

INPLASY PROTOCOL

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Support: CNPq.

**Review Stage at time of this
submission:** Preliminary
searches.

Conflicts of interest:
None declared.

INTRODUCTION

Review question / Objective: Population: adults (aged between 18 and 50 years) with traumatic knee lesions who underwent treatment with mesenchymal stem cells; Intervention: defined by the treatment with mesenchymal stem cells; The comparison

Mesenchymal stem cells for the treatment of articular cartilage defects of the knee: an overview of systematic reviews

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Review question / Objective: Population: adults (aged between 18 and 50 years) with traumatic knee lesions who underwent treatment with mesenchymal stem cells; Intervention: defined by the treatment with mesenchymal stem cells; The comparison group: treatment with autologous chondrocytes or microfracture treatments; Primary outcome: formation of cartilage neo tissue in the defect area, determined by magnetic resonance imaging (MRI) or by direct visualization in second-look knee arthroscopy; Secondary outcomes: based on clinical scores such as visual analog scale (VAS) for pain, Western Ontario and McMaster universities score (WOMAC), knee society score (KSS), Tegner and Lysholm.

INPLASY registration number: This protocol was registered with the International Platform of Registered Systematic Review and Meta-Analysis Protocols (INPLASY) on 30 December 2022 and was last updated on 30 December 2022 (registration number INPLASY2022120114).

group: treatment with autologous chondrocytes or microfracture treatments; Primary outcome: formation of cartilage neo tissue in the defect area, determined by magnetic resonance imaging (MRI) or by direct visualization in second-look knee arthroscopy; Secondary outcomes: based on clinical scores such as visual analog

scale (VAS) for pain, Western Ontario and McMaster universities score (WOMAC), knee society score (KSS), Tegner and Lysholm.

Rationale: Mesenchymal stem cells (MSC) have been considered safe in the clinical scenario due to the lack of major adverse events reported at short- and medium-term. Besides, clinical improvement and positive histological findings may suggest its efficacy (Filardo et al., 2016). MSC can be isolated from bone marrow (Fellows et al., 2016), periosteum (Ferretti & Mattioli-Belmonte, 2014), synovium and synovial fluid (Sousa et al., 2014; Fang et al., 2020; Li et al., 2020), and adipose tissue (Filardo et al., 2013). Nevertheless, evidence that cell-based therapy is superior to other treatment options is scarce (Nakamura et al., 2009), although it presents promising functional outcomes (Chimutengwende-Gordon et al., 2020; Debnath, 2020). Hence, MSC-based therapy efficiency must be improved prior to clinical use (Zha et al., 2021).

Condition being studied: Articular cartilage lesions incidence during arthroscopic procedures varies from 19% to 66%, from which 11% are described as full thickness, localized and adequate for repair (Curl et al., 1997; Hjelle et al., 2002; Aroen et al., 2004). Surgical techniques available for cartilage repair aim to stimulate tissue formation in chondral or osteochondral defects through cell and/or scaffolds implantation in the articular defect (Makris et al., 2015; Kwon et al., 2019; Schreider et al., 2020). However, most methods used in clinical practice lead to fibrocartilage formation and are restricted to small defects (less than 2-4 cm²).

METHODS

Search strategy: Pubmed®, Embase®, Web of Science®, Scopus®, Scielo® and Epistemonikos® searches will be performed using the key words and medical MeSH terms (Cell- and Tissue-Based Therapy) and (cartilage OR chondral OR osteochondral) with no language or time restrictions.

Participant or population: Adults (aged between 18 and 50 years) with traumatic knee lesions who underwent treatment with mesenchymal stem cells.

Intervention: Treatment with mesenchymal stem cells.

Comparator: Autologous chondrocytes or microfracture treatments.

Study designs to be included: Systematic reviews with and without meta analysis.

Eligibility criteria: Eligible systematic reviews will be included if they report treatment of human articular cartilage defects with mesenchymal stem cells.

Information sources: Pubmed®, Embase®, Web of Science®, Scopus®, Scielo® and Epistemonikos®.

Main outcome(s): Primary outcome: formation of cartilage neo tissue in the defect area, determined by magnetic resonance imaging (MRI) or by direct visualization in second-look knee arthroscopy.

Additional outcome(s): Secondary outcomes: clinical scores such as visual analog scale (VAS) for pain, Western Ontario and McMaster universities score (WOMAC), knee society score (KSS), Tegner and Lysholm.

Data management: Search and selection process will be performed by two independent researchers, beginning with title and abstract analysis using Rayyan® tool. Then, full papers will be selected for reading and analysis according to the eligibility criteria (inclusion/exclusion) for data extraction by the five authors. Disagreements between researchers will be solved through careful discussion of the systematic reviews.

Quality assessment / Risk of bias analysis: Evaluation of systematic reviews quality will be conducted independently by two researchers. Methodological quality of each systematic review will be evaluated

with AMSTAR 2. PRISMA 2020 list will be used to assess the quality of each systematic review. GRADE scale will be used to evaluate the quality of evidence provided in the included systematic reviews.

Strategy of data synthesis: A Microsoft Excel® data extraction sheet, developed by the reviewers, will be used to extract data. For each systematic review, the following data will be extracted by two authors (EBS and RA), if available: first author's last name, year of publication, date of last literature research, search database, date of publication, included criteria, number of included studies, number included of RCTs, and number of patients included in the RCTs.

Subgroup analysis: After analysis of the selected systematic reviews, primary studies full texts will be screened for studies regarding treatment of articular cartilage repair with MSC.

Sensitivity analysis: To be determined.

Language restriction: None.

Country(ies) involved: Brazil.

Keywords: Articular cartilage defects; knee; mesenchymal stem cells; overview of systematic reviews.

Dissemination plans: Publication and presentation in conferences.

Contributions of each author:

Author 1 - Eduardo de Sousa - Research design, data screening and extraction, data analysis and draft the manuscript.

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