

REVIEWERS' COMMENTS:

Thank you very much for the in-depth review of the paper and for mentioning some very important points which really helped us to improve the manuscript. We have done additional work and re-written part of the manuscript accordingly. We have also carefully gone through the whole manuscript and did language corrections. All modifications are in red text. We hope that the reviewer's will now find the manuscript substantially revised with respect to the points raised by them. Here is the point-by-point response to the reviewers' comments:

Reviewer #1:

Scientific Quality: Grade C (Good)

Language Quality: Grade C (A great deal of language polishing)

Conclusion: Major revision

Specific Comments to Authors: In the current basic study, the authors introduce the "Combination of Mesenchymal Stem Cells and 3D Collagen Scaffold Preserves Ventricular Remodeling in Rat Myocardial Infarction Model". Overall, the study is clear and well done. But, there are some major points to improve the paper.

1- At the first, there are misspellings and critical grammatical errors in the text which should be corrected (For example: Wistar rats weighing 150-250 gm were used for bone marrow isolation and development of MI model).

We have carefully gone through the whole manuscript and corrected the misspellings, grammatical errors and sentence structure in the revised manuscript.

2- The abbreviations and symbol should be corrected.

Abbreviations and symbols have been corrected in the revised manuscript.

3- Also, the abstract part is long and should be modified.

Abstract part has been modified and reduce in the revised manuscript.

4- The authors should add the "degrees of freedom, F" for any part of quantification results.

Degrees of freedom have now been mentioned in the "Results" part of the revised manuscript as Tables 3A and 3B.

5- Highlights is very long and only the important points should be mentioned.

Highlights have been modified in the revised manuscript.

6- It should be noted that some figures are not in high resolution and should be modified. In other words, some figures are very poor and is not acceptable.

Figures have been processed and converted into high resolution images in the revised manuscript.

Reviewer #2:

Scientific Quality: Grade B (Very good)

Language Quality: Grade B (Minor language polishing)

Conclusion: Minor revision

Specific Comments to Authors: I would like to congratulate the authors for this manuscript. This study is interesting. I have some comments about the manuscript:
Material and methods:

1- Please refer related previous study on the methods that you use.

In this study, some protocols were performed according to manufacturer's instructions, whereas, some procedures were according to the previous reports. We have included references of these papers in the revised manuscript.

2- Please meet the requirement of using SI units.

We have used the SI units in the manuscript.

3- Page 10 line 8: Please clarify the 'triangle Ct' method.

'Triangle Ct' method has been explained in the "Methods", on page 10.

4- Page 10 line 11 and Page 12 last line: Please clarify the 'optimal temperature cutting' abbreviation, whether it is OCT or OTC.

The abbreviation for "Optimal Cutting Temperature" is "OCT". It has been corrected in the methods in the revised manuscript.

5- Discussion: Regarding the scaffold used, please specify possible reasons of choosing non-denatured type 1 collagen scaffold over other scaffolds (e.g., hydrogels/chitosan/biomimetic microcarriers/fibrins).

The reason for selecting non-denatured type 1 collagen scaffold over other scaffolds have now been mentioned in detail in the revised "Discussion", on pages 19 and 20.

6- Please point out the limitations of your study within the methodology.

Study limitations now have been mentioned at the end of "Discussion", on page 24.

7- Please check for mistyped words.

We have carefully gone through the whole manuscript and corrected the mistyped words in the revised manuscript.

Reviewer #3:

Scientific Quality: Grade B (Very good)

Language Quality: Grade B (Minor language polishing)

Conclusion: Minor revision

Specific Comments to Authors: This manuscript is very interesting paper, I benefited a lot from it, it contains very valuable information, a good addition in the field of cardiovascular injuries that many suffer from. It is well organized with all the details of the study. However, the quality of the manuscript can be improved if the authors considered and addressed the following concerns:

1- There are simple words written wrong

We have carefully gone through the whole manuscript and corrected all the wrong sentences and words in the revised manuscript.

2- Please put the names of genes of cardiac markers on the figure 3.

The names of genes have now been mentioned in figure 3 in the revised manuscript.

Reviewer #4:

Scientific Quality: Grade C (Good)

Language Quality: Grade B (Minor language polishing)

Conclusion: Major revision

Specific Comments to Authors: Qazi, et al explored the protective effect of mesenchymal stem cells combined with three-dimensional collagen scaffolds on ventricular remodeling in rat myocardial infarction model. This research is innovative. It has been proved that MSC is used in myocardial infarction model, and MSC and three-dimensional collagen scaffold are also reported in osteoarthritis, but this topic is still valuable at present. However, there is no in-depth mechanism research and no great clinical significance. At the same time, the manuscript also has many places to improve. Nevertheless, there are a number points that may deserve some revisions.

1. Abstract seems a little cumbersome. I think we should simplify the content of the background.

The content of the backgrounds has now been simplified in the revised manuscript.

2. I recommend that the author mark the significance with an asterisk on the graph and express it with N.S. there is no significant difference

We have marked the significance with letters "a, b and c, i.e., ^a $P < 0.05$, ^b $P < 0.01$, and ^c $P < 0.001$ ", as per the guidelines of this journal as mentioned in the manuscript preparation. The guidelines also state that "Data that are not statistically significant should not be denoted, i.e., $P > 0.05$ ". Therefore, we did not mention N.S. on any figure in the manuscript.

3. Figure 3: Gene expression analysis of cardiac markers. The name of each gene should be marked on the figure.

The names of genes have now been mentioned in figure 3 (figure 4 in in the revised manuscript).

4. Fluorescence images showing the expression of cardiac specific proteins. It may be clear on the original picture, but the clarity is very low after the author combines the pictures. Why not use WB quantitative analysis?

We have processed the images and converted them into high resolution images. We expect that the images are now clear.

5. Cardiac function analysis should have pictures of cardiac ultrasound. Quantitative data alone is not enough. Many data of cardiac function analysis can be drawn in a table, perhaps better

Ultrasound images of cardiac function analysis of all the groups have now been included in figure 6. Also the function analysis data have been presented in the form of table, i.e., table 2.

6. The flow of the experiment should be able to draw a flow chart for patients to understand.

A flow chart of experimental design has been included in the revised manuscript as figure 1.

7. The article needs a great deal of language polishing, also, please avoid long sentences.

We have carefully gone through the whole manuscript and corrected for all the English language mistakes. Long sentences have been shortened.

4 LANGUAGE POLISHING REQUIREMENTS FOR REVISED MANUSCRIPTS SUBMITTED BY AUTHORS WHO ARE NON-NATIVE SPEAKERS OF ENGLISH

As the revision process results in changes to the content of the manuscript, language problems may exist in the revised manuscript. Thus, it is necessary to perform further language polishing that will ensure all grammatical, syntactical, formatting and other related errors be resolved, so that the revised manuscript will meet the publication requirement (Grade A).

Authors are requested to send their revised manuscript to a professional English language editing company or a native English-speaking expert to polish the manuscript further. When the authors submit the subsequent polished manuscript to us, they must provide a new language certificate along with the manuscript.

We have carefully gone through the whole manuscript and corrected for all the English language mistakes. Long sentences have been shortened. The author list includes a faculty member of a US university. The manuscript is therefore extensively revised. We hope that all errors have been corrected in the revised manuscript.

Once this step is completed, the manuscript will be quickly accepted and published online. Please visit the following website for the professional English language editing companies we recommend: <https://www.wjgnet.com/bpg/gerinfo/240>.

5 ABBREVIATIONS

In general, do not use non-standard abbreviations, unless they appear at least two times in the text preceding the first usage/definition. Certain commonly used abbreviations, such as DNA, RNA, HIV, LD50, PCR, HBV, ECG, WBC, RBC, CT, ESR, CSF, IgG, ELISA, PBS, ATP, EDTA, and mAb, do not need to be defined and can be used directly.

The basic rules on abbreviations are provided here:

- (1) **Title:** Abbreviations are not permitted. Please spell out any abbreviation in the title.
- (2) **Running title:** Abbreviations are permitted. Also, please shorten the running title to no more than 6 words.
- (3) **Abstract:** Abbreviations must be defined upon first appearance in the Abstract. Example 1: Hepatocellular carcinoma (HCC). Example 2: *Helicobacter pylori* (*H. pylori*).
- (4) **Key Words:** Abbreviations must be defined upon first appearance in the Key Words.

(5) Core Tip: Abbreviations must be defined upon first appearance in the Core Tip. Example 1: Hepatocellular carcinoma (HCC). Example 2: *Helicobacter pylori* (*H. pylori*)

(6) Main Text: Abbreviations must be defined upon first appearance in the Main Text. Example 1: Hepatocellular carcinoma (HCC). Example 2: *Helicobacter pylori* (*H. pylori*)

(7) Article Highlights: Abbreviations must be defined upon first appearance in the Article Highlights. Example 1: Hepatocellular carcinoma (HCC).

Example 2: *Helicobacter pylori* (*H. pylori*)

(8) Figures: Abbreviations are not allowed in the Figure title. For the Figure Legend text, abbreviations are allowed but must be defined upon first appearance in the text. Example 1: A: Hepatocellular carcinoma (HCC) biopsy sample; B: HCC-adjacent tissue sample. For any abbreviation that appears in the Figure itself but is not included in the Figure Legend textual description, it will be defined (separated by semicolons) at the end of the figure legend. Example 2: BMI: Body mass index; US: Ultrasound.

(9) Tables: Abbreviations are not allowed in the Table title. For the Table itself, please verify all abbreviations used in tables are defined (separated by semicolons) directly underneath the table. Example 1: BMI: Body mass index; US: Ultrasound.

We have carefully followed all the mentioned rules for the use of abbreviations in the tables.

6 EDITORIAL OFFICE'S COMMENTS

Authors must revise the manuscript according to the Editorial Office's comments and suggestions, which are listed below:

(1) Science editor:

The authors submitted a manuscript investigating the protective effect of mesenchymal stem cells combined with three-dimensional collagen scaffolds on ventricular remodeling in rat myocardial infarction model. The topic is within the scope of the WJCC. There are 1 table and 9 figures. A total of 37 references are cited, including 15 references published in the last 3 years. There are 6 self-cited references. The authors provided the Biostatistics Review Certificate, Institutional Animal Care and Use Committee Approval Form or Document, and the Institutional Review Board Approval Document. No academic misconduct was found by the Bing search. This is an invited manuscript. This research is innovative. It has been proved that MSC is used in myocardial infarction model, and MSC and three-dimensional collagen scaffold are also reported in osteoarthritis, but this topic is still valuable at present. However, there is no

in-depth mechanism research and no great clinical significance. Some specific comments are listed below.

1. In the Material and methods section, please refer related previous study on the methods that you use. Please meet the requirement of using SI units. Page 10 line 8: Please clarify the 'triangle Ct' method. Page 10 line 11 and Page 12 last line: Please clarify the 'optimal temperature cutting' abbreviation, whether it is OCT or OTC.

In this study, some protocols were performed according to manufacturer's instructions, whereas, some procedures were given references in the revised manuscript.

We have used the SI units in the manuscript.

'Triangle Ct' method has been explained in the "Methods", on page 10.

The abbreviation of "Optimal Cutting Temperature" is "OCT". It has been corrected in the methods, on page 10, in the revised manuscript.

2. In the Discussion section, regarding the scaffold used, please specify possible reasons of choosing non-denatured type 1 collagen scaffold over other scaffolds (e.g., hydrogels/chitosan/biomimetic microcarriers/fibrins). Please point out the limitations of your study within the methodology.

The reasons of choosing non-denatured type 1 collagen scaffold over other scaffolds (e.g., hydrogels/chitosan/biomimetic microcarriers/fibrins) have been mentioned in the "Discussion", on page 20.

Study limitations have been mentioned at the end of "Discussion", on page 25.

3. The abstract part is long and should be modified. The authors should simplify the content of the background.

The content of the backgrounds have been simplified in the revised manuscript.

4. The authors should be added the "degrees of freedom, F" for any part of quantification results.

Degree of freedom has been mentioned in the "Results" part of the revised manuscript.

5. Highlights is very long and only the important points should be mentioned.

Highlights have been modified in the revised manuscript.

6. It should be noted that some figures are not in high resolution and should be modified. In other words, some figures are very poor and are not acceptable. Fluorescence images showing the expression of cardiac specific proteins. It may be clear on the original picture, but the clarity is very low after the authors combine the pictures. Why not use WB quantitative analysis?

We have processed the image and converted it into high resolution image.

7. The authors should mark the significance with an asterisk on the graph and express it with N.S. there is no significant difference.

We have marked the significance with letters "a, b and c, i.e., ^a $P < 0.05$, ^b $P < 0.01$, and ^c $P < 0.001$ ", as per the guidelines of manuscript preparation, we didn't find N.S. on the figures in the "format of manuscript" provided by the journal. The guidelines also stated that "Data that are not statistically significant should not be denoted, i.e., $P > 0.05$ ". Therefore, we did not mention N.S. on any figure in the manuscript.

8. The name of each gene should be marked on Figure 3.

The names of genes have been mentioned in figure 3 of the revised manuscript.

9. Cardiac function analysis should have pictures of cardiac ultrasound. Quantitative data alone is not enough. Many data of cardiac function analysis can be drawn in a table.

Ultrasound images of cardiac function analysis of all the groups have been included in figure 6, also the function analysis data have been presented in the form of table, i.e., table 2.

10. The flow of the experiment should be able to draw a flow chart for patients to understand.

A flow chart of experimental design has been included in the revised manuscript on page 34.

11. The English needs to be improved to a certain extent. There are a lot of errors in grammar and format in the whole manuscript.

We have carefully gone through the whole manuscript and corrected for all the English language mistakes. The author list includes a faculty member of a US university. The manuscript is therefore extensively revised. We hope that all errors have been corrected in the revised manuscript.

Language Quality: Grade B (Minor language polishing)

Scientific Quality: Grade C (Good)

(2) Company editor-in-chief:

I have reviewed the Peer-Review Report, the full text of the manuscript, and the relevant ethics documents, all of which have met the basic publishing requirements of the World Journal of Stem Cells, and the manuscript is conditionally accepted. I have sent the manuscript to the author(s) for its revision according to the Peer-Review Report, Editorial Office's comments and the Criteria for Manuscript Revision by Authors. Before final acceptance, uniform presentation should be used for figures showing the same or similar contents; for example, "Figure 1 Pathological changes of atrophic gastritis after treatment. A: ...; B: ...; C: ...; D: ...; E: ...; F: ...; G: ...".

Please provide decomposable Figures (in which all components are movable and editable), organize them into a single PowerPoint file.

A single PowerPoint file containing all editable contents has been provided.

Please authors are required to provide standard three-line tables, that is, only the top line, bottom line, and column line are displayed, while other table lines are hidden. The contents of each cell in the table should conform to the editing specifications, and the lines of each row or column of the table should be aligned. Do not use carriage returns or spaces to replace lines or vertical lines and do not segment cell content.

Tables are now according to the required format.

Please check and confirm whether the figures are original (i.e. generated de novo by the author(s) for this paper). If the picture is 'original', the author needs to add the following copyright information to the bottom right-hand side of the picture in PowerPoint (PPT): Copyright ©The Author(s) 2022.

All figures are original. The copyright information has been added in the PPT slides.