

## PEER-REVIEW REPORT

**Name of journal:** *World Journal of Stem Cells*

**Manuscript NO:** 76905

**Title:** A Short Review of Therapeutic Applications of Adipose-derived Stromal Vascular Fractions in Osteoarthritis

**Provenance and peer review:** Unsolicited Manuscript; Externally peer reviewed

**Peer-review model:** Single blind

**Reviewer's code:** 05395420

**Position:** Editorial Board

**Academic degree:** MS, PhD

**Professional title:** Assistant Professor

**Reviewer's Country/Territory:** India

**Author's Country/Territory:** China

**Manuscript submission date:** 2022-04-06

**Reviewer chosen by:** AI Technique

**Reviewer accepted review:** 2022-05-20 03:33

**Reviewer performed review:** 2022-05-20 03:46

**Review time:** 1 Hour

Scientific quality	<input type="checkbox"/> Grade A: Excellent <input type="checkbox"/> Grade B: Very good <input type="checkbox"/> Grade C: Good <input checked="" type="checkbox"/> Grade D: Fair <input type="checkbox"/> Grade E: Do not publish
Language quality	<input type="checkbox"/> Grade A: Priority publishing <input checked="" type="checkbox"/> Grade B: Minor language polishing <input type="checkbox"/> Grade C: A great deal of language polishing <input type="checkbox"/> Grade D: Rejection
Conclusion	<input type="checkbox"/> Accept (High priority) <input type="checkbox"/> Accept (General priority) <input type="checkbox"/> Minor revision <input checked="" type="checkbox"/> Major revision <input type="checkbox"/> Rejection
Re-review	<input checked="" type="checkbox"/> Yes <input type="checkbox"/> No



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<b>Peer-reviewer statements</b>	Peer-Review: [ <input checked="" type="radio"/> ] Anonymous [ <input type="radio"/> ] Onymous Conflicts-of-Interest: [ <input type="radio"/> ] Yes [ <input checked="" type="radio"/> ] No
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#### **SPECIFIC COMMENTS TO AUTHORS**

Dear authors I commend you for your work on exploring the utility of SVF in the treatment of OA I have some serious queries which prevent me from considering the work for publication When we look into the available literature on the use of SVF for OA we have abundant literature on the same subject and i do not find any distinct discussion or different perspective that is being communicated to the community through this article. Moreover i find this article to be of review nature but authors claim it to be original research which I could not accept.

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**Peer-review model:** Single blind

**Reviewer's code:** 03676315

**Position:** Peer Reviewer

**Academic degree:** MD

**Professional title:** Associate Professor

**Reviewer's Country/Territory:** Germany

**Author's Country/Territory:** China

**Manuscript submission date:** 2022-04-06

**Reviewer chosen by:** Dong-Mei Wang

**Reviewer accepted review:** 2022-05-25 05:11

**Reviewer performed review:** 2022-05-25 15:17

**Review time:** 10 Hours

Scientific quality	<input type="checkbox"/> Grade A: Excellent <input type="checkbox"/> Grade B: Very good <input checked="" type="checkbox"/> Grade C: Good <input type="checkbox"/> Grade D: Fair <input type="checkbox"/> Grade E: Do not publish
Language quality	<input type="checkbox"/> Grade A: Priority publishing <input checked="" type="checkbox"/> Grade B: Minor language polishing <input type="checkbox"/> Grade C: A great deal of language polishing <input type="checkbox"/> Grade D: Rejection
Conclusion	<input type="checkbox"/> Accept (High priority) <input type="checkbox"/> Accept (General priority) <input type="checkbox"/> Minor revision <input checked="" type="checkbox"/> Major revision <input type="checkbox"/> Rejection
Re-review	<input checked="" type="checkbox"/> Yes <input type="checkbox"/> No

<b>Peer-reviewer statements</b>	Peer-Review: <input checked="" type="radio"/> Anonymous <input type="radio"/> Onymous Conflicts-of-Interest: <input type="radio"/> Yes <input checked="" type="radio"/> No
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## SPECIFIC COMMENTS TO AUTHORS

Dear authors, thanks for submitting your manuscript. It describes the background and stem cell therapy potential of osteoarthritis. Some parts of the manuscript need some major revision to make the manuscript ready for publication. Title: ok Abstract: ok Keywords: words used in the title should not be part of the keywords (e.g. osteoarthritis The "Pathogenesis" part should mention praearthritic deformities. Severe valgus or varus malalginment leads to lateral or medial gonarthrititis. It should further be discussed that frontal malalignment needs to be appreciated and addressed by correction osteotomy when developing a concise treatment plan. The best stem cells alone cannot prevent arthritis in severe malalginment. Also, in the manuscript the role of stem cells in post traumatic arthritis should be discussed. At the end of the discussion, please give a conclusion of your work. The conclusion paragraph should be identified by a common wording like: "In conclusion..." e.g. References: Some references about secondary arthritis should be added and discussed

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**Peer-review model:** Single blind

**Reviewer's code:** 04480049

**Position:** Editorial Board

**Academic degree:** MD, PhD

**Professional title:** Associate Professor, Consultant Physician-Scientist, Staff Physician

**Reviewer's Country/Territory:** Bulgaria

**Author's Country/Territory:** China

**Manuscript submission date:** 2022-04-06

**Reviewer chosen by:** AI Technique

**Reviewer accepted review:** 2022-05-19 08:30

**Reviewer performed review:** 2022-05-26 11:10

**Review time:** 7 Days and 2 Hours

Scientific quality	<input type="checkbox"/> Grade A: Excellent <input checked="" type="checkbox"/> Grade B: Very good <input type="checkbox"/> Grade C: Good <input type="checkbox"/> Grade D: Fair <input type="checkbox"/> Grade E: Do not publish
Language quality	<input type="checkbox"/> Grade A: Priority publishing <input checked="" type="checkbox"/> Grade B: Minor language polishing <input type="checkbox"/> Grade C: A great deal of language polishing <input type="checkbox"/> Grade D: Rejection
Conclusion	<input type="checkbox"/> Accept (High priority) <input type="checkbox"/> Accept (General priority) <input type="checkbox"/> Minor revision <input checked="" type="checkbox"/> Major revision <input type="checkbox"/> Rejection
Re-review	<input checked="" type="checkbox"/> Yes <input type="checkbox"/> No

<b>Peer-reviewer statements</b>	Peer-Review: [ <input checked="" type="radio"/> ] Anonymous [ <input type="radio"/> ] Onymous
	Conflicts-of-Interest: [ <input type="radio"/> ] Yes [ <input checked="" type="radio"/> ] No

## SPECIFIC COMMENTS TO AUTHORS

Overall: The present manuscript is a well written and detailed review focusing on therapeutic applications of adipose-derived stromal vascular fractions. This is a very timely review of a "hot" topic. Abstract: Please fix the definition of osteoarthritis in the abstract. The contemporary concept of osteoarthritis now assumes the disease as a highly heterogeneous disorder characterized by progressive cartilage loss, remodeling of adjacent bones and concomitant low-grade inflammation (PMID: 30911813). Keywords should be preferably selected from the MeSH browser. Minor comments: Introduction: Please, fix those expressions: 1. "OA is a complete joint disease" – OA is considered a whole joint disease. 2. "This disease not only causes" – This disease does not only cause... 3. Economic burden is usually brought to society and not only to the patients. 4. "It is worth noting that, for different genders, the prevalence of OA in females is higher than in males" – "for different genders" is abundant. The introduction should ideally end with the aim of the present manuscript. If it is a review please describe the purpose of this review in addition to its justification. Please discuss further intraarticular injections as a part of a multimodal approach to the osteoarthritic joint. Since you agree that OA is a whole-joint disease, an urge has arisen for the implementation of intraarticular injections in a whole joint approach for the management of KOA (PMID: 32803403) Minor English check may be beneficial.

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**Peer-review model:** Single blind

**Reviewer's code:** 05439875

**Position:** Editorial Board

**Academic degree:** MD

**Professional title:** Assistant Professor

**Reviewer's Country/Territory:** Italy

**Author's Country/Territory:** China

**Manuscript submission date:** 2022-04-06

**Reviewer chosen by:** Dong-Mei Wang

**Reviewer accepted review:** 2022-05-26 07:50

**Reviewer performed review:** 2022-05-26 12:39

**Review time:** 4 Hours

Scientific quality	<input type="checkbox"/> Grade A: Excellent <input type="checkbox"/> Grade B: Very good <input type="checkbox"/> Grade C: Good <input checked="" type="checkbox"/> Grade D: Fair <input type="checkbox"/> Grade E: Do not publish
Language quality	<input type="checkbox"/> Grade A: Priority publishing <input checked="" type="checkbox"/> Grade B: Minor language polishing <input type="checkbox"/> Grade C: A great deal of language polishing <input type="checkbox"/> Grade D: Rejection
Conclusion	<input type="checkbox"/> Accept (High priority) <input type="checkbox"/> Accept (General priority) <input type="checkbox"/> Minor revision <input checked="" type="checkbox"/> Major revision <input type="checkbox"/> Rejection
Re-review	<input checked="" type="checkbox"/> Yes <input type="checkbox"/> No

<b>Peer-reviewer statements</b>	Peer-Review: <input checked="" type="checkbox"/> Anonymous <input type="checkbox"/> Onymous Conflicts-of-Interest: <input type="checkbox"/> Yes <input checked="" type="checkbox"/> No
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## SPECIFIC COMMENTS TO AUTHORS

Dear authors, you performed a review about the available treatment for osteoarthritis, focusing on Adipose-derived Stromal Vascular Fractions. The review is of interest for physician who manage patients with OA. However, the information reported are sometimes vague and not supported by appropriate references. Please address the issue reported below:

- “The primary method of diagnosing OA is imaging examination, which mainly includes X-rays, computed tomography (CT), MRI, ultrasonography, and arthroscopy. X-ray examination is one of the preferred methods for the clinical diagnosis of OA”, please support these information with references such as guidelines or consensus
- Please, discriminate about the different therapeutic approaches considering the stage of the disease
- “According to the International Cartilage Regeneration & Joint Preservation Society (ICRS), exercise is the most effective way to treat OA, as it can reduce joint pain and stiffness. Furthermore, losing weight is also one of the important ways to improve OA.”, please report appropriate reference
- “The injected drugs include glucocorticoids, sodium hyaluronate, platelet-rich plasma (PRP), bone morphogenetic protein 7 (BMP-7), and stem cells”, please argue better the treatment proposed. Read and cite Migliore A, Paoletta M, Moretti A, Liguori S, Iolascon G. The perspectives of intra-articular therapy in the management of osteoarthritis. *Expert Opin Drug Deliv.* 2020 Sep;17(9):1213-1226. doi: 10.1080/17425247.2020.1783234. Epub 2020 Jun 22. PMID: 32543240.
- Recently, a new intrarticular agent is proposed for the treatment of OA. Please, read and cite Moretti A, Paoletta M, Liguori S, Ilardi W, Snichelotto F, Toro G, Gimigliano F, Iolascon G. The Rationale for the Intra-Articular Administration of Clodronate in Osteoarthritis. *Int J Mol Sci.* 2021 Mar 7;22(5):2693. doi:





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10.3390/ijms22052693. PMID: 33799992; PMCID: PMC7962069.

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**Peer-review model:** Single blind

**Reviewer's code:** 02708249

**Position:** Editorial Board

**Academic degree:** PhD

**Professional title:** Full Professor

**Reviewer's Country/Territory:** France

**Author's Country/Territory:** China

**Manuscript submission date:** 2022-04-06

**Reviewer chosen by:** Dong-Mei Wang

**Reviewer accepted review:** 2022-05-27 16:08

**Reviewer performed review:** 2022-06-07 11:40

**Review time:** 10 Days and 19 Hours

Scientific quality	<input type="checkbox"/> Grade A: Excellent <input checked="" type="checkbox"/> Grade B: Very good <input type="checkbox"/> Grade C: Good <input type="checkbox"/> Grade D: Fair <input type="checkbox"/> Grade E: Do not publish
Language quality	<input type="checkbox"/> Grade A: Priority publishing <input checked="" type="checkbox"/> Grade B: Minor language polishing <input type="checkbox"/> Grade C: A great deal of language polishing <input type="checkbox"/> Grade D: Rejection
Conclusion	<input type="checkbox"/> Accept (High priority) <input checked="" type="checkbox"/> Accept (General priority) <input type="checkbox"/> Minor revision <input type="checkbox"/> Major revision <input type="checkbox"/> Rejection
Re-review	<input checked="" type="checkbox"/> Yes <input type="checkbox"/> No



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#### **SPECIFIC COMMENTS TO AUTHORS**

This paper reviews with pathogenesis, diagnosis, and current clinical treatments for OA. The paper is well written. The paper contains minor typos that should be fixed. As the content of the paper relates more to existing studies and techniques for OA treatment, the title is not appropriate. A title such as the following or another would be more appropriate: - A Short Review of Therapeutic Applications of Adipose-derived Stromal Vascular Fractions in Osteoarthritis - Therapeutic Applications of Adipose-derived Stromal Vascular Fractions in Osteoarthritis: A Short Review. In Section Discussion, the following sentence is incomplete: "As a result, it is critical for the early diagnosis and treatment of OA"

## RE-REVIEW REPORT OF REVISED MANUSCRIPT

**Name of journal:** *World Journal of Stem Cells*

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**Provenance and peer review:** Unsolicited Manuscript; Externally peer reviewed

**Peer-review model:** Single blind

**Reviewer's code:** 05395420

**Position:** Editorial Board

**Academic degree:** MS, PhD

**Professional title:** Assistant Professor

**Reviewer's Country/Territory:** India

**Author's Country/Territory:** China

**Manuscript submission date:** 2022-04-06

**Reviewer chosen by:** Ze-Mao Gong

**Reviewer accepted review:** 2022-07-19 13:29

**Reviewer performed review:** 2022-07-19 13:54

**Review time:** 1 Hour

<b>Scientific quality</b>	<input type="checkbox"/> Grade A: Excellent <input type="checkbox"/> Grade B: Very good <input checked="" type="checkbox"/> Grade C: Good <input type="checkbox"/> Grade D: Fair <input type="checkbox"/> Grade E: Do not publish
<b>Language quality</b>	<input type="checkbox"/> Grade A: Priority publishing <input checked="" type="checkbox"/> Grade B: Minor language polishing <input type="checkbox"/> Grade C: A great deal of language polishing <input type="checkbox"/> Grade D: Rejection
<b>Conclusion</b>	<input type="checkbox"/> Accept (High priority) <input type="checkbox"/> Accept (General priority) <input checked="" type="checkbox"/> Minor revision <input type="checkbox"/> Major revision <input type="checkbox"/> Rejection
<b>Peer-reviewer</b>	Peer-Review: <input checked="" type="checkbox"/> Anonymous <input type="checkbox"/> Onymous



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statements

Conflicts-of-Interest: [ ] Yes [Y] No

#### **SPECIFIC COMMENTS TO AUTHORS**

Expand NCT in the Table 1 footer Consequences to be changed in table 2 heading to results In the discussion also comment on the benefit of using AD-based SVF compared to BM-MSCs as AD-MSCs are found to be superior as shown in <https://doi.org/10.1177%2F1947603520951623> Comment and ease of its extraction and its regulations in processing which limit their earlier clinical translation