ISSN 2618-1584 Vol. 5, Issue 5: 11-19, DOI: 10.25236/FMSR.2023.050502

Global trends in disc degeneration and degenerative disc disease: a bibliometric and visualization study

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Abstract: ***Objective:*** *There has been increasing interest in the study of disc degeneration and degenerative disc disease. The purpose of this study was to investigate the global status and trends in this field.* ***Methods:*** *Retrieved 1991-2022 research papers related to disc degeneration and degenerative disc disease from the Science Citation Index-Expanded Web of Science. The source data were studied and indexed using bibliometrics. The visualization study used VOSviewer software to perform literature coupling, co-authorization, co-citation, and co-occurrence analysis to analyze trends in published research on disc degeneration and degenerative disc disease.* ***Results:*** *A total of 2036 literatures were included. Worldwide, the number of related research interests and publications is increasing every year. The United States contributes the most to global research, is cited the most and has the highest H-index. The journal Springer Nature published the most. The University of California, Rush University, Harvard University, Jefferson University and the University of Hong Kong are among the top contributors. Research can be divided into four categories: mechanism studies, animal studies, clinical trials, and tissue engineering. Mechanism research and tissue engineering are expected to be the next hot topics in this field.* ***Conclusions:*** *Judging from current global research trends, there will be an increasing number of papers on disc degeneration and degenerative disc disease. The United States is the largest contributor in this field. Much of the effort has been devoted to the mechanisms and tissue engineering of disc degeneration, such as nucleus pulposus cells and inflammatory responses, which may be the next hot spot in research.*

Keywords: *Intervertebral disc degeneration; Degenerative disc disease; Global trends; Bibliometrics; Visualization research*

1. Introduction

With the continuous exploration of the etiological basis of intervertebral disc degenerative diseases, the causes of intervertebral disc degeneration (resulting from the imbalance of synthesis and catabolism caused by cells, extracellular matrix, growth factors and inflammatory factors) have been gradually identified. At the same time, with the continuous expansion of tissue engineering in the field of orthopedics, more and more clinical and basic researchers try to treat discborne diseases through exogenous interventions, including molecular therapy, cell therapy and gene therapy [1]. In molecular therapy, researchers try to increase anabolic growth factors by reducing inflammatory factors such as TNF-a and IL-8 [2,3]. In terms of cell therapy, studies mainly focus on the introduction of exogenous cells and the in vitro expansion and replantation of autologous nucleus pulposus cells [4,5]. In gene therapy, the side effect of inhibiting inflammatory factors by applying exogenous growth factors has been overcome, which has become a hot topic of researchers' attention [6]. However, the above-mentioned biotherapy also has significant problems. As the pathogenesis of disc degeneration is not fully understood, biotherapy lacks a clear target. Therefore, how to break through the bottleneck of biological therapy depends on further confirmation of the mechanism of disc degeneration, which is also an area that researchers should pay attention to and explore. Of course, before further research and discussion on the mechanism of intervertebral disc degeneration, we need to summarize the current research status of intervertebral disc degeneration and degenerative intervertebral disc disease, and predict the promising keywords and trends. As the core part of scientific research, the amount of publication is an important index to measure the contribution of scientific research. Bibliometrics analysis can provide information based on literature database and bibliometrics characteristics for qualitative and quantitative evaluation of the changing trend of research activities over time. It provides

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a method to capture the development of a certain field and compare the contributions of scholars, journals, institutions and countries [7]. Bibliometric analysis has also been used to develop policy and clinical practice guidelines, and this viable approach has been successfully used to assess trends in research on the spine, sepsis, diabetes, and injuries [8]. As far as we know, in the field of intervertebral disc degeneration, the research results on nucleus pulposus cells and inflammatory responses are relatively hot and few in quantity and quality. Therefore, the objective of this study was to evaluate the current status and trend of research on the mechanisms of disc degeneration, including nucleus pulposus cells and inflammatory responses.

2. Materials and methods

2.1. Data Sources

Bibliometric analysis was performed based on the Science Citation Index-Expanded (SCI-E) of the Web of Science (WoS) which is considered the optimal database for bibliometrics.

2.2. Search strategy

All publications were searched in WoS from January 1, 1991 to December 31, 2022 in the database. In this study, the search criteria were: subject = disc degeneration AND subject = degenerative disc disease AND year of publication = (1991-2022) AND language = (English) AND type of literature = (Article or Review). We have also improved the ability to search for certain countries or regions by indexing countries/regions in WoS.

2.3. Data collection

Download the complete record of each publication from the WoS database, including title, publication year, author's name, nationality, affiliation, publication journal name, keywords and abstract in TXT. Import a file to Microsoft Excel 2017. Two authors (LCS and WWW) independently filtered and extracted data entries and collections. Any disagreement should be discussed to reach a consensus. Finally, the authors manually cleaned and analyzed the data in Microsoft Excel 2017.

2.4. Bibliometric Analysis

The internal function of WoS is used to describe the basic characteristics of the above qualified publications. The H-index is a measure of scientific impact. The H-index indicates that a scholar or country has published h papers, and each paper has been cited by other publications at least h times. Therefore, the H-index reflects both the number of publications and the number of citations per publication [9]. Using R software (version 3. 1. 3), the logistic regression model was used to plot the publication time curve: f (x) =c/ (1+a×exp[-b × (X-1991)]). Where, the independent variable x is the year and f (x) is the cumulative number of publications. The formula T=lna/b+ 1991 is used to calculate the inflection point, which is defined as the time when the publication growth rate changes from positive to negative [10].

2.5. Visual analysis

Visual analysis using VOSviewer (LeidenUniversity, Leiden, the Netherlands) for publications for visual analysis. In this study, VOSviewer was used to conduct bibliographic coupling, coauthorization, co-citation and co-occurrence analysis [11].

3. Results

3.1. Trend

3.1.1. Global Publishing Trends

From 1991 to 2022, a total of 2,269 articles were published globally, which met the search criteria. When looking at the volume of annual publications, most studies were published in 2022 (228 articles, 10. 04%). From 1991 to 2022, the total number of annual global publications showed an overall

ISSN 2618-1584 Vol. 5, Issue 5: 11-19, DOI: 10.25236/FMSR.2023.050502

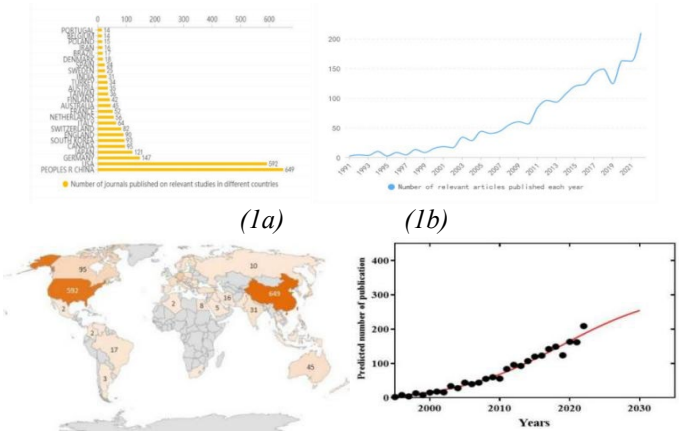
upward trend. In addition, research interest in this field is increasing year by year (Fig. 1a).

3.1.2. National Contributions

A total of 67 countries and regions have contributed to this field. Among these countries, China published the most articles (649, 31. 876%), followed by the United States (592, 29. 077%), Germany (147, 7. 220%), Japan (121, 5. 934%) and Canada (95, 4. 666%) (Fig. 1 b, c).

3.1.3. Global publishing trend prediction

The logistic regression model is used to create a time curve of the number of publications that can predict the future trend [12]. Figure (d) shows a model fitting curve that predicts the growth trend in the number of global publications over the next few years.



(1a) *(1b)* *(1c)* *(1d)*

Figure 1: Global trends and countries in disc degeneration and degenerative disc disease. (a) Publications related to disc degeneration and degenerative disc disease research worldwide number of publications in different years. (b) Number of publications related to disc degeneration and degenerative disc disease by country. (c) World map showing the distribution of Disc degeneration and degenerative disc disease research. (d) Model fit curves predicting the growth trend in the number of global publications related to the field of disc degeneration and degenerative disc disease over the next few years.

3.2. Quality of publications in different countries

3.2.1. Total citation frequency

Papers from the United States had the highest total citation frequency (25,642). China ranked second in total citations (12,647), followed by the United Kingdom (6,340), Germany (3, 876) and Japan (4,742) (Fig. 2a).

3.2.2. Average citations

The highest was Welsh publications (127. 2). Sweden ranked second in average citation frequency (95. 96), followed by Belgium (75. 6), the United Kingdom (66. 62) and Finland (61. 18). Figure 5 lists the top 20 journals with the highest average citation frequency (Fig. 2b).

3.2.3. H-Index

(2a) *(2b)* *(2c)*

Figure 2: Citation frequency and H-index levels of different countries. (a) Total citations of research articles on disc degeneration and degenerative disc disease in different countries. (b) The average number of citations per paper for articles from different countries. (c) H-index of publications in different countries.

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The H-Index of relevant papers in the United States was the highest (84), followed by China (53), Japan (40), South Korea (38) and Canada (37) (Fig. 2c).

3.3. Analysis of global publications

3.3.1. Journal Analysis

There were 255 articles in Spine (IF=3. 269, 2021), 151 articles in European Spine Journal (IF=2. 721, 2021), and 70 articles in Spine Journal (IF=4. 297, 2021). 44 articles on BMC Musculoskeletal Disorders (IF=2. 562, 2021). The Journal of Neurosurgery Spine (IF=5. 526, 2021) has 44 articles on cell therapy for disc degeneration. Figure 3a lists the top 20 journals with the most published studies.

3.3.2. Research Directions

Figure 3b shows the distribution of research directions related to intervertebral disc degeneration and degenerative intervertebral disc disease. The most popular fields of study are orthopedics, neuroscience, surgery, cell biology [13, 14] and experimental research medicine [15, 16].

3.3.3. Institutional output

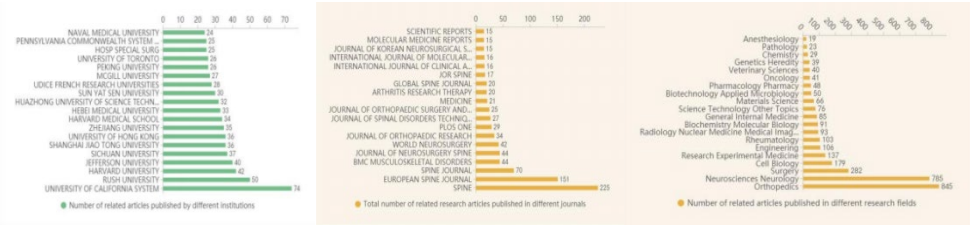
The top 20 institutions with the highest output are listed in Figure 3c. The University of California published the most papers (74), Rush University the second (50), Harvard University the third (42), Jefferson University the fourth (38) and Sichuan University the fifth (37).

3.3.4. Sources of funds

The top 20 funding organizations related to supporting this research field are shown in Figure 3d, with a total of 1242 studies funded. Among them, the National Science Foundation of China (NSFC) funded 258 projects (ranked first), and United States Department of Human Services Department the of Health (USDH) funded 139 projects (ranked second).

3.3.5. Authors

The top 20 authors published a total of 375 papers, representing 18. 418% of all papers in the field (Figure 3e). In the field of disc degeneration and degenerative disc disease, the three authors with the most published papers are Liu H (39), followed by Zhang Y (26) and Wang H (23).



(3a) *(3b)* *(3c)*

(3d) *(3e)*

Figure 3: Global high-contributing journals, research directions, high-impact institutions, authors, and funding for disc degeneration and degenerative disc disease research (a) The world's leading research journals. (b) The sum total of world research directions. (c) High-impact institutions in the world. (d) Major donor funds in the world. (e) Authors of significant influence in the world.

3.4. Bibliographic coupling analysis

Bibliographic coupling is a measurement method that uses citation analysis to establish similarity relationships among documents. The journal names in the total publication are analyzed using VOSviewer.

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3.4.1. Magazines

As shown in Figure 4a, a total of 88 identified journals (defined as a minimum number of publications using more than 5 for a journal) appear in total link strength. The top 5 magazines in terms of total link strength are: Spine (total link strength = 65,437), European Spine Journal (total link strength = 55,629), Spine Journal (total link strength = 27,905), World Neurosurgery (total link strength = 16,465) and BMC Musculoskeletal Disorders (total link strength = 16,449).

3.4.2. Institutions

Papers identified from 70 institutions (defined as an organization using a minimum number of more than 10publications) were analyzed using VOSviewer (Figure 4b). The top five institutions are Rush University (total link strength =25,091times), the University of Hong Kong (total link strength = 22,073times), Jefferson University (total link strength = 19, 861times), the University of Manchester (total link strength =15, 825 times) and Sun Yat-sen University (total link strength = 15,522 times).

3.4.3. Countries

The VOSviewer (Figure 4c) was used to analyse country papers identified in 41 countries (defined as a minimum number of publications using more than 5 in a country). The top five countries in terms of total link strength are the United States (total link strength = 326,243), China (total link strength = 310,595), Germany (total link strength = 112,559), and Switzerland (total link strength = 84,391).

(4a) *(4b)* *(4c)*

Figure 4: Literature coupling analysis of global disc degeneration and degenerative disc disease. (a) Mapping of 88 journals that have been identified as relevant to disc degeneration and degenerative disc disease. (b) Maps of 76 institutions associated with disc degeneration and degenerative disc disease. (c) Mapping related to disc degeneration and degenerative disc disease in 41 countries. The line between the two points in the graph indicates that a similar relationship has been established between the two journals/institutions/countries. The thicker the line, the stronger the connection between the two journals/institutions/countries.

3.5. Co-citation analysis

3.5.1. Publications

403 articles (defined as the minimum number of citations for a document cited more than 20 times) were analyzed using VOS viewer (Figure 5a). The top five studies with the highest total link strength are as follows: Spine journal, September 2001;26 (17) : 1873- 1878 (total link strength = 3145 times) [17] ;Journal of Spine, August 2006;31 (18) : 2151-2161 (total link strength =2242 times) [18];Nat Rev Rheumatol January 2014;10(1) :44-56 (total link strength =2026 times) [19];Arthritis Res Ther 2005;7 (4) 732 (total link strength = 1851 times) [20]and Journal of Spine, June 1995;20 (11) : 1307-1314 (total link strength = 1638 times) [21].

3.5.2. Journals

VOSviewer is used to analyze the journal name of the co-citation analysis (the journal is defined as a source that has been cited at least 20 times). As shown in Figure 5b, 512 identified journals appear in the total link strength. The top 5 journals in terms of total link strength are:Spine (total link strength =694,421), Eur Spine J (total link strength = 237,626), Spine J (total link strength = 153, 172), J Bone Joint Surg Am (total link strength = 101,319), J Neurosurg-Spine (total link strength =113,258).

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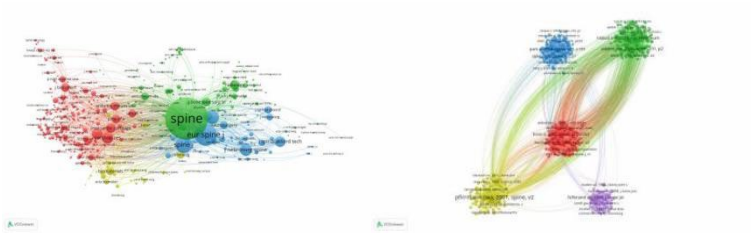


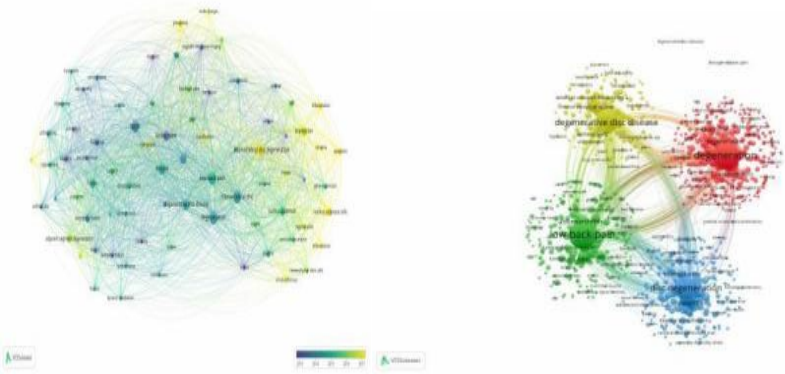
(5a) *(5b)*

Figure 5: Analysis of co-authors of research on global disc degeneration and degenerative disc disease. (a)Link strength diagram of cited frequency of 403 articles in fields related to disc degeneration and degenerative disc disease. (b)Link strength diagram of 512 journals cited in the field of disc degeneration and degenerative disc disease.

3.6. Co-occurrence analysis

The VOSviewer was used to analyze all keywords used in the included study (defined as words used more than 5 times in the title and abstract of all publications). As shown in Figure 6a, the 776 keywords identified were divided into four categories, roughly: "mechanism research ", "animal research ", "clinical research ", and "tissue engineering" (Figure 6a). In the "mechanism study" cluster, the key words are nuclei pulposus, intervertebral disc degeneration, inflammation, and apoptosis. For the "animal research" cluster, the main keywords are: nucleus pulposus stem cells, models. For the "clinical study" cluster, the key words were: low back pain, degenerative disc disease. In the "tissue engineering" cluster, the keywords often used are: spine, in vitro, tissue engineering, nucleus pulposus cells. These results indicate that nucleus pulposus cells and inflammatory responses in the study of intervertebral disc degeneration and degenerative intervertebral disc disease are most prominent in the above four directions [22].

The VOSviewer color-codes keywords (defined as words that have been used more than 40 times in the titles and abstracts of all publications) based on the average time the keywords have appeared in all publications included (Figure 6b). Purple indicates the keyword appears earlier, and yellow indicates the keyword appears later. Before 2014, in the early stages of research, most research was focused on "clinical studies. "According to the latest trends, "mechanism research " and "tissue engineering" will be widely concerned in the future [23].



(6a) *(6b)*

Figure 6: (a)The 776 keywords were grouped together in the areasrelated to disc degeneration and degenerative disc disease. (b)The position of 64 keywords over time in areas related to disc degeneration and degenerative disc disease.

4. Discuss

4.1. Trends in disc degeneration and degenerative disc disease

Bibliometrics and visual analysis can present the current status and predictions of the search field. Therefore, the purpose of this study was to evaluate intervertebral disc degeneration and degenerative

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intervertebral disc disease research, including contributing countries, institutions, funding institutions and research priorities. Recent advances in the study of disc degeneration and degenerative disc disease have been dramatic and exciting. As this study shows, the number of publications per year has increased significantly. In addition, research interest in this field has increased dramatically over the past few years, with a total of 67 countries publishing relevant studies in this field. Based on the available data, we predict the number of future publications. Therefore, more in-depth studies on nucleus pulposus cells and inflammatory responses to disc degeneration and degenerative disc disease will be published in the next few years [24,25]. The current positive results will, in turn, encourage a wide range of researchers to conduct further high-quality research.

4.2. Quality and status of global publications

A country's total citations and H-index represent its academic influence and publication quality [26]. Although the total number of publications in the United States is lower than that in China, the United States contributes the most to global research in terms of total citations and H-index. So, the United States can still be considered a leader in this area. China ranks first in the total number of publications, and second in the total number of citations and H-index. Compared with previous years, the quantity and quality of Chinese publications are increasing and improving year by year, and the research in this field is also in a leading position. With the gradual increase of research funding in China (National Natural Science Foundation: No. 1), the quality of research is expected to improve significantly further.

Springer Nature, Elsevier, Lippincott Williams &Wilkins, Wiley, Sage published more studies on disc degeneration and degenerative disc disease. But Springer Nature, Elsevier, Lippincott Williams &Wilkins publish two to three times as many papers as the fourth-ranked journal, so further research in the field is most likely to come first to those publishers at the top of the list.

In these top five countries, their research institutions are leading the way in the field of disc degeneration and degenerative disc disease, which is in line with their leading position in global publications. And almost all of the top 20 universities are in the top five countries. All these show that the foundation of a country's academic level lies in the establishment of more first-class universities and research institutes. At the same time, we also listed the authors of more published studies in this area, indicating that we can closely follow these authors for further research to obtain the latest advances in disc degeneration and degenerative disc disease.

This study uses bibliographic coupling analysis to establish similarity between publications in terms of journals, institutions and countries. Bibliographic coupling occurs when two works cite the same third work in their bibliography. These data show that Spine is the journal most associated with this field, and that the United States is leading the way in this field. The purpose of co-citation analysis is to investigate the impact of research by counting the number of concurrent citations of research. The present results indicate that the signature study of nucleus pulposus cells and inflammatory responses in disc degeneration and degenerative disc disease has a larger total frequency of induction. In the research field of intervertebral disc degeneration, nucleus pulposus cells and inflammatory response are frequently cited keywords in this field [27].

4.3. Research mainly focused on nucleus pulposus cells and inflammatory response

Based on co-occurrence analysis, we found research directions and hot topics in this field. Keywords in all titles and abstracts included in the study were analyzed to create a co-occurrence network map. Four research directions can be observed from the co-occurrence map (Figure 6a), including mechanism studies, animal studies, clinical trials, and tissue engineering. While this result is consistent with common sense in the field, this study could make future research more clear. In the central position of the co-occurrence map, the weight of key words such as nucleus pulposus cells and inflammatory response is higher, and the display is more prominent. Therefore, further high-quality studies are needed to evaluate the intervertebral disc degeneration and degenerative intervertebral disc disease in nucleus pulposus cells and inflammatory responses in these four directions [28].

Taken together, this study demonstrates the global trend of disc degeneration and degenerative disc disease. The United States and China are the largest contributors to the study, leading global research in the field. The Springer Nature publishing Group has published the most articles related to it. We can predict that more studies on disc degeneration and degenerative disc disease will be published in the coming years. In particular, the mechanism of nucleus pulposus cells and inflammatory response in intervertebral disc degeneration and degenerative intervertebral disc disease as well as tissue

ISSN 2618-1584 Vol. 5, Issue 5: 11-19, DOI: 10.25236/FMSR.2023.050502

engineering research will receive more attention and become a hot spot in the future[29,30].

Acknowledgement

Fund: Health Commission of Shanxi Province (No. : 2020133)

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