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Mesenchymal stem cells in wound healing: A bibliometric analysis as a powerful research tool

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Abstract

Bibliographic analysis is still very rarely used in experimental basic study papers. The comprehensive bibliometric analysis of scientific literature on research progress and challenges in stem cell therapy for diabetic chronic wounds, which was conducted in the work of Shi *et al* can be a case study and a source of valuable information for writing reviews and experimental papers in this field. Basic experimental studies on a role of mesenchymal stem cells (MSCs) in wound healing that are published in 2023-2024, such as Zhang *et al* in 2023, Hu *et al* in 2023, Wang *et al* in 2023 are certainly also subjects for applying this powerful tool to analyze current research, challenges and perspectives in this field. This is due to the fact that these studies have addressed a great variety of aspects of the application of MSCs for the treatment of chronic wounds, such as using both the cells themselves and their various products: Sponges, hydrogels, exosomes, and genetic constructions. Such a wide variety of directions in the field of study and biomedical application of MSCs requires a deep understanding of the current state of research in this area, which can be provided by bibliometric analysis. Thus, the use of such elements of bibliographic analysis as publication count by year and analysis of top-10 keywords calculated independently or cited from bibliometric analysis studies can be safely recommended for every basic study manuscripts, primarily for the "Introduction" section, and review.

Key Words: Bibliometric analysis; Mesenchymal stem cells; Wound healing; Tissue engineering; Dressing; Hydrogels; Matrix; Exosomes

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Core Tip: Bibliographic analysis is still very rarely used in basic studies. Meanwhile, it is a very effective tool to better understand the development of the chosen research area and to analyze the data more broadly, as it is perfectly demonstrated in the work of Shi *et al* in 2024 and in comparisons with basic studies on a role of mesenchymal stem cells in wound healing published. Such elements of bibliographic analysis as publication count by year and analysis of top-10 keywords can be safely recommended for using in every basic study manuscripts.

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INTRODUCTION

As an editor-in-chief, I would like to acknowledge a comprehensive bibliometric analysis of scientific literature on the topic of research progress and challenges in stem cell therapy for diabetic chronic wounds, which was conducted in the work of Shi *et al*[1] in 2024, numerous of basic research papers on this topic of the role of mesenchymal stem cells (MSCs) in chronic wound care published in 2023-2024 years in the *WJSC*. The art of constructing a manuscript of bibliometric analysis allows us to see many important facts and ideas that may remain in the shadows in a manuscript based on the classical format of basic research.

The aim of this work is to try to find elements of bibliometric analysis in conventional basic research papers on this and related topics, and to discern whether the main results of bibliometric analysis on this topic are reflected in the basic research papers. Or, on the contrary, the information presented in ordinary basic research papers contradicts the conclusions of the bibliometric analysis. As a result of this work, we will make recommendations on what role bibliometric analysis should play in experimental study.

BIBLIOMETRIC ANALYSIS

The study of Shi *et al*[1] analyzed the most searched topics within the main research theme in terms of keyword frequency and co-occurrence, as well as papers citations in Scopus, Web of Science Core Collection, VOSviewer, and CiteSpace databases and related software. The results of this study allow identifying the most promising directions in this scientific area: (1) The investigation and application of stem cells for chronic wound healing: “stem cells”, “stromal cells”, “mesenchymal stem cells”, “adipose-derived stem cells”, “endothelial progenitor cells”; (2) The various therapeutic technics for treatment of different diseases associated with chronic wounds: “chronic wounds”, “diabetes mellitus”, “diabetic foot ulcers”, “venous leg ulcers”, “skin”, “double-blind”, “critical limb ischemia”; and (3) The study of mechanisms of wound healing: “diabetic wound healing”, “repair”, “therapy”, “angiogenesis”, “expression”, “biological therapies”, “differentiation”, “proliferation”.

The authors themselves draw the following conclusions: “The priority topics revolved around dressings, extracellular vesicles, wound healing, and adipose stem cells. The results of these analyses will help researchers understand the current research status and provide hopeful directions for future studies. Future research will also focus on the clinical translation of stem cell therapies for diabetic chronic wounds”.

The authors also conducted a complete bibliometric analysis on parameters such as publication count, country (geographical distribution, country/region contributions), affiliation (author institution, institutional collaboration network), author (authors and cocitation author analysis, contributions of different authors), journal (journals and cocited journal analysis), reference (cocited reference analysis). The tables, graphs, network diagrams, heatmaps compiled by the authors give noticeably clear picture of the current development of the topic on the use of stem cell therapy for diabetic foot treatment in the world biomedical science.

Such analysis is of significant help in planning new research in the chosen scientific field, to correct the direction of research when negative results are obtained, to interpret and discuss the obtained data, and to continue the research in the most promising direction.

BASIC RESEARCH STUDIES IN *WJSC*

Despite the fact that the subject of this manuscript is considerably far from the topic of diabetic foot treatment and is quite specific, considering that the source of biomaterial is deer antlers, nevertheless many key words (from keywords list, abstract or repeatedly occurs in the text) from bibliometric analysis of Shi *et al*[1] we can see in this experimental paper: “wound healing”, “repair”, “therapy”, “mesenchyme/mesenchymal stem cells”, “adipose(-derived) mesenchymal stem cells”, “endothelial (progenitor) cells”, “skin/(cutaneous)”, “(extracellular) matrix”, “(gene) expression”, “(cell) proliferation”. On the other hand, keywords such as “foot ulcer”, “chronic wounds”, “diabetic foot”, “critical limb ischemia”

are missing here, which is not surprising since the investigators used a full-thickness cutaneous wound healing rat model. Also the key word "angiogenesis" is missing in the text, which is rather difficult to explain, since the very process of angiogenesis (by expression levels of CD31 - the surface marker of neovascular endothelial cells) during wound healing is investigated in the paper[2].

In the introduction, the authors also indicate many keywords from the bibliometric analysis and generally describe the current state of research in the field close to the results of the bibliographic analysis, although it is on a more distant topic. The authors draw the conclusion that the use of matrix-based wound covers that injectable hydrogels based on antler reserve mesenchymal matrix have clinical benefits for stimulating regenerative wound healing[2], which partially coincides with the conclusions of the authors of the bibliometric analysis[1]. This paper also includes authors affiliated to Chinese institutions, whereas, according to the bibliographic analysis, China is a leader in this scientific field.

However, in the "Introduction" section, the authors do not make any attempts to conduct a bibliographic analysis of their subject matter.

In this experimental paper, we also see a list of keywords given in the bibliographic analysis[1]: "wound healing", "repair", "mesenchymal stem cells", "endothelial (progenitor) cells", "skin", "angiogenesis", "(cell) proliferation". Although some important keywords (directly from the keyword list) of this research paper[3] are not in the top 10 and top 20 keywords of bibliometric analysis by Shi *et al*[1], they can still be seen in the keywords clustering chart in figure 8A [1], such as "exosomes", "collagen/gelatin" as well as "hydrogel" from the last paper[2]. However, such important keywords of the current research work as "sponge", "safety", "hemostasis", "human umbilical cord mesenchymal stem cells" are totally absent in the bibliometric analysis by Shi *et al*[1].

Meanwhile, the conclusions that the authors draw from the results about high efficacy of MSC-derived exosomes loaded onto gelatin sponges for wound healing[3] largely coincide with the conclusions of the bibliometric analysis[1] that the most promising topics are dressings, stem cells, and extracellular vesicles for wound healing. The authors of this paper are also from China.

In this study, the authors also do not make a bibliographic analysis on their field of knowledge according to any of its parameters (number of papers, keywords, *etc.*).

In this experimental research work[4], we see maximum keyword matching with the bibliometric analysis[1] as this study also investigates the treatment of diabetic ulcers. The list of keywords mentioned in the bibliographic analysis of Shi *et al*[1] in this paper is as follows: "wound healing", "diabetic (foot) ulcers", "diabetes mellitus", "mesenchymal stem cells", "adipose-derived mesenchymal stem cells", "endothelial progenitor cells", "skin", "angiogenesis", "(cell) proliferation", "differentiation", "expression", "mechanism". Moreover, authors are from the Peking Union Medical College from the top 10 of most productive affiliations in this scientific field indicated in the paper of Shi *et al*[1]. The authors' conclusions about the prospective use of modified exosomes partially overlap with the findings of the bibliometric analysis[1].

In this study, the authors also do not make any elements of a bibliographic analysis on their research topic.

Although the topic of experimental basic research of Zhang *et al*[5] in 2024 is not related to diabetic skin ulcers, numerous of keywords are mentioned in this study are from the top 10 and top 20 keywords of bibliometric analysis by Shi *et al*[1]: "(bone marrow) mesenchymal stem cells", "angiogenesis", "differentiation", "repair", "healing", "mechanism", (human umbilical vein) endothelial cells", "proliferation", "therap(eutic)". The authors' conclusions about the prospective use of hydrogel loaded with MSC-derived exosomes partially overlap with the findings of the bibliometric analysis[1].

In this study, the authors do not make a bibliographic analysis on the topic of MSC role in bone regeneration.

RESEARCH PAPERS IN OTHER BPG JOURNALS

The case report of Ha *et al*[6] in 2024 in the *World Journal of Clinical Cases* has only 3 of the same keywords as those noted in the bibliographic analysis of Shi *et al*[1]: "diabetic foot ulcers", "wound healing", and "therapy". The keywords relevant to MSCs are not mentioned in this case report. However, among the important keywords, "regenerative medicine" was not mentioned in the work of Shi *et al*[1].

Some keywords familiar to us from the work of Shi *et al*[1] can be found in another case report of McNeil *et al*[7] in 2023 published in the *World Journal of Diabetes*, such as "diabetic foot ulcer(ation)" and "management". However, the authors of this paper use a specific term "diabetes-related foot disease", derived by them even in the title of the paper, which is not present in the study of Shi *et al*[1]. There are also numerous medical terms in this case report that are not mentioned in the bibliographic analysis of Shi *et al*[1]: "lower extremity amputation", "neuropathy", "arterial disease", "infection".

In the work of Sadat-Ali *et al*[8] in 2023 published in *World Journal of Diabetes* just the main keyword "wound heal(ing)" and the general keyword "mechanism" were indicated, since this case report has nothing to do with either diabetes or MSCs.

Thus, case reports devoted to study of chronic wounds published in other BPG journals are less likely to fall into the keyword pool allocated in the bibliographic analysis of Shi *et al*[1] by their keywords. This is not surprising, as these works are largely outside the scope of bibliographic analysis of Shi *et al*[1].

EXAMPLES

Nevertheless, bibliometric analysis as a special form of scientific research is actively developing in the area of wound healing research. In the last few years, numerous papers of this type have appeared, reflecting the roles of various factors in wound healing: Various drugs (curcumin[9], peptides[10]), different (bio)materials (nanomaterials[11], hydrogels based on alginate[12] and glycol chitosan/silk fibroin/chondroitin-6-sulfate/maleic anhydride-modified polyethylene glycol hydrogel[5]), different cell types (MSCs[1,5], macrophages[13]), diseases (diabetes[1,14], post-COVID-19 fibrosis [15], bone fractures[5]), wound dressing[12], extracellular vesicles[5,16], and biofilms[17]. All these papers are similar to Shi *et al*[1] study in their plan and main content, as well as in the methods of analysis used in the work.

Moreover, with the development of on-line tools for processing bibliographic information in such a database of scientific publications as Scopus, Web of Science, and PubMed, there is a growing trend to bring some simple elements of bibliometric analysis, such as the number of publications by year, into review papers. Such examples of review studies are the following papers in the field of wound care: Pollini and Paladini[18] in 2020, Jaldin-Crespo *et al*[19] in 2022, Nandhakumar *et al*[20] in 2022, Zhang *et al*[21] in 2024.

CONCLUSION

Thus, the bibliographic analysis even on a rather distant topic but in framework of the basic theme devoted to the role of mesenchymal stem cells in wound healing can help in selecting the most promising research direction and in the correct treatment of the current topic. This tool for analyzing scientific information is highly effective. In this regard, we recommend using various elements of bibliographic analysis, which can be found in the study of Shi *et al*[1], at least analyzing the number of papers on a topic by year, top-10 keywords in the chosen research area, and numerous papers by main keywords to write the section "Introduction" of basic experimental study manuscripts and review manuscripts in *WJSC*. Alternatively, one could simply actively refer to such bibliometric analysis studies that are closest in the research topic and cite the most interesting data from them, given into the account that there are already quite numerous studies of this type.

FOOTNOTES

Author contributions: Bonartsev AP designed the research study; Voinova VV, Vasina DV, and Bonartsev AP performed the research; Voinova VV and Bonartsev AP wrote the original draft; Vasina DV and Bonartsev AP reviewed and edited the manuscript; All authors have read and approved the final manuscript.

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