analyzed. Methods of qualitative synthesis of clinical and experimental research findings were applied. Results. Literature analysis has shown that mesenchymal stem cells possess a strong potential to stimulate the regeneration of soft tissue structures. They contribute to the reduction of inflammatory responses, promote neoangiogenesis, and enhance reparative processes in muscles, tendons, and ligaments. Most studies report a positive effect of MSCs on functional recovery after trauma, manifested by shortened rehabilitation periods and improved tissue strength. Experimental models have demonstrated the ability of MSCs to integrate into damaged tissues and facilitate their reconstruction. In clinical practice, MSC application was associated with improved clinical and morphological treatment outcomes. An important aspect is the versatility of MSC sources, including bone marrow, adipose tissue, and umbilical cord blood. Several studies confirm the long-term positive effects of MSCs in soft tissue repair. At the same time, unresolved issues remain regarding optimal dosages, administration routes, and control of cell proliferation. A promising direction is the combined use of MSCs with biomaterials and growth factors. Overall, the review highlights significant progress in this field and confirms its high clinical relevance. Conclusions. Over the past decade, substantial progress has been achieved in understanding the role of mesenchymal stem cells in the regeneration of soft tissue structures after trauma. The available data indicate the promising potential of their application and open up new opportunities for the development of innovative regenerative technologies in medicine.
Keywords: mesenchymal stem cells, traumatology, muscles, tendons, ligaments, regeneration.

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ВИКОРИСТАННЯ МЕЗЕНХІМАЛЬНИХ СТОВБУРОВИХ КЛІТИН У ВІДНОВЛЕННІ М'ЯКОТКАНИННИХ СТРУКТУР ПІСЛЯ ТРАВМ: М'ЯЗИ, СУХОЖИЛКИ, ЗВ'ЯЗКИ

Анотація. Травматичні ушкодження м'якотканинних структур, зокрема м'язів, сухожилків і зв'язок, становлять серйозну медичну й соціальну проблему, оскільки вони є одними з найпоширеніших у спортивній практиці та побутових ситуаціях. Їх частота зростає у зв'язку з активним залученням населення до фізичної активності, професійним спортом і високим рівнем травматизму внаслідок аварій та виробничих ушкоджень. Відновлення функціональної спроможності цих структур часто є тривалим і неповним, що знижує якість життя пацієнтів та обмежує їхню працездатність. Сучасні методи терапії нерідко виявляються недостатньо ефективними, що стимулює пошук нових підходів до лікування. Мезенхімальні стовбурові клітини (МСК) зарекомендували себе як перспективний інструмент у відновленні різних тканин і органів, а їхнє застосування у регенерації м'якотканинних структур викликає значний інтерес. Мета статті – узагальнити сучасні дані щодо використання мезенхімальних стовбурових клітин у відновленні м'язів, сухожилків і зв'язок після травм. Матеріали і методи. У статті використано дані, отримані шляхом системного пошуку в наукометричних базах Google Scholar, Scopus, PubMed та Web of Science. Аналізувалися публікації за останні 10 років, що стосуються застосування мезенхімальних стовбурових клітин у відновній медицині. Використано методи якісного узагальнення результатів клінічних і експериментальних досліджень. Результати. Аналіз літератури показав, що мезенхімальні стовбурові клітини мають виражений потенціал до стимуляції регенерації м'якотканинних структур. Вони сприяють зменшенню запальної реакції, стимулюють неоангіогенез та посилюють репаративні процеси у м'язах, сухожилках і зв'язках. Більшість досліджень відзначають позитивний вплив МСК на функціональне відновлення після травм, що проявляється у скороченні термінів реабілітації та підвищенні міцності тканин. В експериментальних моделях продемонстровано здатність МСК інтегруватися у пошкоджені тканини та сприяти їхній реконструкції. У клінічних умовах застосування МСК супроводжувалося покращенням клінічних і морфологічних результатів лікування. Важливим аспектом є універсальність джерел МСК, зокрема кісткового мозку, жирової тканини та пуповинної крові. Окремі дослідження підтверджують довготривалий позитивний ефект після застосування МСК у відновленні м'яких тканин. Водночас залишаються невирішеними питання оптимальних дозувань, методів введення та контролю за проліферацією клітин.

Перспективним напрямом вважається комбіноване застосування МСК із біоматеріалами та факторами росту. Загалом, огляд демонструє значний прогрес у цій сфері та підтверджує високу клінічну значущість напрямку. Висновки. За останнє десятиліття досягнуто суттєвого прогресу у вивченні ролі мезенхімальних стовбурових клітин у регенерації м'якотканинних структур після травм. Отримані дані свідчать про перспективність їхнього використання та відкривають нові можливості для розробки інноваційних відновних технологій у медицині.
Ключові слова: мезенхімальні стовбурові клітини, травматологія, м'язи, сухожилки, зв'язки, регенерація.

Statement of the problem. Traumatic injuries of soft tissue structures, including muscles, tendons, and ligaments, represent one of the most pressing issues in modern medicine and sports science. They not only limit patients' physical activity but also have a significant socio-economic impact, as they lead to prolonged recovery, reduced work capacity, and complications in the rehabilitation process. According to recent reviews, muscle injuries account for up to 55% of all sports-related injuries, with the large muscle groups of the lower limbs being the most vulnerable due to their high load during sports activities and daily functioning [1].

Special attention should be given to sports injuries in young athletes, as this age group is critical for future physical development and professional careers. Epidemiological studies in the United States have shown that more than 8 million sports injuries are recorded annually among children and adolescents, with about 40% of them involving the musculoskeletal system. Most frequently, the lower limbs are affected, including injuries to muscles and tendons, which require particular focus from pediatric sports medicine [2].

Similar trends are observed among adult athletes. A systematic review covering multiple studies revealed that muscle and tendon injuries are the leading types of musculoskeletal damage in adult athletes. They account for up to 40% of total cases, with the most common being strains and partial tears of the muscles of the lower limbs. In addition, a high recurrence rate is observed, which significantly prolongs recovery time and limits athletic careers [3].

Data from Iran, based on an analysis of 2,700 cases over a five-year period, confirm the global relevance of the problem. The authors found that ligament and tendon injuries account for up to 22% of all joint-related trauma. Damage to the ligamentous apparatus of the knee and ankle joints was particularly common, leading to significant limitations in mobility and requiring surgical intervention in a substantial number of cases [4].

Anterior cruciate ligament (ACL) and meniscal injuries are among the most frequent in sports. In certain studies, it was established that among professional athletes, the incidence of ACL injuries reached 3.1 cases per 10,000 hours of play. From the beginning of active sports participation to the occurrence of such an injury, an average of 2 to 5 years usually passes. Moreover, more than 70% of affected individuals report persistent functional limitations even after treatment is completed [5].

An additional complicating factor is the presence of concomitant meniscal injuries. Research has shown that in young athletes undergoing revision ACL reconstruction, meniscal tears were identified in more than 45% of cases. This highlights the high risk of combined injuries, which considerably prolong treatment and rehabilitation periods [6].

Further analysis revealed that delayed ACL reconstruction significantly influences the frequency and type of meniscal damage. Patients who postponed surgical intervention demonstrated a higher incidence of complex and multi-zonal meniscal tears, which complicated recovery and reduced treatment effectiveness [7].

In some sports, the risk of lower limb injuries is especially high. For example, in handball, according to a systematic review, the prevalence of lower limb injuries reached 41.5%, with most cases involving ligament and tendon damage. Such injuries not only remove athletes from training but also substantially affect their future athletic performance [8].

In professional ice hockey, the prevalence of injuries is also high. Among Swiss professional players, injuries related to overuse and acute trauma were reported in 75% of athletes. The most vulnerable areas were the knee and shoulder joints, with a significant proportion of injuries affecting the ligamentous structures [9].

The analysis of injuries in artistic sports, particularly ballet, also deserves special attention. According to a systematic review, the prevalence of musculoskeletal injuries among ballet dancers reached 67%. More than 50% of these cases involved lower limb injuries, including ligament and tendon damage, reflecting the specific biomechanical demands and the high risk of recurrent trauma [10].

Thus, traumatic injuries of muscles, tendons, and ligaments are extremely widespread in both professional and amateur sports, as well as in the general population. Their high incidence, prolonged recovery periods, and risk of recurrence highlight the need for new and more effective methods of treatment and regeneration of soft tissue structures. In this context, the use of mesenchymal stem cells, which have already demonstrated efficacy in the repair of other tissues and organs, has attracted significant interest.

The purpose of the article is to summarize current experience and results of clinical and experimental work on the use of mesenchymal stem cells for the regeneration of soft tissue structures.

Research objects and methods. The search for literature sources was conducted in the search engines Google Scholar, Scopus, PubMed and Web of Science. The search was conducted using keywords according to the title of the article. The search was conducted to a depth of 10 years (the age of publication of the article more than 10 years was an exclusion criterion). PRISMA was used for organization and the PRISMA flow diagram for visualization of the process of selecting publications for review of literary sources in accordance with international standards for writing review articles [11].

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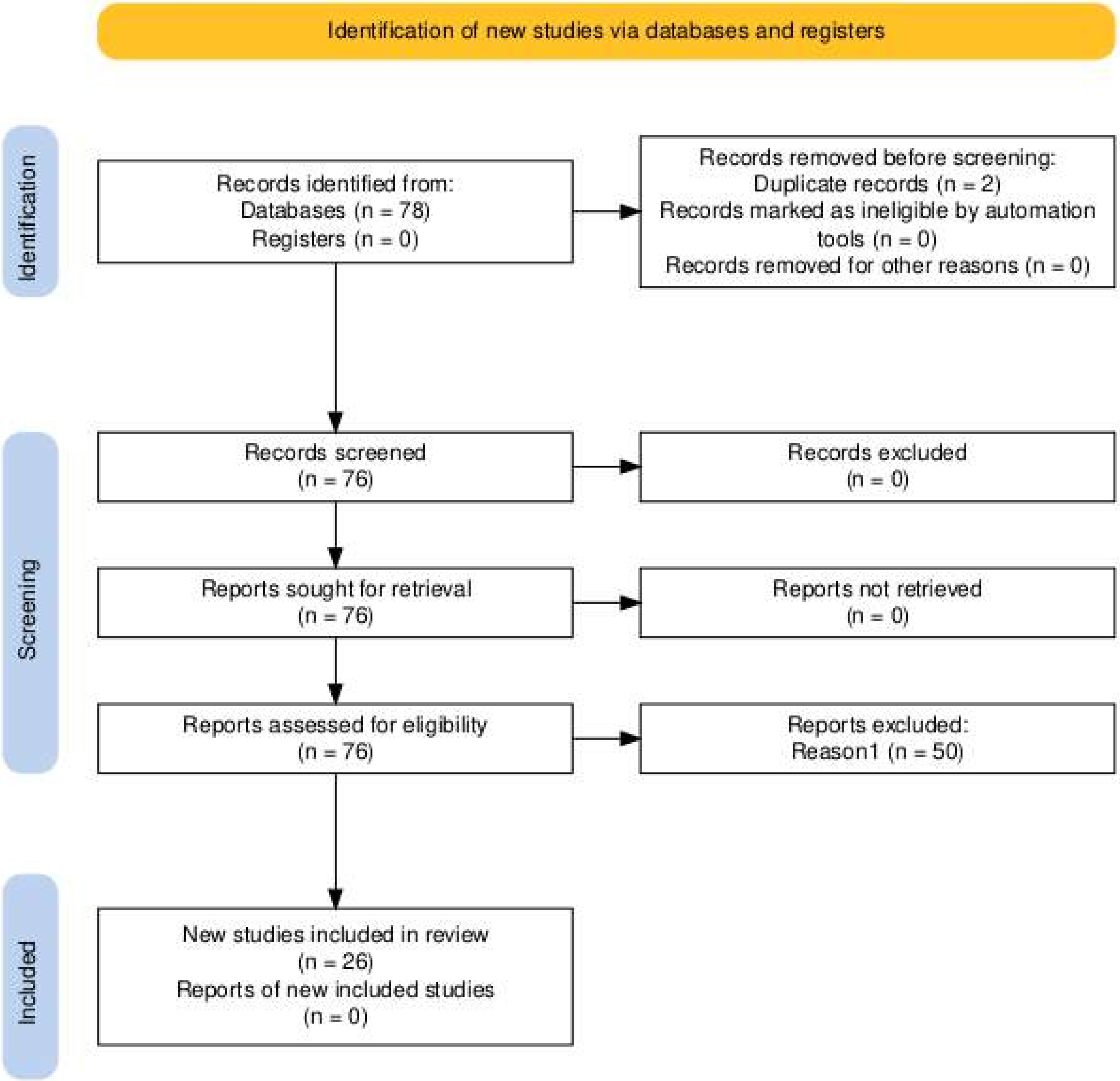

Fig. 1. The PRISMA flow diagram of literary sources search results.

Presentation of the main material.

Research results and their discussion. The use of MSCs in the treatment of tendon and ligament injuries has gained increasing attention from clinicians and researchers in recent years. Cell therapy has demonstrated its ability to accelerate tissue repair, reduce pain severity, and improve functional outcomes. Clinical evidence confirms that MSC administration into the injured area in patients with chronic tendinopathies resulted in significant clinical improvement within the first 6-12 months. This approach allows for a considerable reduction in rehabilitation time compared to traditional conservative or surgical methods [12].

In ligament repair, MSCs have shown potential both as a standalone therapy and in combination with reconstructive procedures. Studies have indicated that cell therapy enhances the mechanical strength of the repaired ligament, improves the organization of collagen fibers, and reduces the risk of excessive scar tissue formation [13].

Biomechanical evaluations have confirmed that MSC application promotes higher-quality tissue regeneration, bringing it closer to physiological parameters.

Particular importance is attributed to MSC therapy in cases of anterior cruciate ligament (ACL) reconstruction. It has been demonstrated that MSCs significantly contribute to the formation of the enthesis – the critical tendon- or graft-to-bone attachment zone. This area is often the weakest link in the recovery process after surgery. Stem cell treatment ensures a more mature fibrocartilaginous transition at the interface, resulting in improved biomechanical strength of the reconstructed graft [14,15]. Such an effect is especially important for athletes who require high reliability and functional stability of the knee joint.

Systematic reviews confirm the efficacy of stem cell therapy in the process of "ligamentization" of tendon grafts following ACL reconstruction. It has been found that recovery in MSC-treated groups occurred faster and tissue integration was of higher quality compared to controls. These differences reached statistical significance ($p<0.05$), confirming the genuine therapeutic effect of the cellular approach [16].

The treatment of chronic tendinopathies with MSCs has shown a marked reduction in pain intensity (by 50–70% from baseline) and improved patient functionality during the first year post-therapy. Similar outcomes have been consistently reported, supporting the consideration of cell therapy as a promising alternative when conventional approaches fail to achieve sufficient efficacy [17].

Beyond direct stem cell use, increasing interest is directed toward cell-derived products, particularly exosomes. Evidence indicates that exosomes derived from tendon cells are capable of regulating the balance between synthesis and degradation of the extracellular matrix. This opens a new direction for the development of cell-free therapies that reduce immunological risks while retaining strong regenerative activity [18].

Further studies confirm that MSCs accelerate the formation of mature fibrocartilaginous tissue at tendon-to-bone junctions. This approach enhances osteointegration and reduces the likelihood of reinjury. Such effects are highly relevant for professional athletes, in whom even minor structural defects in ligaments or tendons can have serious functional consequences [19].

A promising strategy involves stimulating endogenous stem and progenitor cells within tendon and ligament tissues. Under appropriate activation, these cells can generate new, fully functional fibers. This approach could serve as an alternative to exogenous cell transplantation and may help avoid additional invasive interventions [20].

Equally significant are the results of cell therapy in skeletal muscle injuries. MSC administration has been shown to accelerate muscle regeneration, reduce fibrosis, and improve contractile strength. In experimental models, restored muscle mass reached 80-90% of baseline values, indicating the strong regenerative potential of stem cells [21].

An important area of development is the integration of MSCs with tissue engineering technologies. Studies have demonstrated that combining cells with biocompatible scaffolds enables the reconstruction of three-dimensional muscle fiber structures that mimic the natural architecture of muscle tissue. This creates opportunities for the use of bioengineered constructs in cases of large muscle defects, where conventional methods are insufficient [22,23].

Further approaches explore combining cell therapy with bioactive materials, growth factors, and hydrogels. Such integrated strategies promote angiogenesis, ensure even distribution of cells at the injury site, and enhance the quality of regenerated tissue [23].

Recent reviews emphasize that cellular technologies in muscle repair shorten regeneration time, improve the strength of newly formed structures, and reduce the risk of recurrence. Promising avenues also include strategies aimed at activating and supporting the functions of native muscle stem cells. Coordinated interaction between these cells and other cellular populations creates an optimal microenvironment for muscle tissue regeneration [24-26].

Thus, accumulated evidence confirms the high efficacy of MSC therapy in the regeneration of soft tissue structures after injury. It ensures both structural and functional restoration, reduces pain, accelerates rehabilitation, and improves the resilience of repaired tissues to subsequent trauma. The future development of this field will depend on refining delivery methods, combining cell therapy with biomaterials and growth factors, and optimizing strategies for activating endogenous cellular resources. Collectively, these approaches reshape the vision of regenerative medicine and provide a foundation for integrating innovative technologies into clinical practice.

Conclusions. Mesenchymal stem cells demonstrate significant potential in the restoration of soft tissue structures, in particular muscles, tendons and ligaments after traumatic injuries. Their use helps reduce inflammation, stimulates regenerative processes and improves functional treatment results. Despite significant progress in research, the questions of optimal methods of administration, dosage and control of the safety of cell use remain open. Further research should be aimed at improving therapeutic strategies and implementing them in broad clinical practice.

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