Bibliometric Analysis on Genetic Factors of Osteoarthritis Pathogenesis: Characteristics and Trends from 2014 to 2023

Yangguang Lu *, Feitian Ni , Yiran Bu , Jialing Lou , Bohuai Yu , Hongzhi Zhang , Haoyang Li , Yige Zhang , Hantao Hu , Di Lu *

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Article

Bibliometric Analysis on Genetic Factors of Osteoarthritis Pathogenesis: Characteristics and Trends from 2014 to 2023

Yangguang Lu [1,*,†], Feitian Ni [2,†], Yiran Bu [1], Jialing Lou [1], Bohuai Yu [1], Hongzhi Zhang [1], Haoyang Li [1], Yige Zhang [1], Hantao Hu [1] and Di Lu [3,*]

[1] The First School of Medicine, School of Information and Engineering, Wenzhou Medical University, Wenzhou, China
[2] The Second Affiliated College, Zhejiang Chinese Medical University, Hangzhou, China
[3] Department of Orthopaedics, Tongde Hospital of Zhejiang Province, Hangzhou, China
* Correspondence: to: Yangguang Lu (yangg_lu@163.com) and Di Lu (hzludi@126.com).
† These authors have contributed equally to this work and share first authorship.

Abstract: Background: Genetic factors are considered important risk factors for the occurrence of osteoarthritis (OA), which has received extensive attention. This study examined the research on the relationship between genetic factors and the pathogenesis of OA from a bibliometric perspective. **Methods:** We searched Web of Science Core Collection for original and review articles on genetic factors and OA. We used R package "bibliometrix" to perform statistical and visualization analysis of countries, institutions, authors, journals, and keywords. **Results:** A total of 1,127 articles met the inclusion criteria, with an average citation of 20.41 per article. From 2012 to 2022, the average annual growth rate of research in this field was 7.83%. The corresponding authors of the published articles were mainly from China, the USA, and the UK. Boston University emerged as the most active and important institution, while the Osteoarthritis and Cartilage published the most articles in this field. The keywords "polymorphism", "genetic" and "mendelian randomization" indicate the future research directions. **Conclusion:** This bibliometric study provides an overview of the key topics and trends in genetic factors and OA pathogenesis research. The high-frequency keywords suggest the current and potential future focus of this field, involving methods, mechanisms, and populations.

Keywords: bibliometrics; genetic factors; osteoarthritis

INTRODUCTION

Osteoarthritis (OA) is a prevalent degenerative joint disease with an unclear pathogenesis, causing a substantial global impact [1], and serving as one of the leading causes of disability [2]. The effects of OA include progressive destruction of articular cartilage, remodeling of subchondral bone, chondrocyte hypertrophy, and synovial inflammation [3]. OA imposes a significant burden on the global economy and healthcare resources, particularly in Western countries. The overall economic burden of OA in these countries is estimated to range from 1 percent to 2.5 percent of the gross domestic product, with projections showing a substantial increase in prevalence further exacerbating this burden [1]. Epidemiological studies have confirmed the association of OA with factors such as age, body mass index, joint injury, and mechanical stress [4]. Moreover, numerous research reports have elucidated the correlation between primary OA and genetic factors [5], with linkage studies identifying critical loci on chromosomes associated with the heritability of OA [6].

Over the past decade, extensive explorations of molecular genetics in human diseases have been conducted [7], including genome-wide association scans (GWAS) of DNA variants, which locate alleles of single nucleotide polymorphisms (SNPs) in cases and controls, linking DNA variants to diseases[8]. Detailed genetic investigations have led to the annual generation of new reports on OA susceptibility risk loci, aiding in our understanding of how genetic risk influences cellular and tissue aspects of joints [7]. However, despite these genetic insights into OA risk factors, the underlying

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reasons for its development and progression remain largely elusive [9]. Previous researchers have dedicated considerable efforts to exploring the risk factors of OA and have made significant progress. Exploring genes that interact with environmental factors to influence the severity of OA will contribute to a better understanding of disease development mechanisms, enabling the development of rational prevention strategies and gene therapy approaches, with crucial clinical significance and application prospects.

Therefore, it is necessary to understand the research progress and trends regarding genetic factors in the pathogenesis of OA. Bibliometric analysis is a method used to evaluate the characteristics of published scientific research, particularly in specific scientific fields [10]. Its aim is to determine key features of relevant publications, including research topics, methods, authors, institutions, and countries [11]. Compared to other traditional research approaches such as systematic reviews, meta-analyses, or experimental and clinical studies, bibliometric analysis utilizes visualization tools to analyse the published academic literature, providing more in-depth insights and considerable advantages [12]. Importantly, bibliometric analysis can reflect the academic impact of publications, identify hotspots and frontiers, assist researchers in identifying past focuses and trends on specific research topics, and serve as an important indicator for future follow-up studies.

The impact of genetic factors on the pathogenesis of OA has become a popular research topic over the past decade [7]. However, there is currently no bibliometric analysis study in this field. Conducting a bibliometric analysis of the correlation between the pathogenesis and genetic factors of OA can help us systematically review existing evidence, discover new genetic risk variant loci, effect genes, and biological pathways, unveil the molecular mechanisms and genetic heterogeneity of OA, and provide novel insights and targets for early diagnosis, prevention, and treatment of OA. This study aims to introduce the perspective of bibliometrics and explore the research progress of the correlation between genes and the pathogenesis of OA based on the Web of Science database, including clinical studies and animal experiments from 2014 to 2023. This exploration will involve identifying core authors and their research collaborations, institutions, countries and regions, and conducting keyword analysis to reflect global research trends and topic hotspots.

MATERIAL AND METHODS

Data Collection

We extracted relevant research on the genetic factors of osteoarthritis (OA) from the Web of Science Core Collection (WOSCC) database. We limited our search to the Science Citation Index Expanded (SCI-EXPANDED) and the Social Sciences Citation Index (SSCI), which are widely used sources in bibliometric analysis. We chose the Web of Science database because it provides more comprehensive materials for analysing past literature [13] and has higher accuracy in journal categorization compared to other databases [14]. The search was conducted using the keywords "osteoarthritis" and "genetic factors", with the specific search strategy as follows: TS = (Osteoarthr* OR Arthrit*Degenerative OR Degenerative Arthriti* OR Arthros* OR OA) AND TS = (Genetic Factors OR Genetic Variants OR Genetic Loc* OR Loc*Genetic). We retrieved all studies published up to June 28, 2023, without any language restrictions. Considering our aim to explore the research trends and hot topics in this field over the past decade, we only included studies published between 2014 and 2023. Additionally, we excluded types of studies such as Meeting Abstracts, Editorial Materials, News Items, and Letters. The bibliometric data were exported as a plain text file, including complete records and cited references.

Data Analysis

We used Microsoft Excel software to record information such as the number of published articles (by country, institution, journal, and author), references, disciplines, keywords, and development

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trends. For analysis, we utilized the Bibliometrix package in R version 4.2.3 software (Ross Ihaka, Robert Gentleman). Bibliometrix is a commonly used comprehensive bibliometric mapping and analysis tool [15]. We employed this tool to analyse the data and create visual maps and charts as follows: (1) Investigating journal influence through Bradford's Law [16]; (2) Analysing and plotting a Three-Field Plot using Keyword Plus; (3) Examining the temporal trend of main subject terms by drawing bar plots; (4) Assessing publication output by country/ territory and keyword usage through heatmaps and line charts; (5) Exploring collaboration relationships among institutions and countries via network plots.

Additionally, we used the online bibliometric analysis tool available at https://bibliometric.com (accessed on June 29, 2023) to obtain information about authors who made outstanding contributions in this field. This information includes the number of articles, Articles Fractionalized (AF), and citation counts. AF is an indicator used to measure author productivity and can quantify research achievements to some extent [15]. Finally, we employed a knowledge synthesis approach to summarize the specific keywords used in this paper [17]. The process of data collection and analysis was independently conducted by two researchers, and any disagreements were resolved through discussion. The flowchart for publication selection and analysis is presented in Figure 1.

RESULTS

General Features of Publications

A total of 1,127 research papers on the genetic factors underlying the pathogenesis of OA were published between 2014 and 2023. These publications consisted of 913 (81.0%) original articles and 214 (19%) reviews, originating from 529 sources (journals and books). They involved 6,899 authors and cited 51,939 references, with 2,825 keywords. Furthermore, the average citation count per article was 20.41, indicating a significant international collaboration rate of 30.35%. The average lifespan of these articles was 4.3 years, and each article had an average of 8 co-authors. The growth rate of publications from 2014 to 2022 was 7.83%, with a noticeable increase in the number of publications in the past five years, accompanied by a rapid growth in citation frequency (Figure 2). It should be noted that although the research conducted in 2023 has not been fully indexed in the database as of June 28, 2023, a considerable volume of articles has already been published in this field.

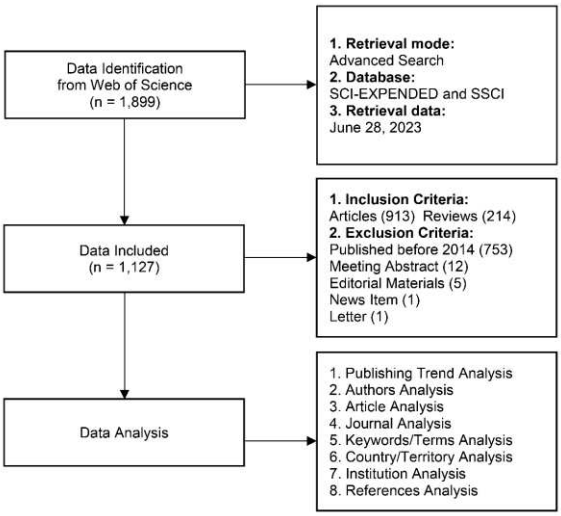

Figure 1. Flowchart of data selection and analysis.

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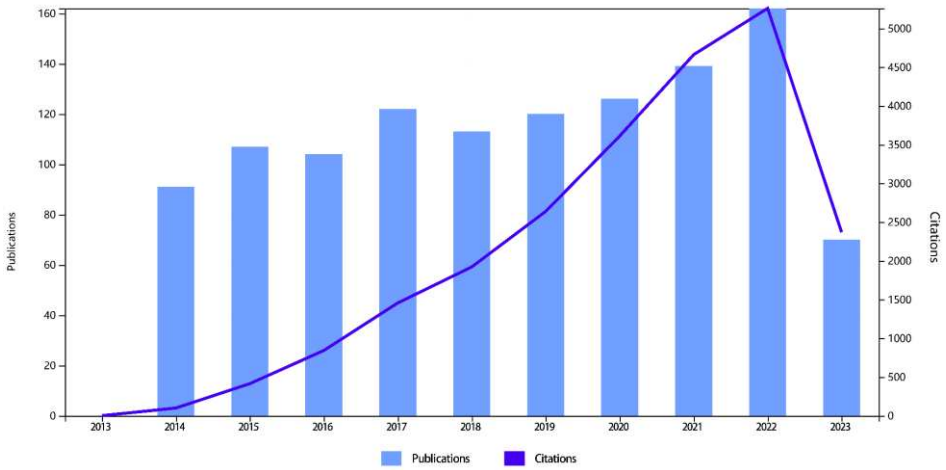

Figure 2. Number of publications and citations per year for studies on Genetic Factors of Osteoarthritis Pathogenesis.

Author Analysis

Table 1 summarizes the top 10 authors who have contributed the most to the research on genetic factors underlying the pathogenesis of OA. Dr. Loughlin J from the United Kingdom ranks first, having published 23 studies in this field over the past decade. His h-index is 4.48, which is the highest among the listed authors in Table 1, indicating significant contributions and achievements in this domain. Following closely is Dr. Zeggini E, also from the United Kingdom, with 17 publications in the last 10 years. The total number of citations for Dr. Zeggini E's work reaches 260, the highest among the listed authors. Additionally, among the top 10 authors, Dr. Wilkinson JM from the United States has the highest average citation count, with each of their articles being cited an average of 15.47 times. In terms of geographical distribution, among these 10 authors, six are from Europe, two are from East Asia, and two are from the United States, which is consistent with the regional distribution of highly influential articles in this field.

Table 1. Top 10 most produced authors on related research.

SCR	Authors	N	AF	TC	CPS	Country
1	Loughlin J	23	4.48	248	10.78	United Kingdom
2	Zeggini E	17	1.40	260	15.29	United Kingdom
3	Meulenbelt I	15	1.61	197	13.13	Netherlands
4	Valdes AM	15	1.73	199	13.27	United Kingdom
5	Wilkinson JM	15	1.84	232	15.47	United States
6	Liu Y	14	1.59	17	1.21	China
7	Zhang F	14	1.73	14	1.00	China
8	Blanco FJ	13	1.45	97	7.46	Spain
9	Jordan JM	13	1.06	93	7.15	United States
10	Rice SJ	13	2.19	91	7.00	United Kingdom

Notes: SCR, Standard competition ranking; N, Number of Articles; AF, Articles Fractionalized; TC, Total Citation; CPS, Citations Per Study.

Top Cited Papers

Table 2 presents the top 10 most cited articles in the research field of genetic factors underlying the pathogenesis of OA. These articles have a minimum total citation count (TC) of 202 [18]. Among

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the two most highly cited articles, one is a Seminar published in The Lancet in 2015, exploring the pathogenesis of OA and potential treatment methods, with 1,604 citations [19]. The second most cited article is a review published in Current Opinion in Rheumatology in 2018, summarizing the research on OA and discussing various risk factors including genetic factors, with 475 citations [20]. Among the top 10 articles with the highest citation counts, four are articles and six are reviews. They primarily involve potential genetic risk factors in the pathogenesis of OA. One study, published by researchers from South Korea in Cell in 2014, specifically highlights the impact of the Zinc-ZIP8-MTF1 axis on OA pathogenesis, elucidating the role of specific gene misexpression as a crucial metabolic regulatory factor in OA progression [21]. Another study indicates the correlation between obesity and OA, with the former being closely associated with genetic factors [22]. Furthermore, a study identifies X-linked hypophosphatemia (XLH) as the most common cause of hereditary phosphate wasting, with OA being one of its common complications [23]. It is worth noting that among the top 10 most cited articles in this field, five originate from Europe [18,19,23–25], three from the United States [20,22,26], and two from East Asia [21,27].

Sources Analysis

Table 3 lists the top 10 journals or book chapters with the highest H-index in the research field of genetic factors in OA etiology. The journal Osteoarthritis and Cartilage has the highest H-index of 17, ranking first among all 529 journals. Annals of the Rheumatic Disease and Plos One closely follow with an H-index of 14 each. Among the top 10 journals with the highest H-index, Osteoarthritis and Cartilage ranks first in both citation count (TC = 933) and number of publications (N = 39). It is important to note that when considering all 529 journals, Lancet has the highest total citation count (N = 1509), despite publishing only one article in the field of genetic factors in OA etiology between 2014 and 2023. According to Bradford's Law [16], Osteoarthritis and Cartilage, Plos One, Annals of the Rheumatic D, and 27 other journals can be considered core journals in the target research field (Figure e-2).

Table 2. Top 10 most cited papers on related research.

SCR	Title	Year	TC	Journal	FA	CA	Country
1	Osteoarthritis	2015	1604	*Lancet*	Glyn-Jones, S.	Palmer, AJR	United Kingdom
2	Epidemiology of osteoarthritis: literature update	2018	475	*Current Opinion in Rheumatology*	Vina, ER	Vina, ER	United States
3	Identification and Specification of the Mouse Skeletal Stem Cell	2015	430	*Cell*	Chan, CKF	Chan, CKF	United Kingdom
4	The Science of Obesity Management: An Endocrine Society Scientific Statement	2018	403	*Endocrine Reviews*	Bray, GA	Bray, GA	United States
5	Role of Thyroid Hormones in Skeletal Development and Bone Maintenance	2016	273	*Endocrine*	Bassett, JHD	Williams, GR	United Kingdom

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				Reviews			
6	Regulation of the Catabolic Cascade in Osteoarthritis by the Zinc-ZIP8-MTF1 Axis	2014	247	*Cell*	Kim, JH	Chun, JS	South Korea
7	Osteoarthritis as a disease of the cartilage pericellular matrix	2018	234	*Matrix Biology*	Guilak, F	Guilak, F	United States
8	Clinical practice recommendations for the diagnosis and management of X-linked hypophosphataemia	2018	225	*Nature Reviews Nephrology*	Haffner, D	Haffner, D	Germany
9	Transforming growth factor-beta in stem cells and tissue homeostasis	2019	221	*Bone Research*	Xu, X	Zhou, XD	China
10	The extracellular matrix as a multitasking player in disease	2019	202	*FEBS Journal*	Theocharis, AD	Theocharis, AD	Greece

Notes: SCR, Standard competition ranking; TC, Total Citation; FA, First Author; CA, Corresponding Author.

Table 3. Top 10 journals with the highest H-index on related research.

SCR	Journal	N	H-index	TC
1	Osteoarthritis and Cartilage	39	17	933
2	Annals of the Rheumatic Disease	21	14	687
3	Plos One	33	14	439
4	Arthritis & Rheumatology	19	13	440
5	International Journal of Molecular Sciences	20	10	505
6	Journal Orthopaedic Research	17	10	320
7	Journal of Bone and Mineral Research	12	10	298
8	Rheumatology	10	8	186
9	Arthritis Research & Therapy	16	8	173
10	Molecular Medicine Reports	10	8	126

Notes: SCR, Standard competition ranking; TC, Total Citations.

Trend Topics and Keywords Analysis

Figure e-1 summarizes the most frequently used topic keywords in the research field from 2014 to 2023, along with their changing trends. The node size represents the frequency of keyword usage, reflecting popular topics and research directions. The most frequently used topic keyword is "expression", appearing 206 times, mainly between 2016 and 2021. "Osteoarthritis" and "association" follow with frequencies of 174 and 154 times, respectively. Knee osteoarthritis, as the most common type of OA [28], appears as a topic keyword 139 times, ranking fourth. It is predominantly cited between 2018 and 2021. In the past two years, "instruments" and "up-regulation" are the most frequently used topic keywords, indicating new research hotspots.

Figures 3(a) and Figure e-3 present the most frequently used keywords by authors from 2014 to 2023 in the form of a heatmap and line graph, respectively, displaying their changing patterns. "Osteoarthritis" has consistently been the most commonly used keyword over the past decade, followed by "polymorphism" and "genetics." In recent years, "Mendelian randomization" and related terms like "GWAS" and "SNP" have gained increasing research interest. This is particularly true as Mendelian randomization has become a hot topic as an evidence-based clinical research method introducing genetic perspectives. GWAS have maintained high popularity in the last three years,

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providing new research evidence for the genetic factors in OA etiology [29]. Additionally, "epigenetics" and "inflammation" have also shown high popularity as keywords in the past two years, indicating potential future research directions.

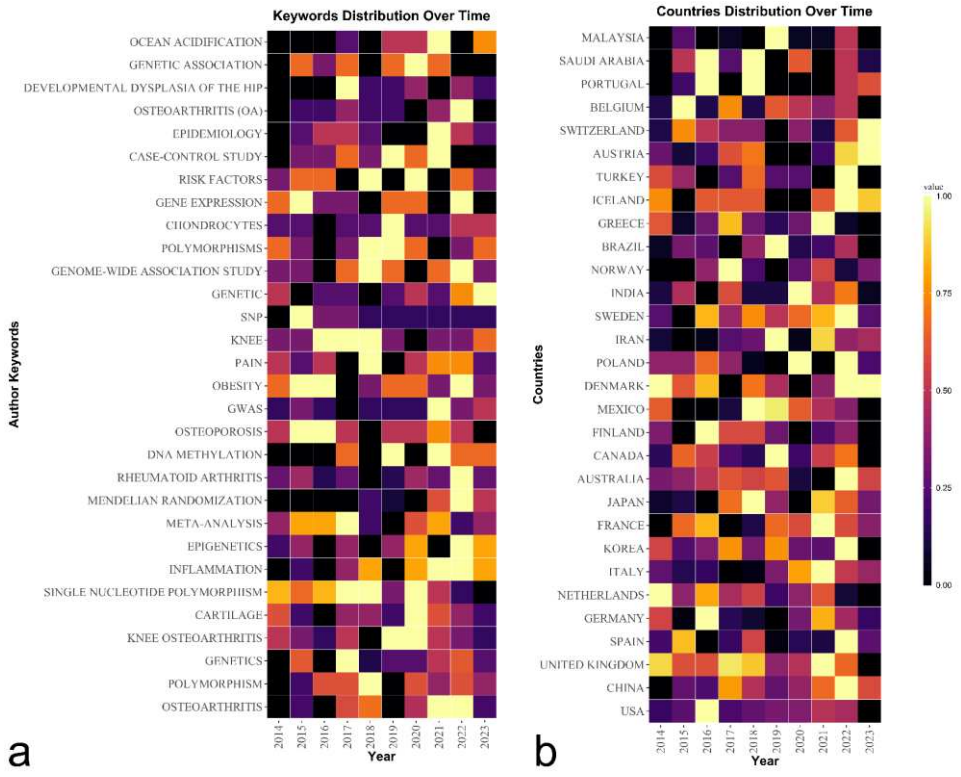

Figure 3. Time trends of the keywords' usage and countries' contribution. (a) Heatmaps of keywords in different time periods; (b) Heatmaps of countries' contribution in different time periods.

Figure 4 represents the Three-Field Plot, where the left-to-right fields represent authors, keywords, and related sources. The node size indicates the frequency or importance of each item, and the lines between nodes represent co-occurrence relationships, with thicker lines indicating higher co-occurrence frequencies or strengths [30]. The keywords "osteoarthritis" and "genetics" are widely used by influential authors. Some keywords representing research methods, such as "meta-analysis", are extensively used by authors like Dr. Reynard IN, Dr. Van Meurs JBJ, Dr. Liu Y, and Dr. Jones G, with BMC Musculoskeletal Disorders having the highest number of publications in this area. "Mendelian randomization" is commonly used by Dr. Wang Y and Dr. Doherty M, with the Journal of Bone and Mineral Research being the most prominent publication venue. Meta-analysis, as a research method that integrates previous studies, can address controversial issues in clinical research and provide evidence for verifying the correlation between genetic factors and OA [31]. Moreover, the keywords "osteoarthritis" and "genetics" have the strongest co-occurrence with the journal Osteoarthritis and Cartilage, while they also appear frequently in other journals like Genes, Clinical Rheumatology, and Arthritis Research & Therapy, all of which are identified as core journals according to Bradford's Law.

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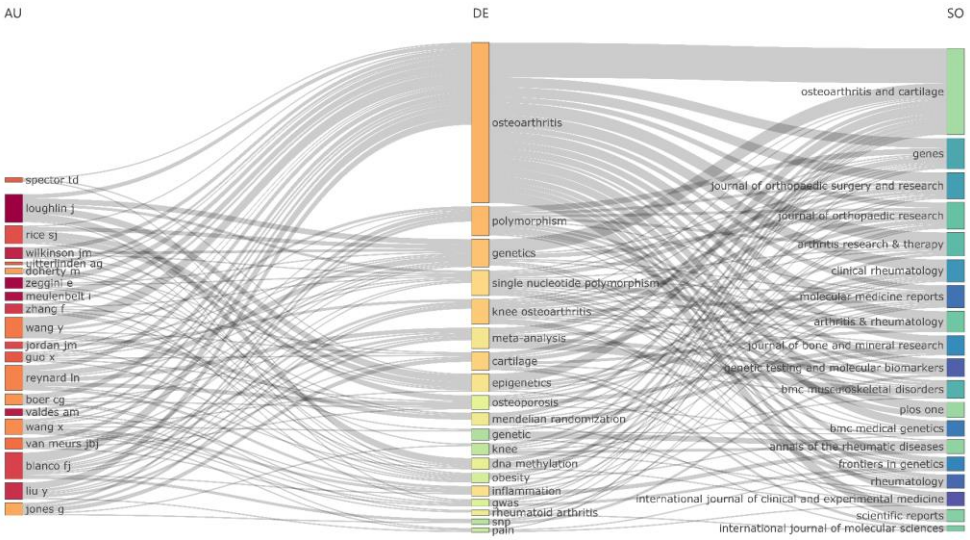

Figure 4. Three-Field plot between authors, keywords, and sources. AU: Author; DE: Keywords; SO: Sources.

Country/Territory Analysis

Table e-1 summarizes the top 10 countries in terms of citation count for articles related to the genetic factors in the pathogenesis of OA published between 2014 and 2023. All these countries have a total citation count exceeding 550. The United States ranks first with a total citation count (TC) of 7149, followed by the United Kingdom with 3424 citations. Moreover, the United Kingdom has an average of 38 citations per article, ranking first among all countries, with a publication count of 469, placing it third among all countries. China has the highest publication count with 285 articles published over the past decade. However, each article from China is cited only 11.5 times on average, placing it last among the top 10 countries with the highest citation count. Netherlands, South Korea, Germany, Spain, Italy, Australia, and Canada have also published over a hundred articles. The inconsistencies in the publication count, total citation count, and average citation count per article may be attributed to variations in high-quality research articles among these countries/regions.

Figures 3(b) and Figure e-4 illustrate the contribution and changes in the number of publications in the field of genetic factors in the pathogenesis of OA by different countries between 2014 and 2023 using heatmap and line graph formats, respectively. The publication counts of the United States, China, and the United Kingdom have maintained high levels throughout this period. In recent years, European countries such as Switzerland, Denmark, Sweden, Spain, Italy, and France have shown an increasing trend in publications in this field.

Figure 5 presents the international research landscape and collaborative relationships in the field of genetic factors related to the pathogenesis of OA. The United States and China have the widest collaboration in this field, co-publishing 59 studies. Additionally, research institutions in the United States have maintained extensive collaborations with the United Kingdom (N = 50), Netherlands (N = 25), Germany (N = 20), Canada (N = 17), Australia (N = 16), Japan (N = 16), and Sweden (N = 16). Research primarily takes place in the United States, Europe, and East Asia, with a lack of studies from Central Asia and Africa. Further discussions are needed regarding the relationship between OA pathogenesis and genetic factors in populations from Central Asia and Africa.

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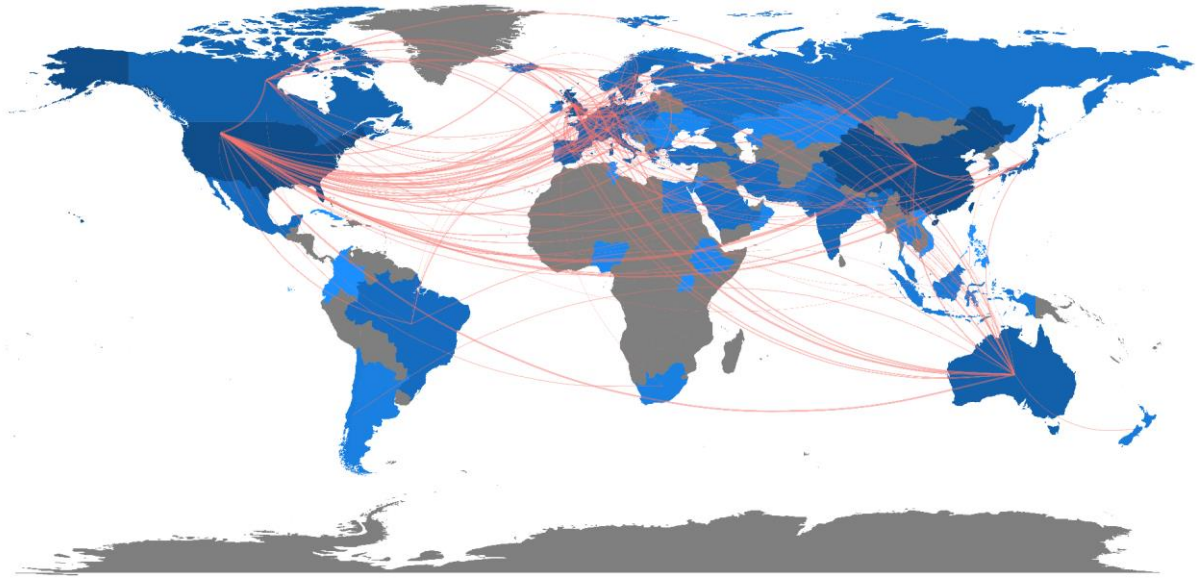

Figure 5. Countries' collaboration world map.

Institution Analysis

Figure 6 displays the institutions engaged in extensive research on the genetic factors in the pathogenesis of OA and their collaboration relationships. The size of each node represents the importance and activity of the respective institution, while the thickness of the connecting lines indicates the level of collaboration between institutions [15]. Boston University, King's College London, University of Sheffield, University of Oxford, and University of Nottingham are ranked highest in terms of importance and activity. Except for Boston University, which is located in the United States, the other four universities are based in the United Kingdom. Among all collaborations in this field, the collaboration between the University of Sheffield and the University of Oxford exhibits the highest level of cooperation. Moreover, the institutions with the highest centrality rankings are Harvard University, University of Edinburgh, Duke University, University of Sydney, and Boston University. Centrality indicates that these nodes act as bridges between two unrelated nodes, signifying their significant role within the structure. These institutions can be referred to as core nodes.

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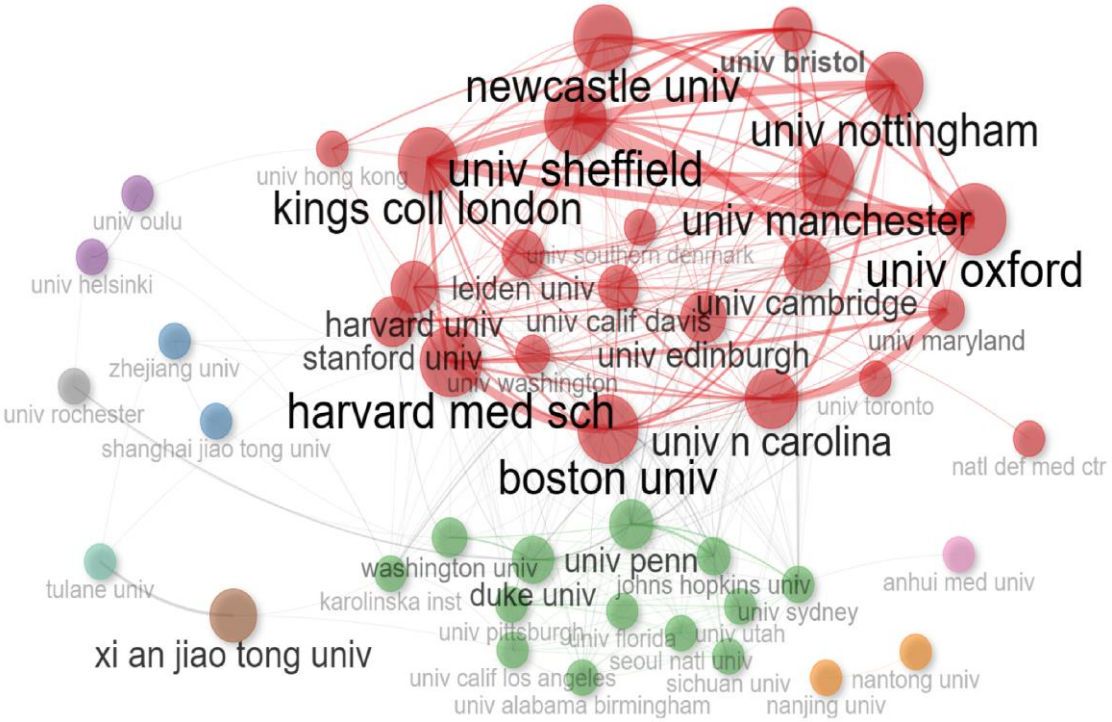

Figure 6. Network analysis of the scientific collaboration between institutions.

Reference Analysis

Table e-2 summarizes the top 10 most cited references in articles published between 2014 and 2023 in the field of genetic factors in the pathogenesis of OA. All these references have been cited more than 40 times in research within this field. Among them, the most cited reference is the study titled "Identification of new susceptibility loci for osteoarthritis (arcOGEN): a genomewide association study" published in The Lancet by Dr. Zeggini E and colleagues in 2012, with 103 citations [32]. Among these 10 references, three studies were published in Nature Genetics and Arthritis & Rheumatology journals, of which two from Nature Genetics were published between 2014 and 2023 [22,33], indicating their greater timeliness. Three studies were published before 2000 [34–36]. Notably, one of the ten references is a meta-analysis study conducted by Eleni Zengini et al., published in Nature Genetics in 2018, providing new evidence through innovative methods.

Figure e-5 represents the Three-Field Plot, where the three fields from left to right represent references, authors, and keywords. The study by Dr. Loughlin J in collaboration with Dr. Zeggini E in 2012 exhibits the strongest co-occurrence. Moreover, this study has been widely cited by influential authors, making outstanding contributions to future research in this field.

DISCUSSION

This study presents the first bibliometric analysis of genetic factors in the pathogenesis of OA. Among the 1127 publications identified from the WOSCC database, approximately four-fifths were original articles, while the remaining one-fifth consisted of reviews. The results indicate a significant increase in the number of relevant publications, particularly after 2020, during the period from 2014 to 2023. It can be predicted that the quantity of related publications will continue to rise in the coming years.

Total citation count serves as an important indicator of interest in a specific research field [37]. In this study, the top 10 most cited articles all investigated the influence of genetics as a potential risk factor for OA. Genetic factors can directly impact OA by affecting joint cartilage structure or bone

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metabolism abnormalities. Furthermore, they may indirectly contribute to the occurrence of OA by influencing risk factors such as obesity and changes in bone density. This suggests that OA may result from polygenic inheritance rather than a single gene defect. The sharp increase in citation counts over the past few years demonstrates the rapid growth of interest in this field, where the role of genetic factors in OA has become a hot topic. Recent years have witnessed the gradual elucidation of genetics' role in the pathogenesis of OA. GWAS-related studies have identified multiple genetic risk variants associated with OA, which may affect cartilage formation and degeneration, as well as joint inflammation and pain [38]. Epigenetic research has discovered a novel DNA methylation modifier that regulates the expression of transcription factors in chondrocytes, thereby impacting cartilage formation and degeneration [39]. Genetic epidemiological studies have also identified certain single-gene mutations or rare variations associated with OA, which may lead to metabolic disorders of cartilage or structural abnormalities in joints [7]. These proposed mechanisms provide new references and inspiration for subsequent research on genetic factors related to OA.

Regarding the publication channels for research on genetic factors in the pathogenesis of OA, we explored different dimensions to determine the contributions of journals to this field and employed Bradford's Law to identify core journals. The total citation count intuitively reflects a journal's influence, while the H-index is a composite quantitative indicator that represents the ratio between the number of publications and their impact [40]. Osteoarthritis and Cartilage has an h-index of 17, a total citation count of 2584, and has published 39 articles, with an average of 66.26 citations per article. Regardless of the dimension considered, it ranks first among all journals. Osteoarthritis and Cartilage is a specialized journal in the field of OA, focusing on research in this area and making significant contributions to exploring genetic factors in OA, thus laying the foundation for future research. The core journals identified by Bradford's Law also demonstrate considerable potential in future research in this field, providing reference sources for future researchers. However, this law only considers the quantity of publications in relevant types of research and does not take into account research quality and influence. It is necessary to synthesize the research achievements published in various journals to better understand the impact of genetics on the pathogenesis of OA.

Currently, the United States has the highest number of papers published on genetic factors in OA pathogenesis, followed by China. Articles published by institutions in the United Kingdom have the highest average citation count, indicating high research quality. Additionally, numerous institutions in the UK and US exhibit significant importance and activity. Generally, a country's economic condition can affect the level and focus of research funding support, thereby influencing its academic capabilities. Therefore, extensive collaboration among research institutions across regions is needed to facilitate global research in this field, furthering the understanding of similarities and differences in the impact of genetic factors on OA pathogenesis within different races.

Keywords can be considered as central elements of specific articles, and the frequency of keywords provides important insights into the main trends within a particular research field [41]. Apart from "osteoarthritis", the most commonly used keyword is "polymorphism." Different variants of the same gene can influence an individual's susceptibility to certain diseases and drug responses [42]. Understanding these variations can enhance our comprehension of the genetic factors involved in the pathogenesis of OA. For instance, polymorphisms in genes such as COL2A1, IL-1, TNF-α, and MMP-3 have been associated with the occurrence, progression, and severity of OA. These gene polymorphisms may contribute to OA development through pathways involving cartilage structure and function, inflammatory response, and activity of matrix-degrading enzymes [43]. This suggests that future studies can identify high-risk or protective polymorphic genes related to OA and explore their associations and mechanisms of action with OA phenotypes and environmental factors. Moreover, these genes can serve as molecular markers for personalized preventive, diagnostic, and treatment strategies for OA patients.

Bibliometrics offers unique advantages in evaluating scientific research in specific fields [10], and our bibliometric analysis exhibits the following strengths. Firstly, our study represents the first

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bibliometric analysis conducted in this field, providing valuable insights for future research. Secondly, our bibliometric analysis is based on the WOSCC database, which employs stringent selection criteria and only includes prominent academic journals across various disciplines, ensuring the quality and authority of the data. Additionally, WOSCC provides comprehensive citation retrieval, granting access to the complete citation network of 1.5 billion references, thus enabling the tracking of research impact and development trends [13,14]. Finally, we performed a detailed bibliometric analysis encompassing countries, institutions, journals, authors, references, and keywords, and visualized the data using the Bibliometrix package and online bibliometric analysis tools, thereby presenting the research development in this field in an intuitive manner.

However, certain limitations of the study should be acknowledged. Firstly, our study only encompassed data from 2014 to 2023. While our objective was to explore research hotspots and development trends in this field over the past decade, insightful studies preceding 2014 may have been excluded. Additionally, some high-quality publications might not have been considered if they are not present in the WOSCC database. Secondly, since our search was conducted in June 2023, the data for 2023 is not entirely included, potentially leading to misunderstandings regarding research hotspots and publication trends. Furthermore, late-published studies may not be accurately identified as hotspots. Lastly, the Bibliometrix package in R tends to favor quantitative analysis, and future research should employ qualitative research methods such as interviews to complement the limitations of quantitative research.

Research on the genetic factors associated with the pathogenesis of OA carries significant clinical implications. Clinicians can identify high-risk populations, perform individualized risk assessments and interventions, and reduce or delay the occurrence and progression of OA. For instance, an OA risk prediction model can be established based on genetic risk variants and other risk factors (such as age, weight, history of trauma) to provide targeted lifestyle guidance (e.g., weight control, appropriate exercise, joint protection) or preventive medication for high-risk individuals [44]. Moreover, novel biomarkers can be developed based on effective genes and biological pathways for early diagnosis, clinical staging, and treatment response monitoring of OA, thereby furnishing evidence for precision medicine [45].

Ultimately, our bibliometric analysis provides guidance and insights for future researchers engaged in this area of study. Future researchers can expand the sample size and coverage of phenotypes, enhance the statistical power and representativeness of genetic research on OA, and discover additional genetic risk variants and impactful genes. Furthermore, researchers can integrate multi-omics data such as functional genomics, transcriptomics, and proteomics to validate the functional effects of independent risk variants (SNVs) associated with OA and elucidate their mechanisms of action and regulatory networks in the pathogenesis of OA [46]. Additionally, new research methods such as meta-analysis and Mendelian randomization can be introduced, and further animal models and clinical trials are necessary to evaluate the impact of OA-related SNVs and impactful genes on the occurrence, development, and treatment of OA, thereby providing stronger evidence to support precision medicine in OA. Lastly, it is imperative to strengthen interdisciplinary, interinstitutional, and international collaborations, share data and resources, conduct global research on the pathogenesis and genetic relevance of OA, promote communication and innovation in genetic research on OA, and provide improved preventive and treatment strategies for OA patients.

CONCLUSION

The surge in research papers dedicated to investigating the pathogenesis and genetic factors associated with OA reflects the growing recognition of the importance of understanding the underlying mechanisms of this complex disease. Collaborative efforts among institutions and researchers worldwide are essential for furthering our knowledge in this field. Identifying hot topics

and actively pursuing research opportunities in these areas will contribute to the development of innovative strategies for the prevention, diagnosis, and treatment of OA.

Supplementary Materials: The following is the supplementary material related to this article: Table S1: Top 10 most cited countries on related research; Table S2: Top 10 most cited references on related research; Figure S1: Time trends of the top-ics during 2014-2023; Figure S2: Core sources identified by Bradford's Law; Figure S3: Line chart of keywords in different time periods; Figure S4: Line chart of countries' contribution in different time periods; Fig-ure S5: Three-Field plot between references, authors, and keywords. CR: References; AU: Authors; DE: Keywords.

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References

1. J. L. Allen, M. E. Cooke, T. Alliston, "ECM stiffness primes the TGF beta pathway to promote chondrocyte differentiation," Molecular Biology of the Cell, vol. 23, no. 18, pp. 3731-3742, 2012.
2. V. Trachana, E. Ntoumou, L. Anastasopoulou, et al., "Studying microRNAs in osteoarthritis: Critical overview of different analytical approaches," Mech Ageing Dev, vol. 171, pp. 15-23, 2018.
3. Y. Zhang, J. Jia, S. Yang, et al., "MicroRNA-21 controls the development of osteoarthritis by targeting GDF-5 in chondrocytes," Exp Mol Med, vol. 46, no. 2, pp. e79, 2014.
4. A. M. Carossino, R. Recenti, R. Carossino, et al., "Methodological models for in vitro amplification and maintenance of human articular chondrocytes from elderly patients," Biogerontology, vol. 8, no. 5, pp. 483-498, 2007.
5. H. J. Kerkhof, R. J. Lories, I. Meulenbelt, et al., "A genome-wide association study identifies an osteoarthritis susceptibility locus on chromosome 7q22," Arthritis Rheum, vol. 62, no. 2, pp. 499-510, 2010.
6. A. M. Valdes, T. D. Spector, "The contribution of genes to osteoarthritis," Med Clin North Am, vol. 93, no. 1, pp. 45-66, x, 2009.
7. G. Aubourg, S. J. Rice, P. Bruce-Wootton, et al., "Genetics of osteoarthritis," Osteoarthritis Cartilage, vol. 30, no. 5, pp. 636-649, 2022.
8. A. Buniello, J. A. L. MacArthur, M. Cerezo, et al., "The NHGRI-EBI GWAS Catalog of published genome-wide association studies, targeted arrays and summary statistics 2019," Nucleic Acids Res, vol. 47, no. D1, pp. D1005-d1012, 2019.
9. K. Chapman, A. M. Valdes, "Genetic factors in OA pathogenesis," Bone, vol. 51, no. 2, pp. 258-264, 2012.
10. O. Ellegaard, J. A. Wallin, "The bibliometric analysis of scholarly production: How great is the impact?," Scientometrics, vol. 105, no. 3, pp. 1809-1831, 2015.
11. V. Durieux, P. A. Gevenois, "Bibliometric indicators: quality measurements of scientific publication," Radiology, vol. 255, no. 2, pp. 342-351, 2010.
12. P. Kokol, H. Blažun Vošner, J. Završnik, "Application of bibliometrics in medicine: a historical bibliometrics analysis," Health Info Libr J, vol. 38, no. 2, pp. 125-138, 2021.

13. A. W. K. Yeung, "Comparison between Scopus, Web of Science, PubMed and publishers for mislabelled review papers," Current Science, vol. 116, no. 11, pp. 1909-+, 2019.
14. Q. Wang, L. Waltman, "Large-scale analysis of the accuracy of the journal classification systems of Web of Science and Scopus," Journal of Informetrics, vol. 10, no. 2, pp. 347-364, 2016.
15. M. Aria, C. Cuccurullo, "bibliometrix: An R-tool for comprehensive science mapping analysis," Journal of Informetrics, vol. 11, no. 4, pp. 959-975, 2017.
16. M. Weinstock, "Bradford's Law," Nature, vol. 233, no. 5319, pp. 434, 1971.
17. R. Whittemore, A. Chao, M. Jang, et al., "Methods for knowledge synthesis: An overview," Heart & Lung, vol. 43, no. 5, pp. 453-461, 2014.
18. A. D. Theocharis, D. Manou, N. K. Karamanos, "The extracellular matrix as a multitasking player in disease," Febs Journal, vol. 286, no. 15, pp. 2830-2869, 2019.
19. S. Glyn-Jones, A. J. R. Palmer, R. Agricola, et al., "Osteoarthritis," Lancet, vol. 386, no. 9991, pp. 376-387, 2015.
20. E. R. Vina, C. K. Kwoh, "Epidemiology of osteoarthritis: literature update," Current Opinion in Rheumatology, vol. 30, no. 2, pp. 160-167, 2018.
21. J. H. Kim, J. Jeon, M. Shin, et al., "Regulation of the Catabolic Cascade in Osteoarthritis by the Zinc-ZIP8-MTF1 Axis," Cell, vol. 156, no. 4, pp. 730-743, 2014.
22. G. A. Bray, W. E. Heisel, A. Afshin, et al., "The Science of Obesity Management: An Endocrine Society Scientific Statement," Endocr Rev, vol. 39, no. 2, pp. 79-132, 2018.
23. D. Haffner, F. Emma, D. M. Eastwood, et al., "Clinical practice recommendations for the diagnosis and management of X-linked hypophosphataemia," Nature Reviews Nephrology, vol. 15, no. 7, pp. 435-455, 2019.
24. C. K. F. Chan, E. Y. Seo, J. Y. Chen, et al., "Identification and Specification of the Mouse Skeletal Stem Cell," Cell, vol. 160, no. 1-2, pp. 285-298, 2015.
25. J. H. D. Bassett, G. R. Williams, "Role of Thyroid Hormones in Skeletal Development and Bone Maintenance," Endocrine Reviews, vol. 37, no. 2, pp. 135-187, 2016.
26. F. Guilak, R. J. Nims, A. Dicks, et al., "Osteoarthritis as a disease of the cartilage pericellular matrix," Matrix Biology, vol. 71-72, pp. 40-50, 2018.
27. X. Xu, L. W. Zheng, Q. Yuan, et al., "Transforming growth factor-beta in stem cells and tissue homeostasis," Bone Research, vol. 6, 2018.
28. L. Sharma, "Osteoarthritis of the Knee," N Engl J Med, vol. 384, no. 1, pp. 51-59, 2021.
29. E. Birney, "Mendelian Randomization," Cold Spring Harb Perspect Med, vol. 12, no. 4, 2022.
30. T. D. Arnold, K. L. Zang, A. Vallejo-Illarramendi, "Deletion of integrin-linked kinase from neural crest cells in mice results in aortic aneurysms and embryonic lethality," Disease Models & Mechanisms, vol. 6, no. 5, pp. 1205-1212, 2013.
31. Y. H. Lee, "An overview of meta-analysis for clinicians," Korean J Intern Med, vol. 33, no. 2, pp. 277-283, 2018.
32. E. Zeggini, K. Panoutsopoulou, L. Southam, et al., "Identification of new susceptibility loci for osteoarthritis (arcOGEN): a genome-wide association study," Lancet, vol. 380, no. 9844, pp. 815-823, 2012.
33. E. Zengini, K. Hatzikotoulas, I. Tachmazidou, et al., "Genome-wide analyses using UK Biobank data provide insights into the genetic architecture of osteoarthritis," Nat Genet, vol. 50, no. 4, pp. 549-558, 2018.
34. J. H. Kellgren, J. S. Lawrence, "Radiological assessment of osteo-arthrosis," Ann Rheum Dis, vol. 16, no. 4, pp. 494-502, 1957.
35. T. D. Spector, F. Cicuttini, J. Baker, et al., "Genetic influences on osteoarthritis in women: a twin study," Bmj, vol. 312, no. 7036, pp. 940-943, 1996.
36. R. Altman, E. Asch, D. Bloch, et al., "Development of criteria for the classification and reporting of osteoarthritis. Classification of osteoarthritis of the knee. Diagnostic and Therapeutic Criteria Committee of the American Rheumatism Association," Arthritis Rheum, vol. 29, no. 8, pp. 1039-1049, 1986.
37. P. O. Seglen, "Citations and journal impact factors: questionable indicators of research quality," Allergy, vol. 52, no. 11, pp. 1050-1056, 1997.
38. C. G. Boer, K. Hatzikotoulas, L. Southam, et al., "Deciphering osteoarthritis genetics across 826,690 individuals from 9 populations," Cell, vol. 184, no. 18, pp. 4784-4818.e4717, 2021.
39. X. B. Zhu, F. Chen, K. Lu, et al., "PPAR gamma preservation via promoter demethylation alleviates osteoarthritis in mice," Annals of the Rheumatic Diseases, vol. 78, no. 10, pp. 1420-1429, 2019.
40. L. Bornmann, H. D. Daniel, "What do we know about the h index?," Journal of the American Society for Information Science and Technology, vol. 58, no. 9, pp. 1381-1385, 2007.
41. X. W. Zhang, H. Lai, F. Zhang, et al., "Visualization and Analysis in the Field of Pan-Cancer Studies and Its Application in Breast Cancer Treatment," Frontiers in Medicine, vol. 8, 2021.

42. Z. Abbaszadeh, S. Çeşmeli, Ç. Biray Avcı, "Crucial players in glycolysis: Cancer progress," Gene, vol. 726, pp. 144158, 2020.
43. Y. Na, R. Bai, Z. Zhao, et al., "IL1R1 gene polymorphisms are associated with knee osteoarthritis risk in the Chinese Han population," Oncotarget, vol. 8, no. 3, pp. 4228-4233, 2017.
44. H. Takahashi, M. Nakajima, K. Ozaki, et al., "Prediction model for knee osteoarthritis based on genetic and clinical information," Arthritis Res Ther, vol. 12, no. 5, pp. R187, 2010.
45. V. B. Kraus, M. A. Karsdal, "Osteoarthritis: Current Molecular Biomarkers and the Way Forward," Calcif Tissue Int, vol. 109, no. 3, pp. 329-338, 2021.
46. S. Graw, K. Chappell, C. L. Washam, et al., "Multi-omics data integration considerations and study design for biological systems and disease," Mol Omics, vol. 17, no. 2, pp. 170-185, 2021.