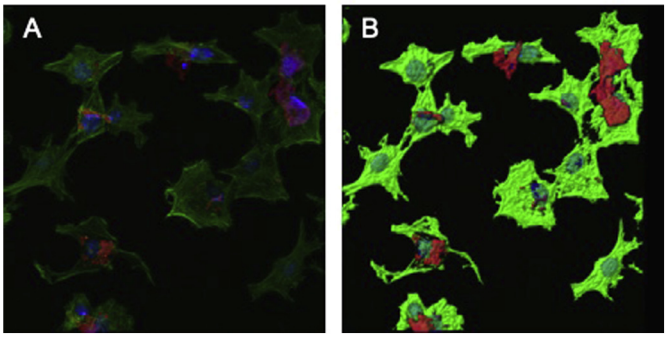

742
STATIN AND NODAL KNEE OSTEOARTHRITIS: A LONGITUDINAL PROPENSITY SCORE-MATCHED STUDY ON THE KNEE OSTEOARTHRITIS FROM THE OSTEOARTHRITIS INITIATIVE (OAI) COHORT

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Purpose: Statins have gained interest as potential disease-modifying osteoarthritis (OA) drugs, but there may be heterogeneity of effect across OA subtypes. We aimed to evaluate the effect of statin on knee OA according to presence of Heberden's nodes (HN), hallmark of nodal OA.
Methods: Using the Osteoarthritis Initiative (OAI) cohort, we conducted a longitudinal propensity-score (PS) matched study. We defined two subcohorts according to the presence of HN (HN^+ and HN^-). Considering per-protocol and new-user approaches, in each subcohort, statin initiators (<1-year of intake before enrollment) and non-initiators (no intake before enrollment) were matched using 1:1 PS-matching method for variables concerning confounding by indication bias (age, sex, diabetes, cardiovascular diseases, smoking, alcohol use). Participants were annually followed for 8-years; adhere to statin and knee OA outcomes were assessed. In each subcohort, the assocoation between statin use and longitudinal knee OA radiographic incidence/progression, and symptom incidence were assesed using Cox proportional regression.
Results: 832-knees (602-subject) and 386-knees (285-subjects) were enrolled in HN^+ and HN^- subcohorts, respectively. In HN^+ subcohort, statin users had 42% lower risk of OA progression in comparison with matched non-users (HR:0.54, 95%CI:0.36-0.93). In contrast, in HN^- subcohort, statin use was not associated with OA progression (HR:1.37, 95%CI:0.74-2.53). No significant associations between statin use and symptom/radiographic incidence were detected in either subcohort.
Conclusions: We found that statin use was associated with reduced risk of radiographic knee OA progression only in subjects with nodal OA. The presence of HN might be considered as an indicator of statin therapy for knee OA progression.

743
CLINICAL OUTCOMES OF HUMAN UMBILICAL CORD BLOOD DERIVED MESENCHYMAL STEM CELLS APPLICATION IN KNEE OSTEOARTHRITIS PATIENTS

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Purpose: There are many animal studies on the articular cartilage regeneration using stem cells, but studies on stem cell treatment on human are rare. For patients with knee osteoarthritis with full thickness cartilage defect (> 2.0 cm^2), we have been using human umbilical cord blood-derived mesenchymal stem cells (hUCB-MSCs) to regenerate articular cartilage since 2012. The purpose of this study is to analyze the effect of hUCB-MSCs based cartilage regeneration surgery on the preoperative and postoperative changes of symptoms, function and arthroscopic findings.
Methods: After standard arthroscopic examination, the cartilage defect site was exposed through small arthrotomy or arthroscopy. Then, multiple drill holes (2-5mm in diameter and 5mm depth) were made approximately 2-3 mm apart at the cartilage defect site, and hUCB-MSCs mixture was implanted in the drill holes of the lesion. Patients with varus or valgus deformity greater than 5 degrees were treated simultaneously with osteotomy. Among 253 patients (276 knees) who underwent hUCB-MSCs surgery from February 2012 to October 2017, we reviewed 64 patients (76 knees) who underwent second-look arthroscopy after postoperatively 1 year. Cartilage regeneration was graded according to Oswestry Arthroscopy Score (OAS). Functional outcomes using subjective International Knee Documentation Committee (IKDC) score, Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC) score, and visual analog scale (VAS) were evaluated at preoperative and postoperative 1 year.
Results: Totally 76 knees (64 patients; mean age, 59.8 ± 8.7 years; age range, 31 to 79 years) underwent second-look arthroscopic surgery at postoperative 1 year. The average preoperative cartilage defect is 4.4 ± 1.1 cm^2 (range, 2.0 to 5.9 cm^2). IKDC score improved from 22.9 points preoperatively to 69.3 points at postoperative 1 year. WOMAC score (mean 52.3 points preoperatively to 13.4 points at postoperative 1 year) and VAS score (mean 7.7 points preoperatively to 1.9 points at postoperative 1 year) all significantly improved at postoperative 1 year. The mean OAS were significantly improved from 5.6 ± 1.8 preoperatively to 2.1 ± 2.4 at postoperative 1 year. There was no complication due to hUCB-MSCs application itself, but in 2 kness, there was poor cartilage regeneration, pain persisted, so converted to TKA.
Conclusions: Although there is no histological study and lifespan of the regenerated cartilage, the cartilage regeneration using hUCB-MSCs showed significant pain and function improvement, and excellent arthroscopic findings of cartilage regeneration. These results suggest that hUCB-MSCs application surgery is good treatment option for patients with severe knee osteoarthritis of relatively younger age to perform TKA surgery.

744
MESENCHYMAL STEM CELLS: WHY INTRA-ARTICULAR? A SYSTEMATIC REVIEW OF ANIMAL STUDIES AND CLINICAL EVIDENCE ON MSC FOR KNEE OSTEOARTHRITIS

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Purpose: To evaluate the preclinical animal studies and clinical studies of MSCs injection for knee osteoarthritis (KOA) and to determine the evidence for a role for MSCs in further studies.
Methods: A systematic search of KOA animal studies and clinical studies published through Aug 2017 was conducted using the PubMed, EMBASE and web of science. Criteria for eligibility were animal studies assessing the therapeutic effects of MSCs intra-articular injection to subjects with KOA. The methodological quality of included animal studies was assessed by the SYRCLE tool for assessing risk of bias in animal intervention studies. Descriptive synthesis was performed. Evidence quality was evaluated based on the CERQual tool. The methodological quality and risk of bias of included systematic reviews was assessed by AMSTAR instrument and ROBIS tool respectively. Best evidence choice procedure was conducted according to the Jadad decision algorithm. The systematic reviews with high methodological quality and low risk of bias were selected ultimately for further evidence synthesis based on the CERQual tool.
Results: Twenty-three KOA animal studies were eligible for inclusion. According to the SYRCLE's tool, all included studies had high risk of bias. Between-study heterogeneity was substantial. The included studies varied in terms of species, modeling methods, MSCs origin, treatment timing, injections frequency, transplantation type and dose of MSCs. The following outcomes, gross morphology, histological analysis, immunohistochemical analysis, radiological evaluation or behavior analysis, were reported in the primary studies. For all outcomes, the evidence quality was low or very low. Four systematic reviews of clinical studies were eligible for inclusion. According to the ROBIS tool, there was one systematic review of clinical studies with low risk of bias and three with high risk of bias. Thus, only one systematic review conducted by Pas et al with highest AMSTAR score and low risk of bias was selected. For all outcomes after evidence synthesis via the CERQual tool, confidence for decision making was either low (self-reported measurement and MRI/histological outcome) or moderate (adverse events).
Conclusions: We do not have absolute confidence to recommend use MSCs injection for KOA clinical trials. Based on the internal and external