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PEER-REVIEW REPORT

Name of journal: *World Journal of Orthopedics*

Manuscript NO: 79974

Title: Comparative effectiveness of adipose-derived mesenchymal stromal cells in the management of knee osteoarthritis: A meta-analysis

Provenance and peer review: Unsolicited manuscript; Externally peer reviewed

Peer-review model: Single blind

Reviewer's code: 06334771
Position: Peer Reviewer
Academic degree: MD

Professional title: Doctor

Reviewer's Country/Territory: China

Author's Country/Territory: South Korea

Manuscript submission date: 2022-09-14

Reviewer chosen by: AI Technique

Reviewer accepted review: 2022-09-18 02:29

Reviewer performed review: 2022-09-21 02:27

Review time: 2 Days and 23 Hours

Scientific quality	[ ] Grade A: Excellent [Y] Grade B: Very good [ ] Grade C: Good [ ] Grade D: Fair [ ] Grade E: Do not publish
Language quality	[Y] Grade A: Priority publishing [ ] Grade B: Minor language polishing [ ] Grade C: A great deal of language polishing [ ] Grade D: Rejection
Conclusion	[ ] Accept (High priority) [Y] Accept (General priority) [ ] Minor revision [ ] Major revision [ ] Rejection
Re-review	[ ] Yes [Y] No

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Peer-reviewer statements	Peer-Review: [Y] Anonymous [ ] Onymous Conflicts-of-Interest: [ ] Yes [Y] No

SPECIFIC COMMENTS TO AUTHORS

The title,abstract and key words can reflect the main subject of the manuscript.In the background, the author can add a little more conflicting references on the evaluation of mesenchymal stem cells from two sources.The methods are detailed and results support the conclusion. Heterogeneity among the majority of the analyzed outcomes may affects the final conclusion.

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Reviewer's code: 03810998
Position: Editorial Board
Academic degree: BSc, MPhil, PhD
Professional title: Associate Professor
Reviewer's Country/Territory: China
Author's Country/Territory: South Korea

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Reviewer accepted review: 2022-10-06 02:46
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Review time: 4 Days and 5 Hours

Scientific quality	[ ] Grade A: Excellent [ ] Grade B: Very good [Y] Grade C: Good [ ] Grade D: Fair [ ] Grade E: Do not publish
Language quality	[Y] Grade A: Priority publishing [ ] Grade B: Minor language polishing [ ] Grade C: A great deal of language polishing [ ] Grade D: Rejection
Conclusion	[ ] Accept (High priority) [ ] Accept (General priority) [Y] Minor revision [ ] Major revision [ ] Rejection
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SPECIFIC COMMENTS TO AUTHORS

First, this article integrated the data of clinical studies involving bone marrow mesenchymal stem cells and adipose-derived mesenchymal stem cells in the treatment of osteoarthritis up to 2021, and compared the therapeutic effects of these two kinds of mesenchymal stem cells on OA by meta-analysis. In this study, multiple scoring criteria were used for comprehensive evaluation, and it was concluded that adipose-derived mesenchymal stem cells may be superior to bone marrow mesenchymal stem cells in the treatment of OA. The results were objective and reliable, and had certain guiding significance for the subsequent research in this field. Second, by integrating and analyzing the results of multiple clinical studies, the author concluded that ADSCs are superior to BMSCs in the treatment of OA. Third, It is mentioned that the authors intend to establish a standardized randomized controlled cohort study comparing the therapeutic effects of ADSCs and BMSCs on OA. In the discussion section, the author proposed that although ADSCs are more effective than BMSCs in the treatment of OA, there are still many shortcomings in the differentiation strategy and storage of ADscs, which need further study by researches in this field. There are some limitations remained to be improved. 1) There are “MSC type” annotation errors in the second column of row 6 and 7 of Table 2. 2) It can be seen from Table II that when AD-MSCs were used as therapeutic agents in the clinical studies included in the analysis, most of the studies only injected different doses of AD-MSCs into the knee joint cavity (7/10). However, when BMSCs were treated, adjuvant therapies such as HA and PRP were often injected at the same time, and BMSCs alone were rarely injected alone (4/12). So, do we need to exclude any increase or decrease in efficacy with or without adjuvant

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therapy when we analyze this data? Or should we eliminate the therapeutic effect of adjuvant therapy and placebo by comparing with the control group in each trial before proceeding to the next step of analysis and comparison between the efficacy of AD-MSCs and BMSCs? 3) It can be seen from Table I that there were no significant differences in age, gender and disease degree among the subjects of each clinical study. The authors also made an analysis after combining the subjects involved in each study into a whole. Could you please add a chart here that lists the number of patients treated with AD-MSCs and BMSCs after all studies were pooled in the manner of a pooled randomized controlled study, and present the number of subjects at each follow-up time point (6/12/24 month)? 4) It has been reported that the proliferative activity and therapeutic capacity of MSCs depend on the underlying disease status of the provider and the site of extraction, especially adipose-derived MSCs. Therefore, could you provide the inclusion and exclusion criteria for the clinical studies included in the analysis? Is there any relevant information about the exclusion of underlying diseases such as diabetes and autoimmune diseases to ensure that the clinical data included in the analysis are more comparable?