Журнал «Перспективи та інновації науки»
(Серія «Педагогіка», Серія «Психологія», Серія «Медицина»)
№ 10(56) 2025

UDC[616.718.05:577.15]-092.9:615.467

https://doi.org/10.52058/2786-4952-2025-10(56)-2164-2172

Fishchenko Volodymyr Oleksandrovych Doctor of Medical Sciences, Professor, Head of the Department of Traumatology and Orthopedics National Pirogov Memorial Medical University, Pirohova, https://orcid.org/0000-0002-4742-9416

Botsul Oleksandr Viktorovych PhD, Assistant of the Department of Traumatology and Orthopedics National Pirogov Memorial Medical University, Vinnytsia, https://orcid.org/0000-0003-0177-2064

Riaboshapko Oleg Mykolayovych PhD, Assistant of the Department of Traumatology and Orthopedics National Pirogov Memorial Medical University, Vinnytsia, https://orcid.org/0000-0002-2071-0371

Makogonchuk Andrii Viktorovych PhD, Associate professor of the Department of Traumatology and Orthopedics National Pirogov Memorial Medical University, Vinnytsya; Vinnytsia, https://orcid.org/0000-0002-5031-5217

Matsipura Maksym Mykolayovych PhD Assistant of the Department of Traumatology and Orthopedics National Pirogov Memorial Medical University, Vinnytsya; Vinnytsia, https://orcid.org/0000-0002-5631-8056

Kyrychenko Vasyl Ivanovych PhD, Associate professor of the Department of Traumatology and Orthopedics National Pirogov Memorial Medical University, Vinnytsya; Vinnytsia, https://orcid.org/0000-0001-5171-4298

Rybinskyi Maksym Volodymyrovych PhD, Associate professor of the Department of Traumatology and Orthopedics National Pirogov Memorial Medical University, Vinnytsya, https://orcid.org/0009-0002-1617-8332

POSSIBILITIES OF USING STEM CELLS FOR THE TREATMENT OF OSTEOCHONDRITIS FRACTURES

Abstract. Transchondral fractures continue to be a challenging orthopedic condition due to impaired blood supply to the subchondral area, leading to detachment of the cartilage-bone fragment. This disease predominantly affects the knee and supracalcaneal joints, has a long course and seriously affects the quality of life of patients in many aspects, affects young, physically active people. The high rate of relapses after conventional surgical treatment prompts the investigation of regenerative treatments, among which cell therapy is a promising approach. The aim of the study is

to review the data of studies in which stem cells are used to treat transchondral fractures. Materials and methods. A search of scientific sources indexed in the databases Scopus, PubMed and Google Scholar was conducted using the advanced search tool using the terms “stem cells” AND “osteochondral lesion” OR “osteochondritis dissecans” AND “cell therapy”. This study demonstrated that the use of MSCs stimulates the activation of bone and cartilage tissue regeneration, as they have the potential to differentiate into osteocytes and chondrocytes. MSC transplantation has a positive effect on fracture healing even in the case of nonunion or chronic inflammation, which allows avoiding invasive surgery in patients with concomitant disease. MSCs have angiogenic, immunomodulatory and antifibrotic effects, which can improve the quality of bone union. Systemic infusion of MSCs enhances mineralization and reduces fibrosis at the fracture site. In osteochondritis dissecans, successful repair of damaged articular surfaces has been described after autologous transplantation of MSCs derived from adipose tissue. Improved limb function (Lisholm score ≥20) has been found after cell therapy in young people. The authors of works in this field emphasize the pathogenetic significance of MSCs in specific injuries of the ankle joint, for which natural recovery is insufficient. The successful treatment of osteochondral lesions of the talus with synovial MSCs with functional recovery after 6 months has also been described. It has been recognized that the location of the cells (bone marrow, adipose tissue or synovium from which they were obtained) affects their osteogenic and chondrogenic potential, which should be taken into account when choosing a graft. Conclusions. Stem cell therapy is a new and well-known procedure for the treatment of transchondral fractures, which demonstrates remodeling of cartilage and bone with minimal invasive destruction. Multicenter studies are needed to standardize the approaches and ensure the availability of these technologies in routine clinical practice.

Keywords: trauma, stem cells, transchondral fractures, cartilage regeneration, cell therapy, tissue engineering, osteochondral defects, joint surface repair.

Фіщенко Володимир Олександрович доктор медичних наук, професор, завідувач кафедри травматології та ортопедії Вінницького національного медичного університету ім. М. І. Пирогова; м. Вінниця, https://orcid.org/0000-0002-4742-9416

Боцул Олександр Вікторович Phd, асистент кафедри травматології та ортопедії Вінницького національного медичного університету ім. М. І. Пирогова; м. Вінниця, https://orcid.org/0000-0003-0177-2064

Рябошапко Олег Миколайович Phd, асистент кафедри травматології та ортопедії Вінницького національного медичного університету ім. М. І. Пирогова; вул. Пирогова 56, м. Вінниця, https://orcid.org/0000-0002-2071-0371

Журнал «Перспективи та інновації науки»
(Серія «Педагогіка», Серія «Психологія», Серія «Медицина»)
№ 10(56) 2025

Макогончук Андрій Вікторович кандидат медичних наук, доцент, доцент кафедри травматології та ортопедії Вінницького національного медичного університету ім. М. І. Пирогова; м. Вінниця, https://orcid.org/0000-0002-5031-5217

Маціпура Максим Миколайович Phd асистент кафедри травматології та ортопедії Вінницького національного медичного університету ім. М. І. Пирогова; м. Вінниця, https://orcid.org/0000-0002-5631-8056

Кириченко Василь Іванович кандидат медичних наук, доцент, доцент кафедри травматології та ортопедії Вінницького національного медичного університету ім. М. І. Пирогова; м. Вінниця, https://orcid.org/0000-0001-5171-4298

Рибінський Максим Володимирович кандидат медичних наук, доцент, доцент кафедри травматології та ортопедії Вінницького національного медичного університету ім. М. І. Пирогова; м. Вінниця, https://orcid.org/0009-0002-1617-8332

МОЖЛИВОСТІ ЗАСТОСУВАННЯ СТОВБУРОВИХ КЛІТИН ДЛЯ ЛІКУВАННЯ ТРАНСХОНДРАЛЬНИХ ПЕРЕЛОМІВ

Анотація. Трансхондральні переломи продовжують бути складним ортопедичним станом через порушення кровопостачання в субхондральній ділянці, що призводить до відшарування хрящово-кісткового фрагмента. Це захворювання переважно вражає колінний та надп'ятковий суглоб, має тривалий перебіг і серйозно впливає на якість життя пацієнтів у багатьох аспектах, вражає молодь, фізично активних людей. Високий рівень рецидивів після звичайного хірургічного лікування спонукає до дослідження регенеративних методів лікування, серед яких перспективним підходом є клітинна терапія. Метою дослідження є огляд даних досліджень, у яких стовбурові клітини використовуються для лікування трансхондральних переломів. Матеріали та методи. Пошук наукових джерел, індексованих у базах даних Scopus, PubMed та Google Scholar, було проведено за допомогою інструменту розширеного пошуку з використанням термінів «стовбурові клітини» ТА «остеохондральне ураження» АБО «розсікаючий остеохондрит» ТА «клітинна терапія». Дане дослідження продемонструвало, що використання МСК стимулює активацію регенерації кісткової та хрящової тканин, оскільки вони мають потенціал для диференціації в остеоцити та хондроцити. Трансплантація МСК позитивно впливає на загоєння переломів навіть у разі незрощення або хронічного запалення, що дозволяє уникнути інвазивної хірургії у пацієнтів із супутнім захворюванням. МСК мають ангіогенний, імуномодулюючий та антифібротичний ефект, що може покращити якість зрощення кісток. Системна інфузія МСК посилює мінералізацію та зменшує фіброз у місці перелому. При розшарованому остеохондриті описано

Журнал «Перспективи та інновації науки»
(Серія «Педагогіка», Серія «Психологія», Серія «Медицина»)
№ 10(56) 2025

успіх відновлення пошкоджених суглобових поверхонь після аутологічної трансплантації МСК, отриманих з жирової тканини. Виявлено покращення функції кінцівок (оцінка Лісгольма ≥20) після клітинної терапії у молодих людей. Автори робіт у даній галузі наголошують на патогенетичному значенні МСК при специфічних травмах гомілковостопного суглоба, для яких природне відновлення є недостатнім. Також описане успішне лікування остеохондральних уражень таранної кістки за допомогою синовіальних МСК з функціональним відновленням через 6 місяців. Було визнано, що місце розташування клітин (кістковий мозок, жирова тканина або синовіальна оболонка, з якої вони були отримані) впливає на їхній остеогенний та хондрогенний потенціал, що слід враховувати при виборі трансплантата. Висновки. Терапія стовбуровими клітинами – це нова та відома процедура лікування трансхондральних переломів, яка демонструє ремоделювання хряща та кістки з мінімальним інвазивним руйнуванням. Для стандартизації підходів та забезпечення доступності цих технологій у звичайній клінічній практиці необхідні багатоцентрові дослідження.

Ключові слова: травма, стовбурові клітини, трансхондральні переломи, регенерація хряща, клітинна терапія, тканинна інженерія, остеохондральні дефекти, відновлення суглобових поверхонь.

Statement of the problem. Osteochondral lesion, osteochondritis dissecans or transchondral fracture is a condition in which the subchondral zone nutrition is disturbed and cartilage piece with its underlying bone are separated. The complication occurs, primarily in the knee joint and less commonly in this ankle or elbow joints of high loads and features of blood supply to epiphyses in the growth zone have [1]. Lesions can also be stable or unstable, the latter of which may involve the development of a loose body within joints that adds to clinical complexity and defines the indications for invasive intervention [2]. Ischemic processes in the subchondral region and microtrauma are implicated in the pathogenesis of this pathology, indicating that several factors contribute to the onset of disease [1].

Based on the findings of imaging techniques, transchondral fractures include chondral, osteochondral, subchondral fractures and osteochdritis dissecans. They are challenging to distinguish without MRI, thus underscoring the significance of an early diagnosis [3]. Fractures of the talus are notoriously difficult to identify and usually remain undiagnosed until chronic pain in the ankle, or limitation of movement is manifested [4]. Medial talar dome fractures are one of the most common types of TDI, necessitating personalized treatment [4].

The frequency of transchondral fractures, especially talar fractures, is highly population-dependent. In an investigation of US military personnel, it was observed with an incident rate of 27 per 100,000 person years; therefore it is clinically relevant in high-intensity exercise environments [5]. Another study demonstrated that a history of previously undiagnosed transchondral fractures was present in as many as 50% of individuals with chronic ankle pain [6]. Among the changing risk factors, their

prevalence increases significantly depending on age, location of lesion and the level of physical activity, especially in youth and athletes [2].

The most common is the Berndt and Harty classification describing four stages of transchondral talar fracture, progressing from cartilage compression to complete dislocation of the fragment with a free body in the joint [7]. The implications of this distinction are important for treatment selection, conservative observation, microfracture, mosaic plastic repair, or stem cell ensilage. Most investigators acknowledge the value of early imaging and risk stratification through MRI and CT images to avoid evolution of the disease.

Apart from the anatomical and functional results, transchondral lesions have significant impact on the patients' QoL. As revealed in the researches of D'Ambrosi et al., larger defects and lesions on medial talus were related to greater scores of pain and lowered levels of physical activity on the SF-36 and AOFAS scales [8]. Mann and Nery present comparable information, in which by passing small volume lesions physical activity limitation can be observed even while playing sports and vigorous household activities [9]. Transchondral fractures are therefore not just an orthopedic issue, but a social one as well; modern reconstructive procedures to achieve optimal structural and functional results in optimizing the quality of life can only be realized through regenerative strategies.

The purpose of the article – to conduct a literature review on the topic of treatment of osteochondritis fractures using stem cells.

Research objects and methods. To achieve the goal of the study, a review of modern literature on the topic of stem cell use in the treatment of osteochondral defects was conducted. For this purpose, a search was conducted for relevant publications related to the topic of the article within the scientific databases Scopus, Google Scholar, and PubMed.

Presentation of the main material.

Research results and their discussion. At present, the use of stem cells in fractures healing process and especially fractyres with transchondral localization is one of most promising regenerative medicine options. The efficacy of the approach is dependent upon the potential of mesenchymal stem cells (MSCs) to differentiate into different cell types like chondrocytes, osteocytes, and other cell types for bone and cartilage tissue regeneration. As reported by Fayaz et al., MSC implantation may favor recovery even in case of delayed consolidation or non-union of fractures, especially in an unvascularized or chronically inflamed environment [10]. Tseng et al. also point out that, in these cases, the application of stem cells avoids conventional invasive procedures which is an advantage especially for patients with comorbidities [11].

According to Wang and coauthors in their reviewMSCs are the ones with the greatest potential for repairing bone tissue because of their high proliferative capacity and for releasing mediators that promote endogenous healing [12]. They exert some of their actions through induction of angiogenesis, immune response modulation and tissue regeneration. Granero-Moltó et al. [13] provided evidence that systemic

Журнал «Перспективи та інновації науки»
(Серія «Педагогіка», Серія «Психологія», Серія «Медицина»)
№ 10(56) 2025

administration of MSCs improves the quality of fracture healing, reduces fibrosis and increases bone mineralization.

Special mention should be given to stem cells in the therapy of osteochondritis dissecans, which is actually a transchondral fracture. Freitag et al reported successful knee joint healing of a large osteochondral defect following failed surgery, although in this case autologous adipose MSCs were used [14]. The same result was reported by Park and Oh, including a fully rehabilitated teenage athlete after MSC treatment on recurrent osteochondritis [15]. Positive time-related dynamics was demonstrated following local injection of autologous MSC in the defect area of the patellar joint in a juvenile osteochondritis patient by Russo et al [16].

Clinical studies prove that, even in chronic joint damage stem cells can cause functional status and pain reduction. In particular, Teo et al. showed that Lysholm score increase ≥20 compared with the baseline among adolescent and young adults with patellar osteochondritis treated with cell therapy [17]. Tribe et al. regarding the use of MSCs as a pathogenetically justified strategy against ankle joint injuries such as transchondral fractures, in view of its extremely low self-regenerative potential [18].

And we also need to think about the origin of cell source. Angthong and Kunkanjanawan published a method for obtaining MSCs from the synovial membrane of ankle joints, which led to restoration of cartilage defects in osteochondral lesions of the talus - patients had lower pain level and improved functional status after 6 months [19]. El-Jawhari et al. has shown that osteogenic differentiation is less extensive in monolayers of bone marrow, adipose tissue, and synovium multipotent mesenchymal cells than chondrogenic differentiation, a factor to be considered when selecting a source of transplant [20].

Therefore, promising and even clinically appealing application of stem cell therapy for transchondral fractures, especially Osteochondritis dissecans. Regenerative properties of MSC in combination with advanced surgical techniques open new perspectives for management of complicated lesions on the articular surfaces. But multicenter randomized studies are warranted to adopt such approaches in broader clinical practice.

Conclusions. Currently, stem cell use in the management of fractures, particularly transchondral is considered one of the most promising directions for regenerative medicine. Mesenchymal stem cells (MSCs) have gained the greatest interest, because of their potential to differentiate into chondrocytes and osteocytes, in addition to promoting regeneration, angiogenesis and immune modulation. The efficacy of MSC treatment in osteochondritis dissecans has also been confirmed in single clinical cases and sets of studies conducted on young patients and athletes. The selection of the source of cells, defect type and transplantation pattern still remain the determining factors for success, although it is encouraging. Additional multicentered studies are needed in order to standardize methods and apply them to more common clinical practices.

References

1. Andriolo, L., Crawford, D. C., Reale, D., Zaffagnini, S., Candrian, C., Cavicchioli, A., & Filardo, G. (2020). Osteochondritis dissecans of the knee: etiology and pathogenetic mechanisms. A systematic review. *Cartilage*, *11*(3), 273-290.

2. Konarski, W., Poboży, T., Konarska, K., Derczyński, M., & Kotela, I. (2024). Understanding osteochondritis dissecans: a narrative review of the disease commonly affecting children and adolescents. *Children*, *11*(4), 498.

3. Bohndorf, K. (1996). Injuries at the articulating surfaces of bone (chondral, osteochondral, subchondral fractures and osteochondrosis dissecans). *European journal of radiology*, *22*(1), 22-29.

4. Flick, A. B., & Gould, N. (1985). Osteochondritis dissecans of the talus (transchondral fractures of the talus): review of the literature and new surgical approach for medial dome lesions. *Foot & ankle*, *5*(4), 165-185.

5. Orr, J. D., Dawson, L. K., Garcia, E. S. J., & Kirk, K. L. (2011). Incidence of osteochondral lesions of the talus in the United States military. *Foot & Ankle International*, *32*(10), 948-954.

6. Mandracchia, V. J., Buddecke, D. E., & Giesking, J. L. (1999). Osteochondral lesions of the talar dome: a comprehensive review with retrospective study. *Clinics in podiatric medicine and surgery*, *16*(4), 725-742.

7. Berndt, A. L., & Harty, M. (2004). Transchondral fractures (osteochondritis dissecans) of the talus. *JBJS*, *86*(6), 1336.

8. D'Ambrosi, R., Maccario, C., Serra, N., Ursino, C., & Usuelli, F. G. (2018). Relationship between symptomatic osteochondral lesions of the talus and quality of life, body mass index, age, size and anatomic location. *Foot and Ankle Surgery*, *24*(4), 365-372.

9. Mann, T. S., & Nery, C. (2024). Osteochondral lesion of the talus: quality of life, lesion site, and lesion size. *Foot and Ankle Clinics*, *29*(2), 213-224.

10. Fayaz, H. C., Giannoudis, P. V., Vrahas, M. S., Smith, R. M., Moran, C., Pape, H. C., ... & Jupiter, J. B. (2011). The role of stem cells in fracture healing and nonunion. *International orthopaedics*, *35*(11), 1587-1597.

11. Tseng, S. S., Lee, M. A., & Reddi, A. H. (2008). Nonunions and the potential of stem cells in fracture-healing. *JBJS*, *90*(Supplement_1), 92-98.

12. Wang, X., Wang, Y., Gou, W., Lu, Q., Peng, J., & Lu, S. (2013). Role of mesenchymal stem cells in bone regeneration and fracture repair: a review. *International orthopaedics*, *37*(12), 2491-2498.

13. Granero-Moltó, F., Weis, J. A., Miga, M. I., Landis, B., Myers, T. J., O'Rear, L., ... & Spagnoli, A. (2009). Regenerative effects of transplanted mesenchymal stem cells in fracture healing. *Stem cells*, *27*(8), 1887-1898.

14. Freitag, J., Shah, K., Wickham, J., Boyd, R., & Tenen, A. (2017). The effect of autologous adipose derived mesenchymal stem cell therapy in the treatment of a large osteochondral defect of the knee following unsuccessful surgical intervention of osteochondritis dissecans–a case study. *BMC musculoskeletal disorders*, *18*(1), 298.

15. Park, H. S., & Oh, J. K. (2025). Successful Rehabilitation Following Stem Cell Therapy for Large Knee Osteochondritis Dissecans in an Adolescent Wrestler. *Journal of Sport Rehabilitation*, *1*(aop), 1-6.

16. Russo, A., Coco, V., & Zaffagnini, S. (2020). The effect of autologous adipose derived mesenchymal stem cell therapy on juvenile osteochondritis dissecans of the patella: a case study. *Journal of Surgical Case Reports*, *2020*(8), rjaa274.

17. Teo, B. J., Buhary, K., Tai, B. C., & Hui, J. H. (2013). Cell-based therapy improves function in adolescents and young adults with patellar osteochondritis dissecans. *Clinical Orthopaedics and Related Research®*, *471*(4), 1152-1158.

18. Tribe, H. C., McEwan, J., Taylor, H., Oreffo, R. O., & Tare, R. S. (2017). Mesenchymal stem cells: potential role in the treatment of osteochondral lesions of the ankle. *Biotechnology journal*, *12*(12), 1700070.

19. Angthong, C., & Kunkanjanawan, H. (2020). Ankle synovium-derived mesenchymal stem cells for the treatment of osteochondral lesion of the talus: a novel cell harvesting technique and clinical applications. *Eur Rev Med Pharmacol Sci*, *24*(16), 8273-80.

20. El-Jawhari, J. J., Brockett, C. L., Ktistakis, I., Jones, E., & Giannoudis, P. V. (2018). The regenerative therapies of the ankle degeneration: a focus on multipotential mesenchymal stromal cells. *Regenerative Medicine*, *13*(2), 175-188.

Література

1. Andriolo, L., Crawford, D. C., Reale, D., Zaffagnini, S., Candrian, C., Cavicchioli, A., & Filardo, G. (2020). Osteochondritis dissecans of the knee: etiology and pathogenetic mechanisms. A systematic review. *Cartilage*, *11*(3), 273-290.

2. Konarski, W., Poboży, T., Konarska, K., Derczyński, M., & Kotela, I. (2024). Understanding osteochondritis dissecans: a narrative review of the disease commonly affecting children and adolescents. *Children*, *11*(4), 498.

3. Bohndorf, K. (1996). Injuries at the articulating surfaces of bone (chondral, osteochondral, subchondral fractures and osteochondrosis dissecans). *European journal of radiology*, *22*(1), 22-29.

4. Flick, A. B., & Gould, N. (1985). Osteochondritis dissecans of the talus (transchondral fractures of the talus): review of the literature and new surgical approach for medial dome lesions. *Foot & ankle*, *5*(4), 165-185.

5. Orr, J. D., Dawson, L. K., Garcia, E. S. J., & Kirk, K. L. (2011). Incidence of osteochondral lesions of the talus in the United States military. *Foot & Ankle International*, *32*(10), 948-954.

6. Mandracchia, V. J., Buddecke, D. E., & Giesking, J. L. (1999). Osteochondral lesions of the talar dome: a comprehensive review with retrospective study. *Clinics in podiatric medicine and surgery*, *16*(4), 725-742.

7. Berndt, A. L., & Harty, M. (2004). Transchondral fractures (osteochondritis dissecans) of the talus. *JBJS*, *86*(6), 1336.

8. D'Ambrosi, R., Maccario, C., Serra, N., Ursino, C., & Usuelli, F. G. (2018). Relationship between symptomatic osteochondral lesions of the talus and quality of life, body mass index, age, size and anatomic location. *Foot and Ankle Surgery*, *24*(4), 365-372.

9. Mann, T. S., & Nery, C. (2024). Osteochondral lesion of the talus: quality of life, lesion site, and lesion size. *Foot and Ankle Clinics*, *29*(2), 213-224.

10. Fayaz, H. C., Giannoudis, P. V., Vrahas, M. S., Smith, R. M., Moran, C., Pape, H. C., ... & Jupiter, J. B. (2011). The role of stem cells in fracture healing and nonunion. *International orthopaedics*, *35*(11), 1587-1597.

11. Tseng, S. S., Lee, M. A., & Reddi, A. H. (2008). Nonunions and the potential of stem cells in fracture-healing. *JBJS*, *90*(Supplement_1), 92-98.

12. Wang, X., Wang, Y., Gou, W., Lu, Q., Peng, J., & Lu, S. (2013). Role of mesenchymal stem cells in bone regeneration and fracture repair: a review. *International orthopaedics*, *37*(12), 2491-2498.

13. Granero-Moltó, F., Weis, J. A., Miga, M. I., Landis, B., Myers, T. J., O'Rear, L., ... & Spagnoli, A. (2009). Regenerative effects of transplanted mesenchymal stem cells in fracture healing. *Stem cells*, *27*(8), 1887-1898.

14. Freitag, J., Shah, K., Wickham, J., Boyd, R., & Tenen, A. (2017). The effect of autologous adipose derived mesenchymal stem cell therapy in the treatment of a large osteochondral defect of the knee following unsuccessful surgical intervention of osteochondritis dissecans–a case study. *BMC musculoskeletal disorders*, *18*(1), 298.

15. Park, H. S., & Oh, J. K. (2025). Successful Rehabilitation Following Stem Cell Therapy for Large Knee Osteochondritis Dissecans in an Adolescent Wrestler. *Journal of Sport Rehabilitation*, *1*(aop), 1-6.

16. Russo, A., Coco, V., & Zaffagnini, S. (2020). The effect of autologous adipose derived mesenchymal stem cell therapy on juvenile osteochondritis dissecans of the patella: a case study. *Journal of Surgical Case Reports*, *2020*(8), rjaa274.

17. Teo, B. J., Buhary, K., Tai, B. C., & Hui, J. H. (2013). Cell-based therapy improves function in adolescents and young adults with patellar osteochondritis dissecans. *Clinical Orthopaedics and Related Research®*, *471*(4), 1152-1158.

18. Tribe, H. C., McEwan, J., Taylor, H., Oreffo, R. O., & Tare, R. S. (2017). Mesenchymal stem cells: potential role in the treatment of osteochondral lesions of the ankle. *Biotechnology journal*, *12*(12), 1700070.

19. Angthong, C., & Kunkanjanawan, H. (2020). Ankle synovium-derived mesenchymal stem cells for the treatment of osteochondral lesion of the talus: a novel cell harvesting technique and clinical applications. *Eur Rev Med Pharmacol Sci*, *24*(16), 8273-80.

20. El-Jawhari, J. J., Brockett, C. L., Ktistakis, I., Jones, E., & Giannoudis, P. V. (2018). The regenerative therapies of the ankle degeneration: a focus on multipotential mesenchymal stromal cells. *Regenerative Medicine*, *13*(2), 175-188.