ISAKOS CONGRESS 2023

Boston
Massachusetts
June 18–June 21

# Advanced therapy with mesenchymal stromal cell for knee osteoarthritis or chondral lesions systematic review.

Caio Tabet MD
Rafael Pacheco MD, PhD
Ana Martimbianco PhD
Daniela Bueno DDS, PhD
Rachel Riera MD, PhD
Arnaldo J. Hernandez MD, PhD
Tiago Fernandes MD, PhD

ISAKOS CONGRESS 2023

Boston
Massachusetts
June 18–June 21


- Sports Medicine Division, Institute of Orthopaedics and Traumatology, University of São Paulo. São Paulo, Brazil.
- Hospital Sírio-Libanês. São Paulo, Brazil.


- The authors declare no conflict of interest.

# Introduction

- Chondral lesion and osteoarthritis are associated with great morbidity and economic burden. Mesenchymal stromal cells (MSCs) has been gaining ground due to their intrinsic role in the repair and regeneration of joint tissues.

# Objective

- To assess the efficacy and safety of MSC therapy for treating knee osteoarthritis or chondral lesions.

# Methods

- A prospectively registered  systematic review and metanalysis of randomized controlled trials (RCTs) following Cochrane and PRISMA statements.
- Were included only parallel RCTs comparing MSC advanced therapy (autologous or allogeneic, combined or not with biocompatible materials) with any other therapy, whose participants were patients with knee osteoarthritis (primary or secondary) or chondral lesions, at any stage.

# Methods

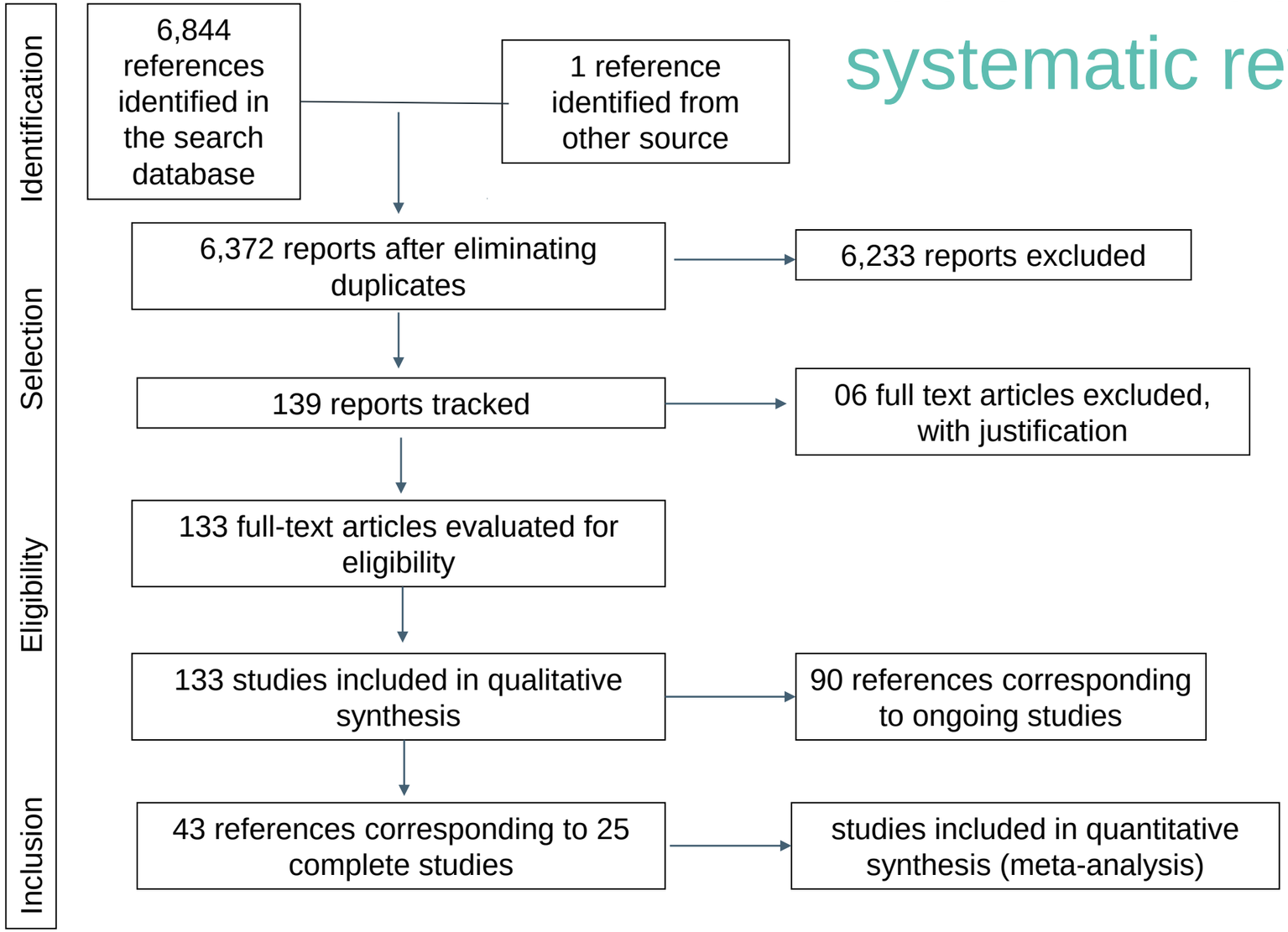
- For efficacy and safety, we considered the following outcomes: pain, physical function and serious adverse events as primary outcomes; quality of life, any adverse effects, and second-look intervention as secondary outcomes.

- A broad search of the literature was performed using electronic and hand search. There was no restriction regarding date, language or status of publication. Sensitive search strategies were developed for the following databases: CENTRAL; BASE; LILACS; MEDLINE; Peter; SPORTDiscus; ClinicalTrials.gov; Open Grey.

# Results

- The selection process was carried out in two stages by two independent reviewers. The searches retrieved 6,844 references (473 duplicates). 1 reference was identified from other source.
- The reading of 6,372 titles and abstracts resulted in the exclusion of 6,233.
- After reading the full text of the 139 remaining references (second step), 6 were excluded, 133 references were included: 43 corresponding to 25 complete studies and 90 ongoing.

# Table 1. Phases of the systematic review



# Results

- Serious adverse events:
  - There was no SAE with the MSC therapy interventions or the comparison interventions in the 25 included studies.

- Adverse events:
  - There was no standardization of AE reporting across studies, resulting in different reporting criteria.
  - Despite the heterogeneity, the studies reported similar AEs between the intervention and comparison groups.

# Results

- Clinical outcomes (pain and function):
  - Most of them reported tendency of better results with MSC therapy.
  - Most of the results were not statistically relevant.

- Considerations:
  - The included studies were highly heterogeneous regarding the tissue source of MSC, obtaining method, processing technique, final cell concentration and comparative therapy.
  - Most of them were focused on surrogate endpoints, such as MRI cartilage changes.

# Conclusion

- MSC therapies have not been fully optimized, requiring standardization of methods and better definition of efficacy and safety in well-designed studies.

# References


1. Chu CR, Rodeo S, Bhutani N, Goodrich LR, Huard J, Irrgang J, et al. Optimizing Clinical Use of Biologics in Orthopaedic Surgery: Consensus Recommendations From the 2018 AAOS/NIH U-13 Conference. J Am Acad Orthop Surg. 2019 Jan 15;27(2):e50–63.

2. Lim H-C, Park Y-B, Ha C-W, Cole BJ, Lee B-K, Jeong H-J, et al. Allogeneic Umbilical Cord Blood-Derived Mesenchymal Stem Cell Implantation Versus Microfracture for Large, Full-Thickness Cartilage Defects in Older Patients: A Multicenter Randomized Clinical Trial and Extended 5-Year Clinical Follow-up. Orthop J Sports Med. 2021 Jan 12;9(1):2325967120973052.

3. Wang Y, Jin W, Liu H, Cui Y, Mao Q, Fei Z, et al. [curative effect of human umbilical cord mesenchymal stem cells by intra-articular injection for degenerative knee osteoarthritis]. Zhongguo Xiu Fu Chong Jian Wai Ke Za Zhi. 2016 Dec 8;30(12):1472–7.

4. Gupta PK, Chullikana A, Rengasamy M, Shetty N, Pandey V, Agarwal V, et al. Efficacy and safety of adult human bone marrow-derived, cultured, pooled, allogeneic mesenchymal stromal cells (Stempeucel®): preclinical and

clinical trial in osteoarthritis of the knee joint. Arthritis Res Ther. 2016 Dec 20;18(1):301.

5.Fiolin J, Dilogo IH, Lubis AMT, Pawitan JA, Liem IK, Pandelaki J, et al. Functional and radiological comparison of umbilical cord mesenchymal stem cells, somatotropin, and hyaluronic acid injection for cartilage repair in early osteoarthritis of the knee: A randomized controlled trial. Orthop J Sports Med. 2020 May 1;8(5_suppl5):2325967120S0004.

6. Wong KL, Lee KBL, Tai BC, Law P, Lee EH, Hui JHP. Injectable cultured bone marrow-derived mesenchymal stem cells in varus knees with cartilage defects undergoing high tibial osteotomy: a prospective, randomized controlled clinical trial with 2 years' follow-up. Arthroscopy. 2013 Dec;29(12):2020–8.

7. Fernandes TL, Cortez de SantAnna JP, Frisene I, Gazarini JP, Gomes Pinheiro CC, Gomoll AH, et al. Systematic review of human dental pulp stem cells for cartilage regeneration. Tissue Eng Part B Rev. 2020 Feb;26(1):1–12.

8. Fernandes TL, Shimomura K, Hart DA, Boffa A, Nakamura N. Cartilage lesions and osteoarthritis: cell therapy. In: Filardo G, Mandelbaum BR, Muschler GF, Rodeo SA, Nakamura N, editors. Orthobiologics: injectable therapies for the musculoskeletal system. Cham: Springer International Publishing; 2022. p. 301–14.

9. Bastos R, Mathias M, Andrade R, Amaral RJFC, Schott V, Balduino A, et al. Intra-articular injection of culture-expanded mesenchymal stem cells with or without addition of platelet-rich plasma is effective in decreasing pain and symptoms in knee osteoarthritis: a controlled, double-blind clinical trial. Knee Surg Sports Traumatol Arthrosc. 2020 Jun;28(6):1989–99.

10. Lamo-Espinosa JM, Mora G, Blanco JF, Granero-Moltó F, Nuñez-Córdoba JM, Sánchez-Echenique C, et al. Intra-articular injection of two different doses of autologous bone marrow mesenchymal stem cells versus hyaluronic acid in the treatment of knee osteoarthritis: multicenter randomized controlled clinical trial (phase I/II). J Transl Med. 2016 Aug 26;14(1):246.

11. Lamo-Espinosa JM, Mora G, Blanco JF, Granero-Moltó F, Núñez-Córdoba JM, López-Elío S, et al. Intra-articular injection of two different doses of autologous bone marrow mesenchymal stem cells versus hyaluronic acid in the treatment of knee osteoarthritis: long-term follow up of a multicenter randomized controlled clinical trial (phase I/II). J Transl Med. 2018 Jul 31;16(1):213.

12. Akgun I, Unlu MC, Erdal OA, Ogut T, Erturk M, Ovali E, et al. Matrix-induced autologous mesenchymal stem cell implantation versus matrix-induced autologous chondrocyte implantation in the treatment of chondral defects of the knee: a 2-year randomized study. Arch Orthop Trauma Surg. 2015 Feb;135(2):251–63.

13. Zhao X, Ruan J, Tang H, Li J, Shi Y, Li M, et al. Multi-compositional MRI evaluation of repair cartilage in knee osteoarthritis with treatment of allogeneic human adipose-derived mesenchymal progenitor cells. Stem Cell Res Ther. 2019 Oct 21;10(1):308.

14. Lu L, Dai C, Du H, Li S, Ye P, Zhang L, et al. Intra-articular injections of allogeneic human adipose-derived mesenchymal progenitor cells in patients with symptomatic bilateral knee osteoarthritis: a Phase I pilot study. Regen Med. 2020 May;15(5):1625–36.