

RESEARCH TRENDS OF MICRORNA STUDIES IN ORTHOPEDICS: A BIBLIOMETRIC ANALYSIS STUDY

ORTOPEDİDE MİKORNA ÇALIŞMALARININ ARAŞTIRMA EĞİLİMLERİ: BİBLİYOMETRİK ANALİZ ÇALIŞMASI

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ABSTRACT

Introduction: MicroRNA (miRNA) is a molecule consisting of a single nucleotide sequence. Its discovery is considered one of the most recent scientific breakthroughs. MicroRNA offers significant potential for both diagnostic and therapeutic applications. Although microRNA has been extensively studied in many fields, including orthopaedics, a bibliometric analysis specific to orthopaedics has not been performed in recent years. We aimed to summarise the comprehensive information map, development landscape, and future directions of microRNA studies published in orthopaedic research.

Methods: In this study, we used a bibliometric approach. The Web of Science database was used to retrieve microRNA studies published in orthopaedic research between 2003 and 2022. Biblioshiny and VOSviewer tools were used for analysis.

Results: A total of 292 research articles on miRNA were published in the field of orthopaedics by 1601 authors. The annual growth rate was 23.12%. 2021 was the year with the highest number of articles (n=62) and citations (n=946). The studies were published across 28 countries, with the majority originating from China (n=182, 62.329%) and the United States (n=52, 17.808%). China's publications continued to increase compared to other countries.

Conclusions: Although the number of publications is low compared to other research areas, global research on microRNA in orthopaedics has gained more attention in the last decade. Our results provide useful information for researchers to grasp the basic knowledge structure and identify current research hotspots, potential partners, and future research frontiers in this field.

Keywords: Bibliometric analysis, MicroRNA, miRNAs, Orthopaedics

ÖZET

Giriş: MikroRNA (miRNA) tek bir nükleotid dizisinden oluşan bir moleküldür. Keşfi en son bilimsel buluşlardan biri olarak kabul edilmektedir. MikroRNA hem tanı hem de tedavi için büyük umut vaat etmektedir. MikroRNA, ortopedi de dahil olmak üzere birçok alanda kapsamlı olarak çalışılmış olmasına rağmen, son yıllarda ortopediye özgü bir bibliyometrik analiz yapılmamıştır. Ortopedik araştırmalarda yayınlanan mikroRNA çalışmalarının kapsamlı bilgi haritasını, gelişim ortamını ve gelecekteki yönelimlerini özetlemeyi amaçladık.

Yöntemler: Bu çalışmada bibliyometrik bir yaklaşım kullandık. Web of Science veri tabanı, 2003 ve 2022 yılları arasında ortopedik araştırmalarda yayınlanan mikroRNA çalışmalarını almak için kullanıldı. Analiz için Biblioshiny ve VOSviewer araçları kullanıldı.

Bulgular: Ortopedi alanında 1601 yazar tarafından miRNA ile ilgili toplam 292 araştırma makalesi yayınlandı. Yıllık büyüme oranı %23,12 idi. 2021 yılı en fazla makale (n=62) ve atıf (n=946) alan yıl oldu. Yayınlar, çoğunluğu Çin (n=182, %62,329) ve Amerika Birleşik Devletleri'nden (n=52, %17,808) olmak üzere 28 ülkeden geldi. Çin'in yayınları diğer ülkelere kıyasla artmaya devam etmiştir.

Sonuç: Yayın sayısı diğer araştırma alanlarına kıyasla düşük olsa da ortopedide mikroRNA üzerine yapılan küresel araştırmalar son on yılda daha fazla dikkat çekmiştir. Sonuçlarımız, araştırmacıların temel bilgi yapısını kavramaları ve bu alandaki mevcut araştırma noktalarını, potansiyel ortakları ve gelecekteki araştırma sınırlarını belirlemeleri için yararlı bilgiler sağlamaktadır.

Anahtar Kelimeler: Bibliyometrik analiz, MikroRNA, miRNA'lar, Ortopedi

INTRODUCTION

MicroRNAs (miRNAs) are short ribonucleic acid (RNA) molecules between 19 and 25 nucleotides in size that control the post-transcriptional silencing of target genes. A single miRNA can affect the expression of numerous genes involved in a functionally interconnected pathway and target hundreds of miRNAs (1). MiRNAs can be isolated from cells, tissues, and other body fluids (serum, plasma,

tears, saliva, urine, feces, synovial fluid, follicle fluid, gastric juice, pancreatic juice, bile, etc.) (2,3).

In the two decades since the discovery of the first miRNA, the study of miRNA biology has grown significantly (4). More than 1,000 human miRNAs have been identified, and miRNAs regulate more than 50% of the protein-coding genes in mammals (5). At the preclinical stage, miRNA mimics and inhibitors are being developed as

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Received date: 20.03.2024 **Accepted date:** 29.05.2024

Cite as: Dülgeroğlu TC, Kurt M, Gökmen MY, Uluöz M. Research Trends of MicroRNA Studies in Orthopedics: A Bibliometric Analysis Study. *Eskisehir Med J.* 2024; 5(3): 117-121. doi: 10.48176/esmj.2024.170.

novel therapeutics (1). In addition, miRNAs have the potential to be used as biomarkers for diagnostic purposes (6). Numerous technology platforms have been created for miRNA isolation, quantification, profiling, target detection, and alteration of miRNA levels in vitro and in vivo (1). The ambiguity of reference expression levels, the lack of standardization, the considerable experimental heterogeneity (both technical and study design/population), and the ability of miRNA to target many miRNAs, i.e., genes, make research into miRNA biomarkers difficult. Combining miRNAs may be more efficient than using a single marker (6).

Orthopaedics is a subspecialty of surgical medicine that focuses on the treatment of musculoskeletal disorders, and the field of orthopaedic research continues to expand to address the growing global burden of various diseases, including musculoskeletal injuries and malignancies. Basic biological and mechanical research is advancing rapidly, providing opportunities to translate these discoveries into clinical applications (7). MiRNA studies in orthopaedics have been published on several topics (8-11). A previous systematic review also looked at the possible links between miRNAs and sarcopenia, osteoarthritis, and age-related fractures/osteoporosis. However, the results of the included studies were mixed (6).

The bibliometric method is a technique that quantitatively assesses the contribution of a field of study by using statistical and mathematical techniques to analyze the literature (12). Due to the recent explosion of scientific publications and the accessibility of several freeware bibliometric tools, the application of bibliometric analysis in the medical sciences has grown significantly (13-18). Although there are few publications on miRNA in the literature (19,20), a bibliometric analysis of miRNA studies in orthopaedics has not been published.

The aim of this study was to investigate the trends of miRNA studies in orthopaedics and to provide guidance for future studies.

MATERIALS AND METHODS

Bibliometric data source and search techniques

The Web of Science Core Collection (WoSCC) was selected as the primary data source. The following search methodology was used to search the scientific literature by TOPIC (the titles, abstracts and author keywords) MicroRNA (topic) OR miRNAs (topic) OR microRNA (topic) OR RNA, micro (topic) OR miRNA (topic) OR primary microRNA (topic) OR microRNA, primary (topic) OR primary miRNA (topic) OR miRNA, Primary (Topic) OR pri-miRNA (Topic) OR pri-miRNA (Topic) OR RNA, Small Temporal (Topic) OR Temporal RNA, Small (Topic) OR stRNA (Topic) OR Small Temporal RNA (Topic) OR pre-miRNA (Topic) OR pre miRNA (Topic).

As a time frame of 20 years was set, only articles

published between 2003 and 2022 were included. Only original articles were selected as document type, and the language of publication was not restricted to a specific language. Orthopaedics was chosen as the field of research. The study methodology is described in Appendix 1.

Bibliometric analysis

In the final step, 292 articles were collected and exported as plain text files for the registries. The data, including highly cited publications, journals, countries and institutions, were imported into Microsoft Excel 2019 for analysis, ranking, and counting. Bibliometric maps of bibliographic couplings between journals and countries were created and examined using the VOSviewer software (version 1.6.18) from Leiden University, the Netherlands (21). The *Biblioshiny Bibliometrics* software generated bar charts and additional bibliometric data, such as a comprehensive science mapping analysis (22).

The most productive journals, countries, and institutions were ranked using traditional bibliometric techniques. According to Hirsch, the H-index was used to assess the quantity and quality of research output by authors, countries, and institutions (23). Journal Impact Factor (IF) was obtained using the Thomson Reuters Journal Citation Report. On 3 March 2023, the citation analysis was completed in a single day to avoid bias from daily database updates. The extracted information was collected and analyzed using indicators studied in previous bibliometric studies (13-20).

RESULTS

A total of 292 miRNA-related research articles were found in the field of orthopaedic research. The annual growth rate of these articles was 23.12%. The miRNA research articles published in the field of orthopaedics were written by 1601 authors. The international co-authorship rate was 11.3% (Figure 1). Between 2003 and 2022, an average of 19.05 articles were published per year. A summary of the general characteristics of miRNA studies published in the field of orthopaedics between 2003 and 2022 is described in Figure 1.

Although the number of publications was irregular, the number of articles per year increased after 2010. 2021 was the year with the highest number of published articles



Figure 1: Summary of main characteristics of miRNA studies published between 2003 and 2022 in the field of orthopaedics

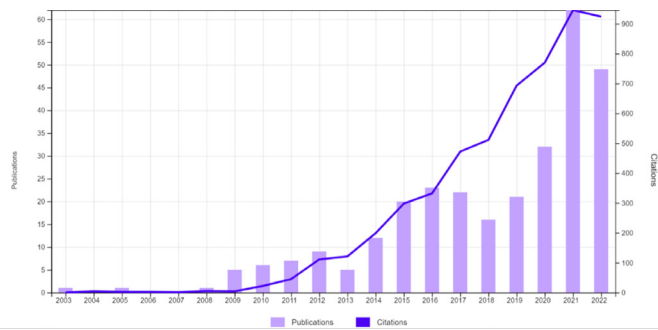


Figure 2: Annual publications and citations between 2003-2022

($n=62$, 21.233%) and the highest number of citations ($n=946$) (Figure 2).

96.575% of the articles were indexed in the Science Citation Index Expanded (SCI-EXPANDED) and 2.397% in the Emerging Sources Citation Index (ESCI). 98.630% of the publications were in English, and 1.37% in German. Publications were often published as Open Access (71.918%). These publications were cited 5563 times, with an average citation count of 19.05 and an average H-index of 39.

A total of 182 articles were published in China; these publications were cited 2386 times, with an average citation count of 13.11 and an average H-index of 26.

There were 52 publications from the USA. These publications were cited 1283 times (average number of citations: 24.67) and had an average H-index of 22.

The retrieved publications came from 28 different countries and were published in 39 peer-reviewed journals. The countries contributing to miRNA research in orthopaedics are shown in Table 1.

Although most miRNA-related articles in orthopaedics were produced in China (182; 62.329%), other top contributors included the USA (52; 17.808%), Japan (20; 6.849%), and Germany (9; 3.082%). As can be seen from the graph analyzing the number of publications by country by year, publications from China continue to increase compared to other countries (Figure 3).

The institutions/universities that contributed most to the literature on miRNA in orthopaedics were Harvard University ($n=16$, 5.479%) in the USA and Sun Yat-sen University ($n=15$, 5.137%) in China. The vast majority of publications were published by Chinese institutions and universities. There were also contributions from institutions and universities in the USA and Japan (Table 2).

A total of 325 funding bodies sponsored publications. The vast majority of scientific papers on miRNA in orthopaedics were funded by institutions from China and the USA (Table 3).

The journal that published the most scientific articles on miRNA in orthopaedics was the *Journal of Orthopaedic Surgery and Research* ($n=75$). The journals with the next highest number of articles were *Osteoarthritis and Cartilage*

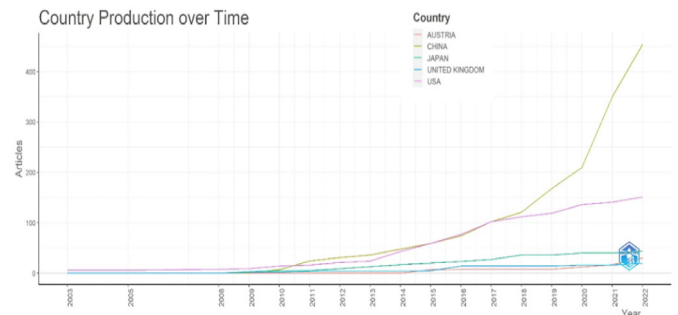


Figure 3: Country production over time-related to miRNA in orthopaedic

($n=32$), *Connective Tissue Research* ($n=25$), *Journal of Orthopaedic Research* ($n=25$), and *BMC Musculoskeletal Disorders* ($n=23$). According to the five-year Thomson Reuters' Journal Citation Report, Osteoarthritis and Cartilage had the highest impact factor (7.326) among all the most important journals publishing on miRNA in orthopaedics, followed by *Bone and Joint Research* (4.535) and *Connective Tissue Research* (3.723) (Table 4). The increase in the number of articles in the *Journal of Orthopaedic Surgery and Research*, which has published an increasing number of articles on this topic since 2020, is particularly noteworthy (Figure 4).

The minimum number of journal publications was then set to at least three papers. A linkage analysis of 37 journals was performed, and 5244 link strengths were found. The *Journal of Orthopaedic Surgery and Research* ($n=1343$), *Connective Tissue Research* ($n=776$), and *Spine* ($n=434$) had the highest total link strengths (Figure 5).

The minimum number of publications per country was set to at least three articles, and we performed a bibliographic linkage analysis using VosViewer. A total of 28 countries were analyzed, and 7036 linkage strengths were found. China ($n=3803$), the USA ($n=3636$), and Japan ($n=1361$) had the highest total link strengths.

The top 25 most cited articles on miRNA in orthopaedics and the number of citations are shown in Table 5.

DISCUSSION

This article uses bibliometric analysis from different perspectives to provide an overview of the current state and worldwide patterns of miRNA research in orthopaedics. It identifies leading academics, institutions, nations, and their collaborations, focusing on significant papers that have been highly cited. These findings are likely to have a significant impact on the direction of future clinical trials and research.

Using the Web of Science (WoS) database, we retrieved 292 relevant papers published between 2003 and 2022 for the current study. Worldwide, 28 different countries contributed to these publications. From 2003 to 2022, global contributions showed an upward trend, with a notable increase starting in 2010. These articles grew by

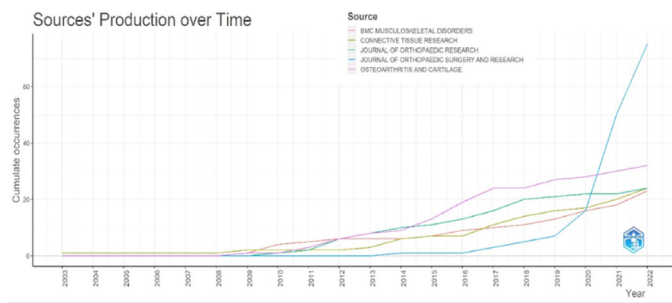


Figure 4: Annual publications of the top five journals with the highest number of articles on miRNA in orthopaedics

23.12% per year. The majority of publications in the field of orthopaedic miRNA research came from China. The highest number of published articles ($n=62$, 21.233%) and the highest number of citations ($n=946$) occurred in 2021. A total of 182 studies were published in China. These articles were cited 2386 times, with an average of 13.11 citations per article. Although China (182; 62.329%) provided the majority of miRNA-related orthopaedic publications, the USA (52; 17.808%), Japan (20; 6.849%), and Germany (9; 3.082%) also contributed significantly. When comparing the number of publications by country and year, China's publications are still growing faster than other countries.

A total of 1601 authors contributed to these studies, with authors from China contributing the most to miRNA studies. The two institutions/universities that contributed most to the literature on miRNA in orthopaedics were Harvard University ($n=16$, 5.479%) in the USA and Sun Yat-sen University ($n=15$, 5.137%) in China. The vast majority of publications came from Chinese institutes and universities. Institutions and universities from the USA and Japan also contributed the largest number of articles.

Citations are a metric used to assess the scientific importance of articles (10-20). In this analysis, we identified the journals, their impact factors, and the top 25 most cited papers with the most significant number of publications on miRNA in the field of orthopaedics. Scientists can use this information to quickly and easily find the most important publications. We collected journal data to determine which journals were interested in this area. When we analyzed the number of journal publications, we found that at least ten articles were published in nine journals, the majority of which were orthopaedic journals. The majority of the studies were published in journals and medical journals of significant academic importance, according to an evaluation of these results taken as a whole. *The Journal of Orthopaedic Surgery and Research* is the most relevant and influential journal on miRNA in orthopaedics, according to the bibliographic links of the journals in Vosviewer. The majority of papers were related to orthopaedics or neurosurgery, and the most prominent elements were in the red circles. This finding suggests that orthopaedic journals focus more on relevant research.

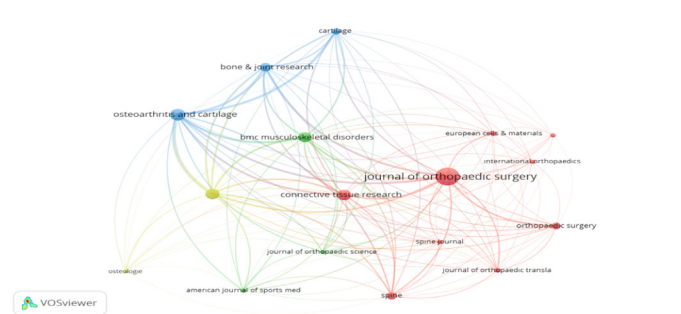


Figure 5: Bibliographic coupling between journals with a minimum of three articles on miRNA

It is worth noting that the top two articles were published in 2009, more than 13 years ago. Therefore, they have had ample opportunity to combine these high citation counts, contributing to their top rankings. The average number of citations for the articles is 19.05. All but one of the articles perform much better than the average citation count of the top five articles (range 18.07-12.44). This shows that these publications have a lot of influence in the industry. A disadvantage of the average citation count is that it does not accurately reflect how the impact of an article has changed over time (24,25). For example, a paper published three decades ago and highly regarded and cited at the time may still have a high average citation score even though it hasn't been cited for a long time. O'Neill et al (24) suggested that when comparing articles from different time periods, the mean citation score can help determine a paper's immediate impact.

Limitations

There are a number of limitations to this study. First, since our bibliometric study is based on the WoS database, it may not include all publications from other, more popular databases such as Scopus and PubMed. Second, we excluded conference proceedings from our study because they may be published twice as conference abstracts and journal articles. However, some potentially useful information might be lost. Thirdly, the number of citations is often used to measure the quality of articles. We evaluated the top 25 most cited articles to find publications in orthopaedics with significant academic impact, although it's possible that we may have missed some in other fields of study. Fourth, we only performed the widely used bibliographic coupling and co-citation analysis to determine the connectivity between institutions, journals, and countries. The co-authorship and citation analysis visualization technique can also provide insightful data for bibliometrics. The current study certainly missed some important facts.

CONCLUSION

The use of miRNA in orthopaedics has been on the rise since 2010. Academics and institutions in China and the United States play an important role in this field. The Journal

of Orthopaedic Surgery and Research (ISSN:1749-799X) is the journal with the strongest correlation and academic influence in this field. Most of this research was published in orthopaedic journals and had a high academic impact. While the current number of studies is limited, there is a clear need for further research in this field.

Ethics Committee Approval: Not applicable.

Informed Consent: Not applicable.

Authorship Contributions: Idea/Concept: TCD, Design: TCG, MK, Supervision: TCG, MU Data Collection or Processing: TCD, MK, MYG, Analysis or Interpretation: TCD, MYG, Literature Search: TCD, MK, MYG, Writing: TCD, MYG Critical Review: MYG, MU, References And Fundings: -, Materials: TCD, MK.

Conflict of Interest: No conflict of interest was declared by the authors.

Financial Disclosure: The authors declare that they have no relevant financial.

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