Global research in cartilage defects: a bibliometric and visualized study

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Research

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Abstract

Objective: Cartilage defects represent an area of intense research interest worldwide among basic scientists and clinicians. This study evaluates the current global status of research into cartilage defects and predicts future trends through bibliometric and visualized analyses.

Method: Publications from 1980 to 2018 on research into cartilage defects were obtained from the Science Citation Index-Expanded Web of Science. Bibliometric methods were used to analyze and index the source data. For visualization studies, VOSviewer software was used conduct bibliographic coupling, co-authoring, co-citation, and co-occurrence analyses.

Result: A total of 9,194 publications were included in this study. The total number of publications in the field is generally on the rise, but in recent years the rate of increase in publications and relative research interest have declined. The USA made the greatest contribution to research on cartilage defects, with the highest number of citations and H-index. *The American Journal of Sports Medicine* published the highest number of articles, and Harvard University had the highest institutional contribution to the field. The most prominent research directions relating to cartilage defects are clinical studies, tissue engineering studies, chondrocyte-based studies, and stem cell-related studies.

Conclusion: The number of publications per year on cartilage defects will likely stabilize in the next 10 years based on current global trends. Future research in the field will likely focus on clinical studies and new directions based on regenerative medicine.

Introduction

Cartilage is a highly specialized type of connective tissue that contains a single cell type, namely chondrocytes, and a low cell density [1]. Rich extracellular matrix and lack of blood vessels are two major characteristics of cartilage tissue, giving it unique structural characteristics that result in unusual rigidity and resilience to fulfil its biological functions [2]. However, the avascular and aneural structure of cartilage makes tissue repair very difficult once it has been damaged. Since the nutritional supply of cartilage mainly comes from the surrounding interstitial fluid by diffusion, it cannot satisfy the high metabolic demands of damaged cartilage tissues undergoing repair [3]. Cartilage in different parts of the body consists of three main subtypes with differences in their biological roles: hyaline cartilage, elastic cartilage and fibrocartilage. As the most abundant form of cartilage in the human body, hyaline cartilage covers articular surfaces and has critical roles of enabling joint movement and shock absorbance. The extracellular matrix components specific to different types of cartilage, such as type II collagen in hyaline cartilage and elastin in elastic cartilage, which are critical for the biological function of these tissues, are very difficult to restore after damage [1, 4]. Repair often results in replacement of the extracellular matrix with type I collagen to form tissue that more closely resembles fibrocartilage and does not fulfil the functions of the original tissue.

The goals of treatment for cartilage injuries are to effectively fill the defect area, to regenerate the native extracellular matrix, and to restore the mechanical properties of local repair sites. However, current treatments are still faced with significant challenges and long-term repair of cartilage is often unsatisfactory, which may contribute to other pathologies such as fibrosis and osteoarthritis. Basic science research into cartilage restoration has focused on regeneration mechanisms at the cellular level and the construction of various tissue engineered cartilage systems [5-8]. In clinical research, particularly for articular cartilage, several surgical and autologous chondrocyte implantation (ACI) techniques have been used for damage repair and have been continuously optimized [9-12]. In addition, there has been recent research targeting the regulation of cartilage phenotype during repair, to address the challenges of cell hypertrophy at the chondrocyte level *in vitro* and excessive fibrosis at the tissue level *in vivo* [13, 14].

As a core part of scientific research, publishing is an important indicator of the global trends in a particular field of research. Publication data can be used to qualitatively and quantitatively evaluate research trends over time and analyze the contributions of scholars, journals, institutions and countries in the field through bibliometric analysis [15]. In medical research, bibliometric analysis can also contribute to the development of relevant policies and clinical guidelines to aid treatment of specific diseases [16]. Existing research has demonstrated that bibliometric analyses can assess research trends in areas such as sepsis [17], diabetes mellitus [18], and the spine [19]. This study aims to analyze existing research in the literature relating to cartilage defects through bibliometric and visualized analyses, to reveal global trends and predict future developments that would be useful for gaining a broad understanding of the field by basic scientists and clinicians alike.

Materials And Methods

Data source

Publication data was obtained from Science Citation Index-Expanded (SCI-E) of the Web of Science (WoS), which is a database suitable for use in bibliometric analysis, according to methods similar to that employed in previous studies [20].

Search strategy

Publications were retrieved from the WoS database on 23 October 2019 according to appropriate search terms, which were set to: theme = cartilage defects AND publishing year = (1980–2018) AND Language = (English) AND Document types = (ARTICLE OR REVIEW). The search for publications from specific countries or regions was refined by selecting for country/region in WoS.

Data collection

TXT files containing the full information for all publications were downloaded from the WoS database. The title, year, journal, author, nationalities, affiliations, keywords and abstract of publications included in the TXT files were imported into Microsoft Excel 2019. The data entry and collection process were

performed and verified by two authors independently (HL and YZ). Finally, the data was manually organized and analyzed in Microsoft Excel 2019.

Bibliometric analysis

Functional metrics in WoS were used to evaluate the basic characteristics of retrieved publications. The H-index represents an H number of papers that have been published by a scholar or country, where each paper has been quoted by at least H other publications [21]. This measurement of the impact of scientific research by an individual entity reflects both the number of publications and the number of citations per publication [22]. Relative research interests (RRI) represents the ratio of the number of publications in a certain field over the number of all-field publications per year. The time curve of publications was plotted by R software (version 3.1.3). The logistic regression model: $f(x) = c/(1+a\times exp[-b\times(x-1994)])$ was used, in which the variable x represented the year and $f(x)$ represented the cumulative amount of papers. The inflection point, defined as the time at which the growth rate of publications changeed from positive to negative, was calculated using the formula $T = lna/b+1994$.

Visualized analysis

VOSviewer (Leiden University, The Netherlands) was used to conduct visualized analyses of the retrieved publications [23], through bibliographic coupling, co-authorship, co-citation and co-occurrence analyses.

Results

Trends in global publication

Amount of global publications

Within the time period of 1980 to 2018, we retrieved 9,194 publications that met the search criteria. A plot of the global number of publications on research into cartilage defects showed that 2017 had the highest number of publications, with 662 documents that accounted for 7.2% of total publications in the field (Figure 1A). Although the number of global publications in the field showed an exponential increase between 1980 and 2018, the rate of increase has slowed in recent years and led to a gradual decline in relative research interest.

Contributions of countries

Publications from 61 countries worldwide have contributed to research into cartilage defects (Figure 1B). From the top 20 countries in the field (Figure 1C), the USA made the highest contribution to publication number (3,510 articles accounting for 35.88% of total publications), followed by Germany (1,110 articles, 11.35%), China (1,083 articles, 11.07%), and Japan (910 articles, 9.30%).

Global publication trends

To predict future publishing trends, a time curve was constructed to show the number of publications through a logistic regression model (Figure 1D). As predicted by the model, the rate of increase in publications on cartilage defects may slow down in the next 10 years, and annual publication number may tend to stabilize.

Publications from different countries

Total citation frequency

The USA had the highest number of citations for their publications on cartilage defects, with a total exceeding 15,000 citations (Figure 2A). This was followed by Germany and Japan with total citation numbers of 36,866 and 27,420, respectively.

Average citation frequency

Sweden had the highest average citation frequency for their publications on cartilage defects at 86.26 citations per publication (Figure 2B). This was followed by Switzerland (44.68 citations) and the USA (43.18 citations).

H-index

H-index for publications on cartilage defects is highest for the USA (172), followed by Germany (87) and Japan (78).

Analysis of contributions to the field

Journals

Among all journals which have published articles on cartilage defects, *The American Journal of Sports Medicine* (2018 impact factor [IF] = 6.093) contributed the highest total number of publications, comprising 399 articles over nearly 40 years which accounted for 4.08% of publications in the field (Figure 3A). This was followed by *Osteoarthritis and Cartilage* (2018 IF = 4.879) and *Knee Surgery Sports Traumatology Arthroscopy* (2018 IF = 3.149) which contributed 310 and 272 articles respectively over the same time period.

Funding sources

The United States Department of Health Human Services and the National Institutes of Health were the funding sources with the highest contributions to publications on cartilage defects, with comparable contributions at 1195 and 1194 publications respectively (Figure 3B). These were followed by the National Natural Science Foundation of China and the NIH National Institute of Arthritis Musculoskeletal Skin Diseases.

Research orientation

Among the different research orientations covered by publications on cartilage defects, the three most prominent areas were orthopedics, surgery and engineering (Figure 3C). These were followed by materials science, sport sciences and cell biology.

Institutions

Harvard University had by far the highest number of publications (264 articles) on cartilage defects compared to other institutions (Figure 3D). This was followed by Monash University and the Hospital for Special Surgery.

Authors

Among the top contributing authors to publications on cartilage defects, Cicuttini FM was ranked first with 115 articles (Figure 3E). All other authors have not published more than 100 articles in the field.

Bibliographic coupling analysis

In bibliographic coupling analysis, citations of the included publications were used to establish similarity relationships between documents.

Journals

Among the 331 journals that have established similarity links through publications on cartilage defects (Figure 4A), bibliographic coupling analysis showed that those with the highest total link strength were: *The American Journal of Sports Medicine* (916,442 times), *Knee Surgery Sports Traumatology Arthroscopy* (607,470 times), *Osteoarthritis and Cartilage* (510,569 times), *Journal of Orthopaedic Research* (398,928 times), and *Arthroscopy: The Journal of Arthroscopic & Related Surgery* (373,134 times).

Institutions

A total of 819 research institutions were identified with at least 5 publications on cartilage defects (Figure 4B). Bibliographic coupling analysis showed that the institutions with the highest total link strength were: Harvard University (673,638 times), Medical University of Vienna (379,172 times), University of California San Diego (368,682 times), Hospital for Special Surgery (366,866 times), and Rush University (348,134 times).

Countries

A total of 55 countries were identified with at least 5 publications on cartilage defects (Figure 4C). Bibliographic coupling analysis showed that the countries with the highest total link strength were: USA (4,193,325 times), Germany (2,278,658 times), Japan (1,493,899 times), China (1,157,471 times), and England (972,769 times).

Co-authorship analysis

In co-authorship analysis, the correlation between items was determined by their number of co-authored publications.

Authors

A total of 1,890 authors were identified with at least 5 publications on cartilage defects (Figure 5A). Co-authorship analysis showed that the authors with the highest total link strength were: Cicuttini FM (509 times), Jones G (431 times), Filardo G (325 times), Kon E (314 times), and Ding CH (287 times).

Institutions

From the 819 institutions identified to have at least 5 publications on cartilage defects (Figure 5B), co-authorship analysis showed that the institutions with the highest total link strength were: Harvard University (380 times), Monash University (290 times), University of Tasmania (167 times), Hospital for Special Surgery (162 times), and University of Pittsburgh (158 times).

Countries

From the 55 countries identified to have at least 5 publications on cartilage defects (Figure 5C), co-authorship analysis showed that the countries with the highest total link strength were: USA (1,326 times), Germany (680 times), Switzerland (447 times), England (405 times), and China (375 times).

Co-citation analysis

In co-citation analysis, the correlation between items was determined by the number of times that they were cited together.

References

A total of 2,179 cited references were identified that have been cited at least 20 times in research on cartilage defects (Figure 6A). Co-citation analysis showed that the references with the highest total link strength were: Brittberg M, 1994, *New Eng J Med* (21,515 times) [11]; Peterson L, 2000, *Clin Orthop Relat Res* (8,796 times) [24]; Knutsen G, 2004, *J Bone Joint Surg Am* (8,121 times) [25]; Steadman JR, 2004, *Arthroscopy* (7,136 times) [26]; and Shapiro F, 1993, *J Bone Joint Surg Am* (6,972 times) [27].

Journals

A total of 1,301 journals were identified that had at least 20 co-cited references in research on cartilage defects (Figure 6B). Co-citation analysis showed that the journals with the highest total link strength were: *Journal of Bone and Joint Surgery* (592,100 times), *Biomaterials* (541,148 times), *The American Journal of Sports Medicine* (495,983 times), *Clinical Orthopaedics and Related Research* (478,843 times), and *Osteoarthritis and Cartilage* (460,793 times).

Co-occurrence analysis

Co-occurrence analysis is performed to identify keywords in a particular research area that indicate the most popular topics and point to future developments in the field (28).

A total of 2,626 keywords were identified that had appeared at least 5 times in the title and abstract of all included publications. The co-occurrence map showed that these keywords were generally divided into four clusters (Figure 7A). Main keywords for ‘clinical studies’ were knee, defects, osteoarthritis, transplantation, and microfracture. Main keywords for ‘tissue engineering studies’ were repair, tissue, in-vitro, full-thickness defects, and collagen. Main keywords for ‘chondrocyte-based studies’ were chondrocytes, differentiation, expression, growth, and cells. Main keywords in ‘stem cell-related studies’ were marrow stromal cells, progenitor cells, and human bone-marrow.

The keywords were also colored according to the average time that they appeared in all included publications (Figure 7B). Earlier keywords were shown in blue and later keywords in red, while those in the middle were shown in green or yellow. Early research on cartilage defects tended to focus on chondrocyte implantation and osteochondral lesions, while the latest research shows heightened interest in stem cells, mechanistic pathways, and various biomaterials.

Discussion

Bibliometric analysis and visualization studies can be used to assess the current state of a research field and predict future trends based on existing publications. This is the first study to utilize such methods to assess the global contributions of countries, institutions, journals, and authors to publications on cartilage defects, and to perform bibliographic coupling, co-authorship, co-citation and co-occurrence analyses of these entities. Based on our analysis, it is evident that although the total number of studies continues to increase in the field, the rate of increase has declined in recent years. These trends are possibly influenced by developments in clinical treatments and tissue engineering approaches related to cartilage defects in the last few decades. For instance, the development of new treatment techniques such as ACI for cartilage defects, and the exciting prospect of being able to tissue engineer artificial cartilage using cells and biomaterials in the 1990s to 2000s were possibly responsible for the exponential increase in related publications during this time period [12, 29]. However, with greater understanding gained in recent years relating to the low regenerative capacity of cartilage, difficulties in replicating its zonal architecture and in integrating engineered and native tissues, and in replicating its functional properties using the available cell sources and biomaterials, scientists and clinicians are beginning to understand the challenges associated with long-term cartilage repair [29]. This has possibly led to a decline in the overall rate of publication in research relating to cartilage defects, but increased depth and quality of the research into previously unexplored approaches and mechanistic pathways.

Our analysis showed that the USA is the top contributing country to global research on cartilage defects, judging by a number of parameters including the total number of publications and citations, H-index, funding source and contributing institutions. Interestingly, although both Germany and China are highly

ranked and comparable in the number of publications in the field, the citation count and H-index of Germany is consistent with its ranking in publication number while China only ranks 6th and 7th respectively. This is likely due to greater emphasis on the number of publications rather than publication quality in the current Chinese evaluation system [30]. Nevertheless, with increased funding injected by the National Natural Science Foundation of China as one of the top funders in the field, the quality of publications will potentially increase in future years to match the amount of publication output.

Among the top six journals with the highest number of publications on cartilage defects, half of them have a focus on clinical research (*The American Journal of Sports Medicine, Knee Surgery Sports Traumatology Arthroscopy,* and *Arthroscopy: The Journal of Arthroscopic & Related Surgery*), suggesting that clinical research on cartilage defects have attracted significant attention over the past 40 years. These same journals are likely to be the main publishing channels for future clinical research in the field. As a major output channel for basic science studies, the high ranking of *Biomaterials* in the top contributing journals on cartilage defects suggests that approaches relating to biomaterials and tissue engineering have been the focus of significant research interest over the past few decades.

Bibliographic coupling occurs when two publications cite a common third work in their references, which establishes a similarity relationship between these publications. From our bibliographic coupling analysis of journals, institutions and countries, we observed that *The American Journal of Sports Medicine* was the most relevant journal for research on cartilage defects, while Harvard University and the USA were the leading institution and country in the field respectively. Co-authorship analysis assesses the collaborating relationship between authors, institutions or countries. Items with higher total link strength for co-authored publications are considered more willing to cooperate. In terms of institutions and countries, the results of bibliographic coupling and co-authorship analyses showed a certain degree of correspondence, suggesting that collaborative research might help to promote the influence of individual institutions and countries in this field. Co-citation analysis evaluates the impact of publications or journals by counting the number of times that they were cited together. In terms of the top journals, the results of co-citation analysis mostly overlapped with rankings by bibliographic coupling and overall publication number. The only exception was the *Journal of Bone and Joint Surgery*, which was highly ranked for co-citations but not for the other two measurements, possibly suggesting that publications by this journal on cartilage defects are proportionally more likely to attract a large number of citations.

Mapping of co-occurrence networks for keywords arising from research on cartilage defects revealed interesting trends on current and future directions. The most prominent keywords including knee, defects and repair occurred in the clusters on ‘clinical studies’ and ‘tissue engineering studies’, verifying that these are the two most popular research categories in the field. Further interesting observations arose when a different color code was introduced to differentiate the same co-occurrence map by the time of appearance of the keywords. Keywords on the periphery of all four clusters, which were represented by small-sized points due to their lower frequency of appearance, and which have not yet made significant connections with other keywords were mostly colored towards the red end of the spectrum. These included keywords such as bone marrow lesions, design, in-vitro chondrogenesis, and neural crest. It can

be anticipated that these represent very recent, innovative developments in research relating to cartilage defects that may give rise to the next breakthroughs in our future understanding of the field.

Conclusion

This was the first study to evaluate global trends in research on cartilage defects. The USA and Harvard University were respectively the top contributing country and institution, while *The American Journal of Sports Medicine* could be considered the most relevant journal in the field. Although the rate of publication output will likely stabilize over the next 10 years, exciting developments in the field will likely bring new insights in our understanding of biomaterials design, mechanistic pathways and clinical treatments relating to cartilage defects.

Declarations

Funding

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Conflict of interest

The authors declare that they have no conflicts of interest.

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Figures

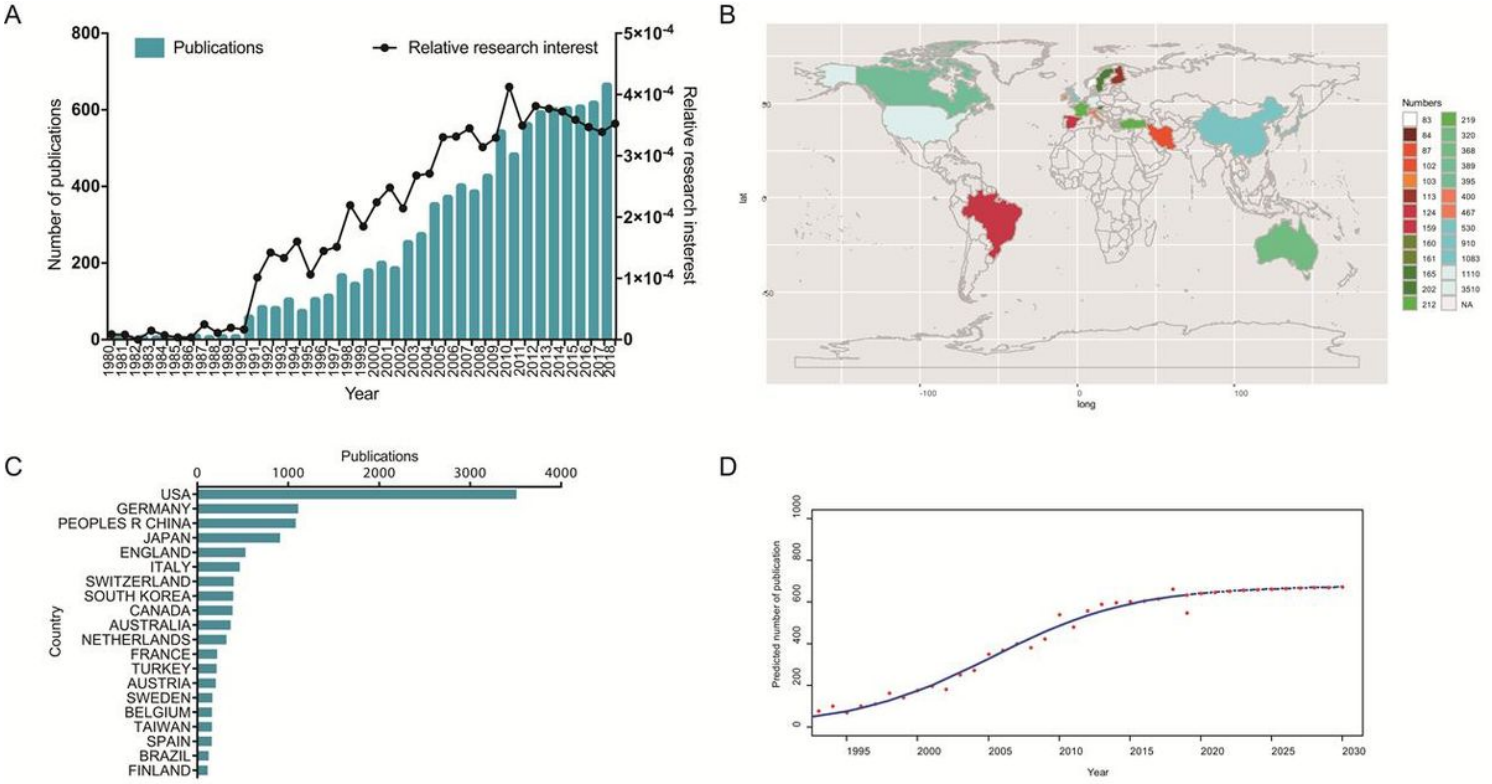

Figure 1

Trends in global publications on cartilage defects. (A) The global number and relative research interests of publications in the field. The histogram represents the single-year publication numbers, and the curve represents the relative research interests. (B) World map showing the distribution of publications in the field. (C) The number of publications from the top 20 countries. (D) Model of growth trends in worldwide publications to predict future publication trends.

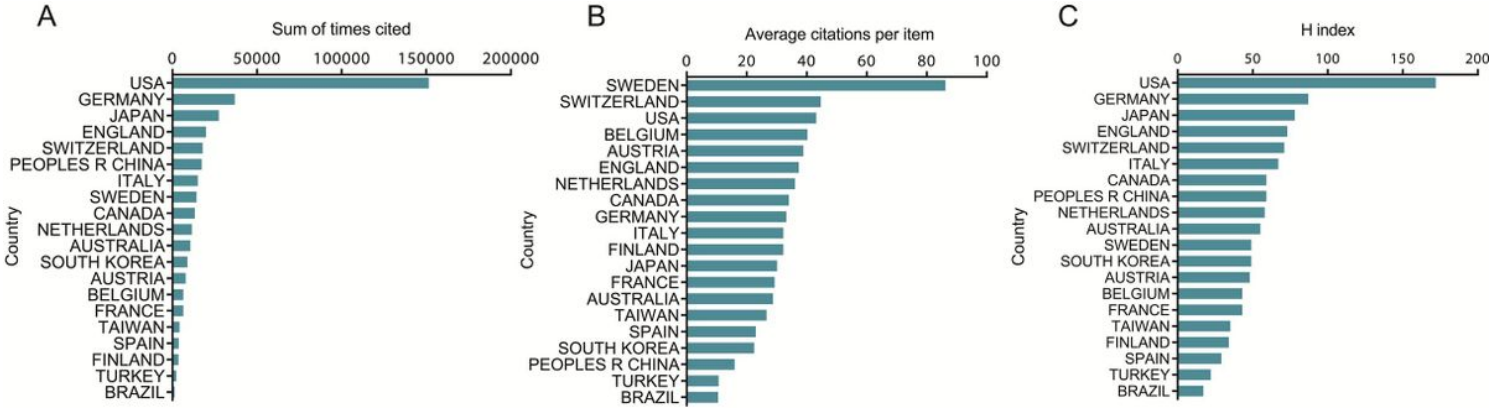

Figure 2

Publications from different countries on cartilage defects. (A) Total citation frequency for publications from different countries. (B) Average citations per publication for different countries. (C) H-index of publications for different countries.

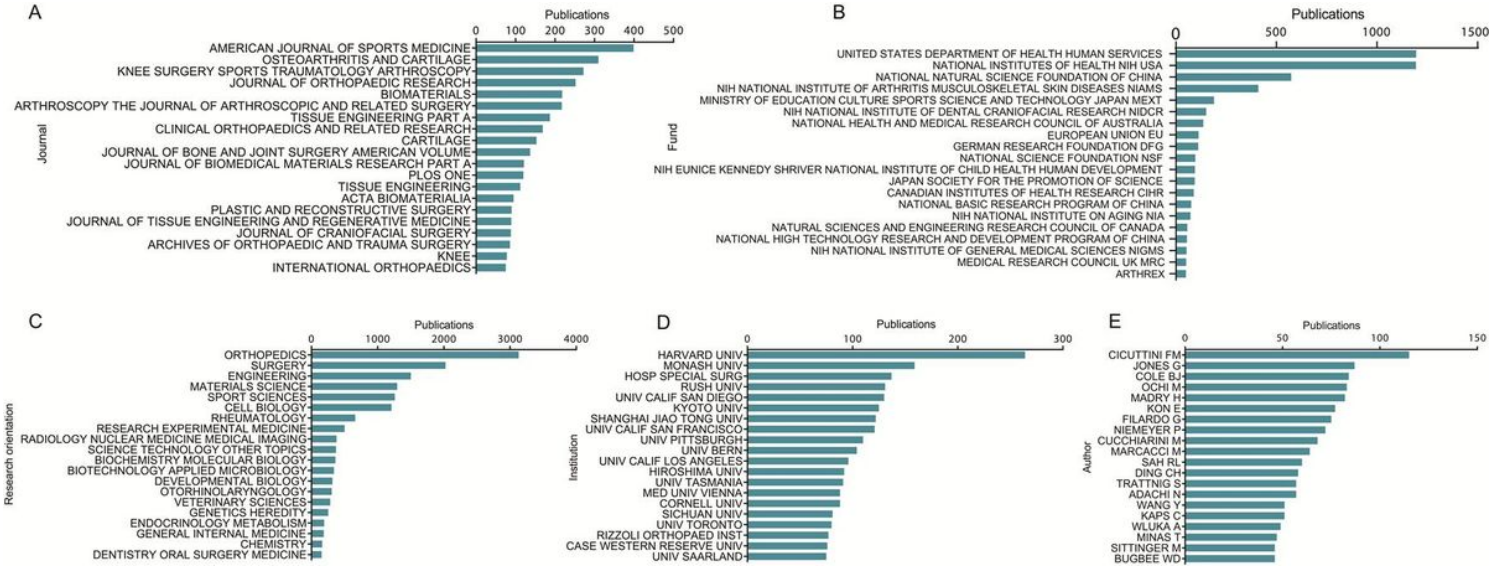

Figure 3

Analysis of contributions to global research on cartilage defects. (A) The top 20 publishing journals. (B) The top 20 funding sources contributing to the research. (C) The top 20 research orientations in the field. (D) The top 20 publishing institutions. (E) The top 20 contributing authors to the field.

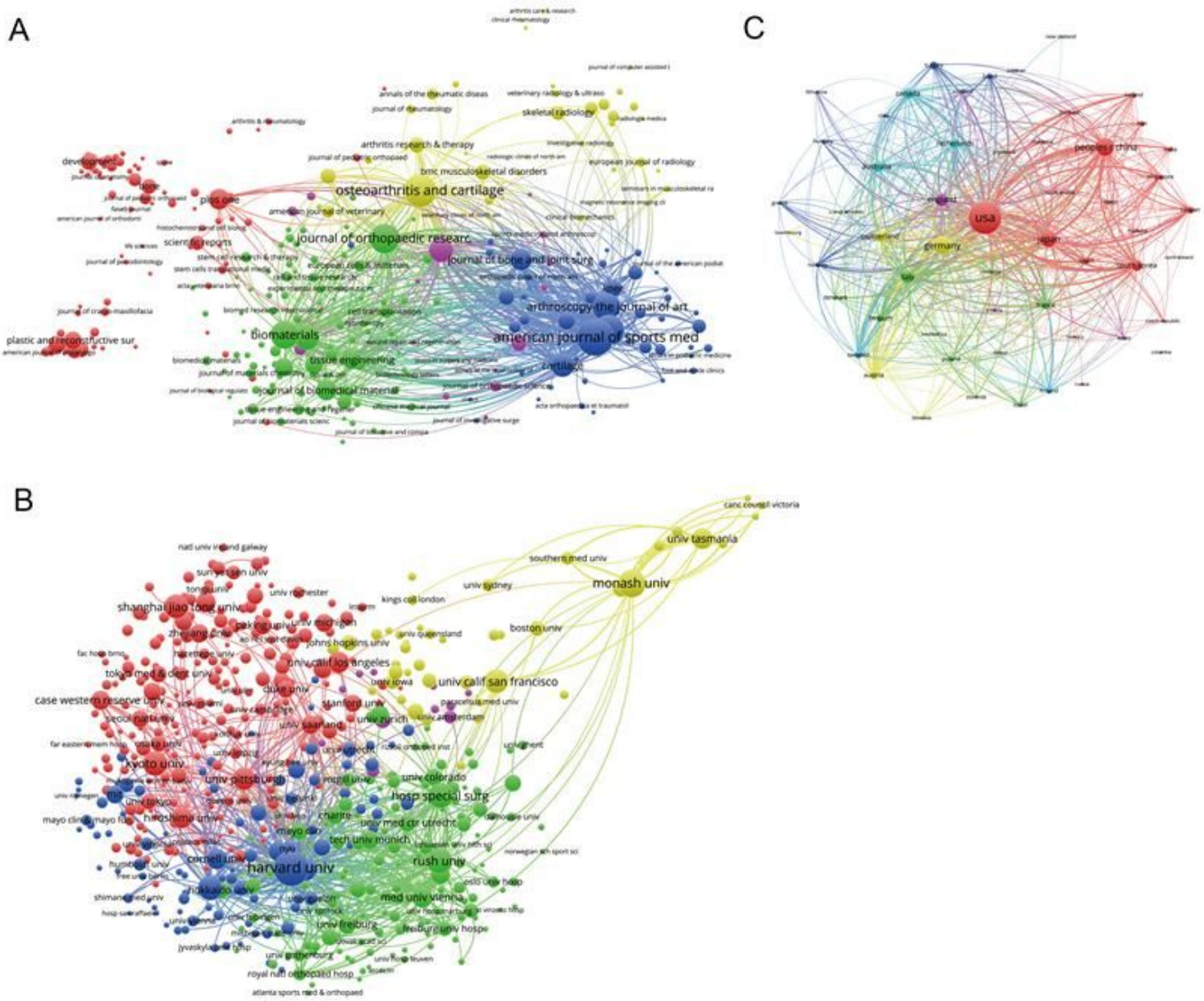

Figure 4

Bibliographic coupling analysis of global research on cartilage defects. Mapping of the (A) 331 identified journals, (B) 819 institutions, and (C) 55 countries through bibliographic coupling. The line between two points indicates that the two entities had established a similarity relationship. A thicker line indicates a closer link between the two entities.

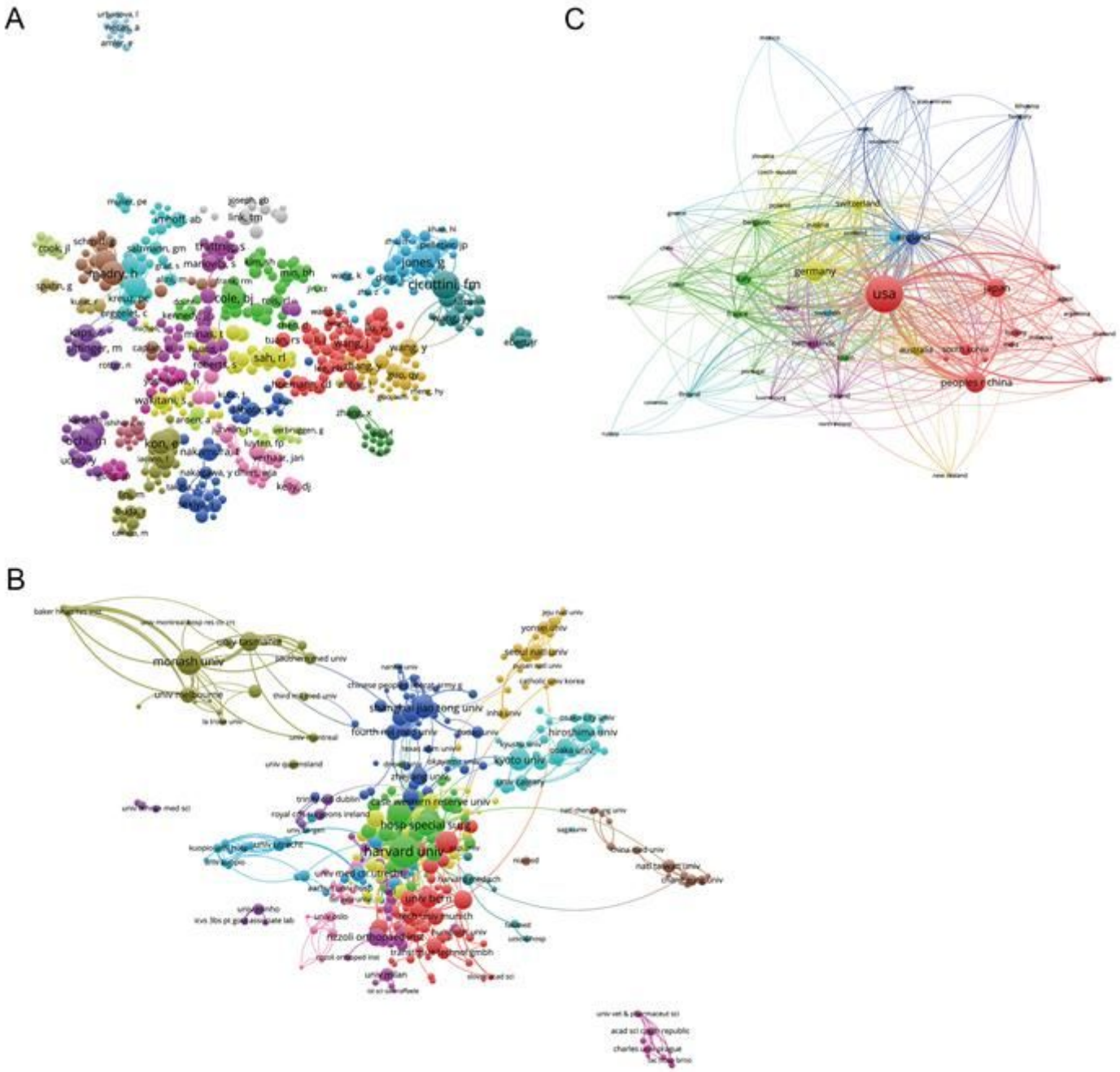

Figure 5

Co-authorship analysis of global research on cartilage defects. Mapping of the (A) 1,890 identified authors, (B) 819 institutions, and (C) 55 countries through co-authorship analysis. The size of the points represents the co-authorship frequency. The line between two points indicates that the two entities had established a collaboration. A thicker line indicates a closer collaboration between the two entities.

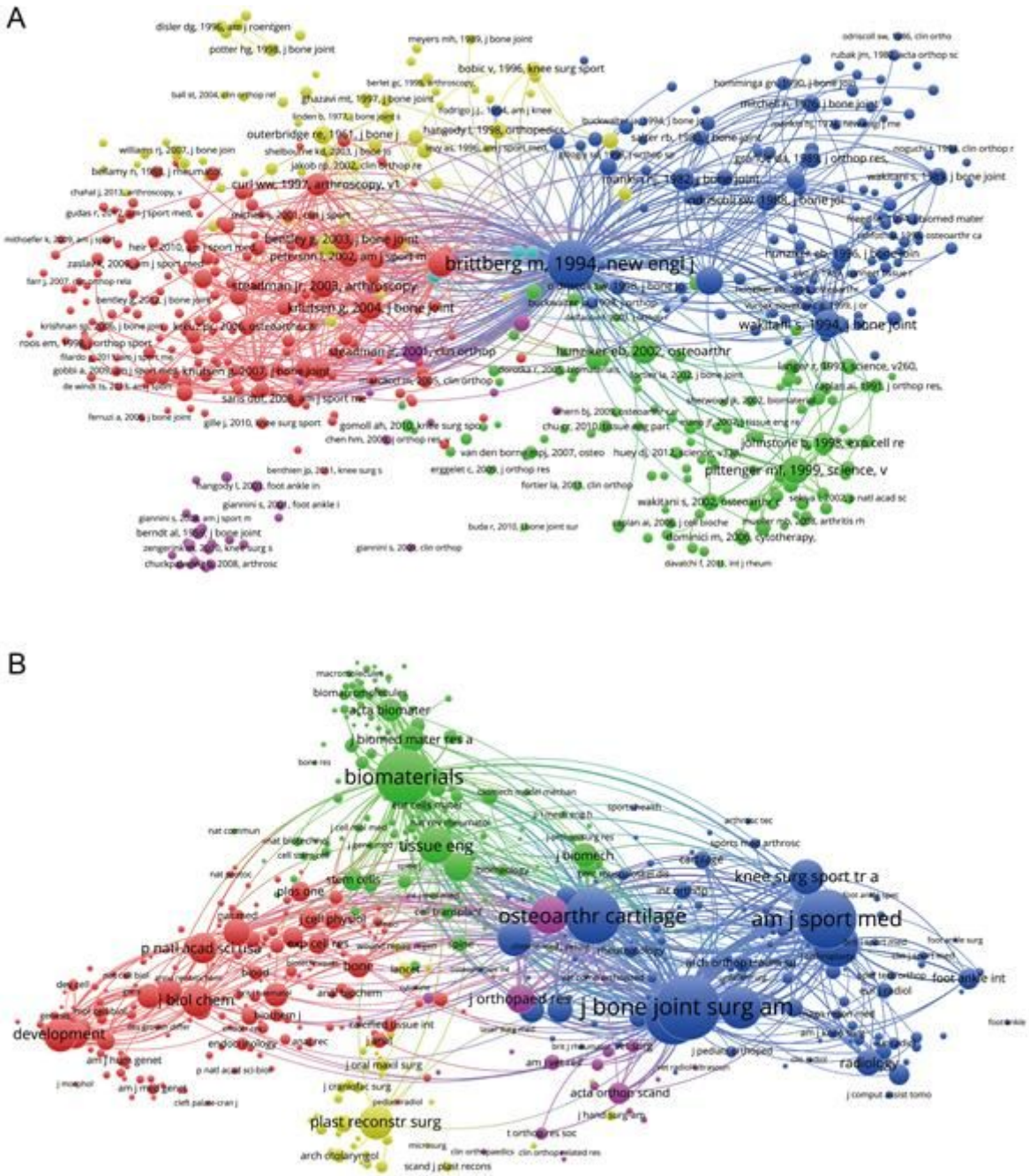

Figure 6

Co-citation analysis of global research on cartilage defects. Mapping of the (A) 2,179 cited references and (B) 1,301 journals through co-citation analysis. The size of the points represents the citation frequency. A line between two points means that both were cited in one paper or journal. A shorter line indicates a closer link between two papers or journals. Points with the same color belong to the same research direction.

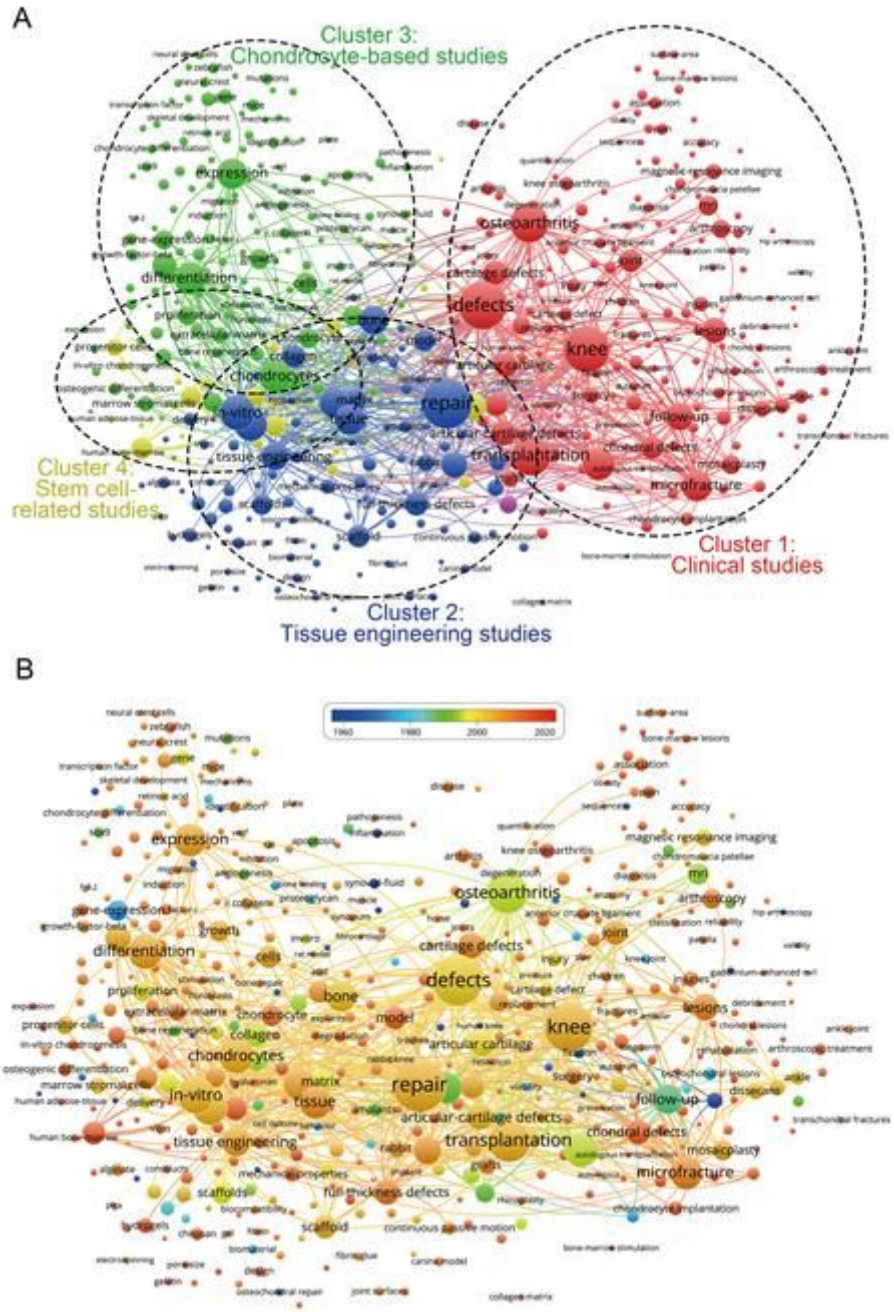

Figure 7

Co-occurrence analysis of global research on cartilage defects. (A) Mapping of keywords relating to research on cartilage defects. The keywords are broadly divided into four clusters: clinical studies (red), tissue engineering studies (blue), chondrocyte-based studies (green), and stem cell-related studies (yellow). The size of the points represents the frequency of appearance. (B) Distribution of keywords according to their mean time period of appearance in the literature. Keywords in blue appeared earlier than those in green and yellow, while keywords in red appeared the latest.