The Global State and Development Trends of Research in Periprosthetic Joint Infection: A Bibliometric and Visualized Study

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Abstract

Background: Periprosthetic Joint Infection (PJI) remains a great challenge for joint orthopedic surgeons. The purpose of this study is to identify promising research directions by comprehensively analyze the global status and development trend of research in PJI based on bibliometrics and visual analysis.

Methods: Overall the literature about PJI from 1994 to 2020 was searched from Web of Science Core Collection (WOSCC). The extracted data (author, journal, institution, country or region, research orientation, support fund, Cited situation) were analyzed by bibliometrics. VOSviewer was used for bibliographic coupling, co-citation, co-authorship, co-occurrence analysis. According to the results of visual analysis, this paper explores the global status and hot prediction direction of PJI.

Results: A total of 2,283 eligible publications were retrieved. In terms of the trend of previous years, an increasing number of PJI publications will be published. Among the countries in the world, the United States has the largest contribution to the field of PJI. Although "Journal of Arthroplasty" has published the largest number of articles, the most influential journal is "Clinical Orthopaedics and Related Research". Thomas Jefferson University has the largest number of publications of any organization. The study of PJI can be divided into four clusters: "Study on diagnosis", "Related risk factors", "Study on treatment", and "Study on anti-biofilm in vitro". The diagnosis and risk factors of PJI is considered to be a hot direction in the future direction.

Conclusions: In recent years, the literature related to PJI has presented a continuous growth trend. The United States is the largest contributor to this field. More attention should be paid to the diagnostic and risk factors of PJI, which may be the future hot spots in this field.

Introduction

Total joint replacement is a prevalent procedure in orthopaedics, with about 800,000 total joint replacements [TJA] performed each year in the United Kingdom and the United States. It is expected that the number of TJA will continue to rise in the coming years to decades [1-3]. However, 0.6-3% of these patients who underwent primary TJA will suffer from [Periprosthetic Joint Infection \(PJI\)](#) [4, 5]. The prevention, diagnosis, and treatment of PJI is still a global problem. Besides, it costs a tremendous amount of funds for treatment, increases mortality, and seriously affects the physical and mental health and quality of life of patients [6-10]. What's more, PJI will bring frightening sequelae to patients, such as a severe decline in joint function, depression, and even amputation [11]. Due to these factors, PJI has become a research hotspot for joint orthopedic surgeons. Nevertheless, there is no systematic investigation on the development trends and global situation of PJI. Bibliometrics is a multi-system discipline based on qualitative and quantitative functions, which integrates mathematics, statistics, philology, and other disciplines [12]. As a burgeoning method, it has been widely used in the evaluation of research hotspots in various medical fields [13]. To scientifically identify promising research

directions, this study comprehensively analyzed the global research status and development trends of PJI through bibliometrics and visual analysis.

Methods

Data source and search strategies

The Web of Science Core Collection(WOSCC) is recognized as the most suitable online database for bibliometric analysis[14]. We used the advanced retrieval function in the Web of Science (WOS) database to access overall the literature from 1994 to May 9, 2020 (27 years) by entering an accurate retrieval format. To eliminate the bias caused by the timely updating of the literature, the literature retrieval and download were completed within 5 hours. The retrieval strategies of this study are as follows: Ts=(Periprosthetic joint infection OR prosthesis-related infections) AND Language: (English). Besides, some restrictions are made on the literature types, such as letters, reviews, conference papers, etc., which are excluded, and only articles and reviews are included.

Data collection

Literature retrieval and data collection were carried out separately by two examiners, (Zhang and Zhu), who are familiar with the WOS database retrieval system. Any controversial documents are referred to the third author (Zeng) to make a decision. The reviewer uses the functions of "create Citation report" and "analyze search results" in WOSCC to save all data in batches into the TXT document format, and enter them into Microsoft Excel2019 after detailed arrangement. Data extraction includes: publication time of each literature, author, journal, institution, country or region, research orientation, support fund, h-index, average citations per item, total cited frequency of publications, title, abstract, and keywords.

Bibliometric and Visualized analysis

The main characteristics of all the included literature (country, journal, institution, author, fund, research direction, citation, h-index) were displayed in pictures made by Microsoft Excel2019. Among them, it includes the distribution map of PJI research on the world map. The H index is a comprehensive quantitative indicator used to measure the quantity and level of researchers' academic output[14]. In addition, the annual publication number of PJI and the predicted growth trend for 2020-2030 are also analyzed and presented in the form of a line graph. Then import the TXT file into the VOS viewer version 1.6.15 (Van Eck and Walt-man, Leiden University, Leiden, The Netherlands) for visual analysis of the literature[15]. Visual analysis of literature includes four aspects: bibliographic coupling, co-authorship, co-citation and co-occurrence of keywords. The larger the shape of the label in overall the visualization diagrams, the greater the frequency or significance of the label.

Results

Analysis of publication trends—distribution and quality

The output and trend of related Publication

A total of 2,283 eligible publications were retrieved, including 2022 articles and 261 reviews. It can be noted that from 1994 to 2020, the number of related publications of PJI presents a growing trend over time. In particular, more than 100 publications have been published annually since 2013. Moreover, the curvilinear model predicts that more than 700 publications will be published by 2030 (Fig 1a).

Analysis of countries [or regions] distribution

Overall included PJI related literatures come from 69 different countries or regions. Among them, the United States (1010,44.24%) is the country that contributes the most to PJI research, and Germany ranks the second in the number of publications (287,12.571%), followed by China (159,6.956%), the United Kingdom (156,6.833%) and Italy (118,5.169%). Publications in other countries are below 100 (Fig 2a, b)

Evaluation of the Quality of publications

The quality of publications is evaluated according to the three quantitative indicators of h-index, average citations per item, and total cited frequency of publications. As can be seen from the bar chart (Fig3a), the top 5 h-index countries are the United States (79), Germany (35), the United Kingdom (27), Switzerland (27), and Spain (22). As for the average cited index, Switzerland (42.2) ranked first, Switzerland (30.6) ranked second, followed by USA (27.16), AUSTRIA (21.39), UK (20.43) (Fig3b). The top five countries in Total cited frequency are USA (27434), Germany (4525), UK (3187), Switzerland (2540), and Italy (1506), respectively (Fig3c).

Characteristic of publications

Institution contributions

Regarding institutional output, the top five were Thomas Jefferson Univ (157) Mayo Clin (122), Thomas Jefferson Univ Hosp (83), Rush Univ (81), and Rothman Inst (57) (Fig4a).

Authors contributions

Surprisingly, Professor, Parvizi J published 209 studies, nearly four times the number of studies published by second Della Valle CJ (58) and third Tan TL (52). The number of articles published by other authors in the top 10 is less than 50 (Fig4b).

Research orientation

Currently, the popular research directions are orthopedics (1511) surgery (707), and infectious disease (175). The top ten research fields are shown in Figure 4c.

Journals of publishing researches

In terms of journals publishing researches on PJI, the Journal of Arthroplasty, with an impact factor (IF) of 3.524 (2019), has published as many as 467 studies, ranking first. Additionally, Clinical Orthopaedics and Related Research (IF=4.154 (2019)) and Journal of Bone and Joint Surgery American Volume (IF=4.716 (2019)) ranked second and third with published 191 studies and 124 studies respectively. Publications from these three journals accounted for about one-third (34.11%) of the total (Fig4d).

Funds Name

The United States Department of Health Human Services (71) is the largest funding source for research. This was followed by the National Institutes of Health NIH USA (70) and the Natural Science Foundation of China National (43). The three funds are from the United States and China, respectively (Fig4e).

Visualized analysis

Generally speaking, total link strength (TLS) is the primary parameter used to identify the relative importance of a node in visual analysis results. TLS is positively correlated with the significance of the nodes.

Visual analysis of Bibliographic coupling

The visualization tool VOS viewer was used to perform Bibliographic coupling analysis of overall included publications according to three subgroups: Countries, Institutions, and Journals. When establishing a national Bibliographic coupling analysis, the minimum threshold of documents is set to 3, which is finally shown in figure 5a for 48 countries. Among them, the top three TLS are USA (658209), Germany (286828), and UK (182405). Similarly, in the analysis grouped by organization, 181 organization names are shown in the visual diagram (Fig5b). The top three organizations in TLS are Thomas Jefferson Univ (181425), Mayo Clin (124305), and Rush Univ (115770). In the analysis grouped by source journals, the order of the top three journals in TLS is exactly the same as the ranking order of the number of posts, which are Journal of Arthroplasty (273081), Clinical Orthopaedics and Related Research (126052), and Journal of Bone and Joint Surgery American Volume (108129) respectively (Fig5c).

Visual analysis of co-citation

The cited references and cited sources were grouped for co-citation analysis. The co-citation analysis was carried out according to the cited references and cited sources. The significance of creating co-citation analysis is that we can know the number of times several references are cited at the same time according to TLS. Only references that have been cited more than 30 times are shown in figure 6a. The results indicated that the top three references for TLS were "Parvizi J, 2011, Clin Orthop Relat R, v469, p3022," "Trampuz A, 2007, New Engl J Med, v357, p654", and "Zimmerli W, 2004, New Engl J Med, v351, p1645". It can be found that most of the studies with high co-citation are published in high-level journals. In addition, the minimum threshold for cited sources is set to 30. Finally, 266 journals were presented in the network map (Fig6b). The top three journals in TLS are Clinical Orthopaedics and Related Research

(133158), Journal of Arthroplasty (120641), and Journal of Bone and Joint Surgery American Volume (118879), which are also fairly influential in the field of orthopedic.

Visual analysis of co-authorship

It can clearly understand the close degree of cooperation between the nodes of countries, between the nodes of authors, and between the nodes of institutions by creating co-authorship analysis. The minimum threshold of publications was set to 5, which showed the 43 nodes of countries, 316 nodes of author, and 118 nodes of institutions in Fig7. The top three countries in TLS are the USA (260), the UK (169), and Germany (166). The top three authors in TLS were Della Valle CJ (516), Parvizi J (181), Tan TL (156). The top three institutions in TLS were Thomas Jefferson Univ (156) Rush Univ (116), and Mayo Clin (102).

Visual analysis of Key Word Co-occurrence

The co-occurrence analysis of keywords is a crucial means to find the current research hotspots of PJI. The principle is to determine the significance of keywords by counting the number of occurrences of keywords in the titles and abstracts of all included literatures. In this analysis, select the counting method as binary counting and set the minimum co-occurrence number to 20. In the end, the visualization map generally presents 660 terms in four clusters, which are "Study on diagnosis of PJI" (red), "Related risk factors of PJI" (blue), "Study on treatment of PJI" (green), and "Study on anti-biofilm in vitro" (yellow) (Fig8a).

In the "Study on diagnosis of PJI" cluster, the most eye-catching keywords are sensitivity, accuracy, biomarkers, value, and culture. In the cluster of "Related risk factors of PJI", the keywords with more repetitions are obesity, risk, body mass index (BMI), age, gender and diabetes. In the "Study on treatment of PJI" clusters, the most popular keywords are debridement, outcome, reconstruction, score, and components. In the "Study on anti-biofilm in vitro" cluster, the most prominent keywords are antibiotics, pathogen, prevention, activity, bacteria, strains. These four categories represent the main research direction of PJI. Besides, an overlap visualization diagram of colour variation with the time axis (2014-2017) was drawn according to the approximate year in which keywords appear (Fig8b). Although studies concentrated on all four areas before 2015, after 2016, most studies focused on risk factors and diagnosis of PJI.

Discussion

Through a systematic bibliometric analysis of the global status quo and development trends of PJI, this study will help scholars to recognize hot directions, influential cooperative institutions and countries in the field of PJI, so as to provide a shortcut for later research. Our global bibliometric analysis of PJI shows that the number of articles about PJI has increased significantly in the last five years. This may be because the larger base of TJA leads to an increase in the number of patients with PJI, coupled with the difficulty of treatment and enormous damage caused by PJI, so it will cause a growing number of

orthopaedic experts to pay attention to the study of PJI. Furthermore, it is scientifically predicted that the output of PJI-related articles will continue to increase over time.

As one of the most developed countries in the world, the United States has published the most articles related to PJI. This is mainly attributed to the United States having the most advanced scientific and technological strength and the strongest economic strength around the world. The H index and average citation frequency often represent the quality of research published in a country. Admittedly, the quality of articles in the United States ranks first. Therefore, the United States is the country with the largest contribution in the field of PJI. In addition, Germany and the UK, as countries second only to the United States, have also made considerable contributions in the field of PJI. Although the number of PJI articles in China ranks third in the world, it is lagged far behind by other countries in the H index and average citation frequency rankings. We consider that this may be because Chinese scholars have always advocated the number of articles while neglecting the quality of the articles themselves. Thomas Jefferson University (USA), Mayo Clin (USA), and Thomas Jefferson University Hospital (USA) are the institutions that publish the most papers related to PJI. These three institutions are all from the USA, which once again confirms the pivotal position of the USA in the PJI field. Paryizi J is the author with the most published PJI-related papers, accounting for 9.15% of the total. This ratio is enough to show that Paryizi J is a leader in the PJI field and represents the leading level in the PJI field. Perhaps, the research direction of his team will be the primary development research direction of PJI in the future. The results of bibliographic coupling analysis indicate that "Journal of Arthroplasty" is the journal with the highest similarity in the PJI field. The results of co-citation analysis show that "Clinical Orthopaedics and Related Research" is the journal with the most cited frequency in the field of PJI. Coincidentally, the most frequently cited single article is "Definition of periprosthetic joint infection: is there a consensus?" published by Professor Parvizi J on "Clinical Orthopaedics and Related Research". Through the co-author analysis, we found that the United States is the most willing to cooperate with other countries, mainly with Canada, China, South Korea, and Japan.

The co-occurrence analysis of keywords can objectively present the hot spots and future research trends of PJI. Therefore, we focus on the detailed analysis of the four clusters obtained from the co-occurrence analysis network diagram.

Cluster1 is "Study on diagnosis of PJI". Since the birth of TJA, the diagnosis of PJI has been a great challenge for clinicians. At present, a large number of diagnostic methods continue to emerge[16]. The more common biomarkers are serum biomarker detection (α -defensin, erythrocyte sedimentation rate, c reactive protein, D-Dimer, procalcitonin, interleukin-6), bacterial culture, joint fluid analysis, (leukocyte esterase), histopathological analysis (frozen section), imaging examination (bone imaging, leukocyte labeling imaging) and molecular biology technique (PCR). Unfortunately, there is still no diagnostic method that can achieve 100% diagnostic accuracy. Plenty of studies have shown that the biomarkers of synovial fluid represented by α -defensin are promising diagnostic indicators[17-19]. The rapid, accurate, simple, and economical diagnosis represented by Leucocyte esterase test paper will be the development direction some time[20, 21]. However, the diagnostic criteria that can determine the clinical treatment

strategy should be to improve the positive rate of bacterial culture to distinguish PJI from aseptic loosening. With the continuous development of science and technology, more novel detection methods will appear, and more research on PJI diagnosis will increase accordingly.

Cluster2 is "Related risk factors of PJI". Prior to TJA, if risk factors for PJI are accurately identified, some preventive measures can be taken to reduce infection rates. At present, the certain risk factors that have been confirmed to cause PJI are as follows: post-Traumatic OA, glucocorticoids > 10mg per day training, alcohol and IVDU, morbidities (diabetes, liver disease, connective tissue disorders) and so on[22]. Several studies have shown that the incidence and mortality of PJI patients can be reduced by avoiding or improving these risk factors[23, 24]. However, there are still many uncertain risk factors for PJI for clinicians. Based on the current refractory nature of PJI, it may be an innovative and advantageous idea to prevent the occurrence of PJI. The timeline prediction chart also confirms that after 2017, a large number of studies have focused on the risk factors of PJI. As a consequence, this aspect will be the main research hotspot of PJI.

Cluster 3 is "Study on treatment of PJI". The ultimate goal of the treatment of periprosthetic infection is to eradicate the infection, eliminate pain, and restore joint function[25]. Up to now, the treatments widely used by clinicians include antibiotic treatment, irrigation, debridement, two-stage revision, replacement of gasket debridement (retention of the prosthesis), arthrotomy, arthrodesis, and so on. Among them, the second-stage revision is the most widely used technique by clinicians, and it is recognized as the preferred method for the treatment of PJI after total knee arthroplasty[25, 26]. Although these treatments can alleviate patients' pain to some extent and effectively control the infection, there is still no therapeutic regimen that can eradicate PJI. The search for more reliable and inexpensive treatments may be the research direction of future.

Cluster 4 is "Study on anti-biofilm in vitro". Biofilms are polysaccharides secreted by bacteria, such as polysaccharide matrix, fibrin, lipoprotein. After the formation of biofilm, it can form a protective coating on the microflora, so that the antibiotics cannot penetrate and thus play an antibacterial role[27, 28]. In vitro studies are mainly about PJI biofilm sterilization resistant (traditional Chinese medicine monomer, antibiotics, Bacteriophage, immunotherapy, enzymatic, ultrasound), modified plant material, and inhibition of quorum sensing, etc. Among them, the anti-biofilm regimen is mainly a combination of antibiotics and surgical treatment. In the future, innovation may be made in the research and development of new antibiotics with better permeability. Furthermore, the research on prosthesis materials and quorum sensing inhibition will become the focus and hotspot in the future. Although these research directions are still in their infancy, basic experimental research is the cornerstone of clinical research. It is believed that the basic research results of PJI will have a revolutionary impact.

To the best of our knowledge, our research is the first time to systematically and objectively analyze the global status quo and development trends of PJI. However, we hold the view that this study has the following limitations. Because only English publications are included in this study, it is limited by the use

of language. Moreover, as the online database is updated continuously, and new research is published every day, our research needs to be updated accordingly.

Conclusion

This study provides the global status and development trend of PJI. There will be a growing number of articles of PJI published based on the development trend in recent years. Up till now, the United States is the country that has the largest contribution for PJI research. Paryizi J is the leading expert in the field of PJI. We predict that the diagnosis and risk factors of PJI will be the hot research direction in this field in the future.

Abbreviations

PJI: [Periprosthetic Joint Infection](#); WOSCC: Web of Science Core Collection; TJA: total joint arthroplasty; WOS: Web of Science; IF: impact factor; TLS: total link strength

Declaration

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Declaration of conflicting interest

The authors declare that there are no conflicts of interest.

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Author Contributions

All authors contributed to the study conception and design. Haitao Zhang and Yinuo Fan conceived and designed the work. Material preparation and data collection and analysis were performed by Haitao Zhang, Yinuo Fan, Pengfei Xin, Wenjun Feng, Houran Cao, Jie Li, Peng Deng. The first draft of the manuscript was written by Haitao Zhang. Jianchun Zeng and Yirong Zeng commented on previous versions of the manuscript. All authors read and approved the final manuscript.

Availability of data and materials

The authors declare that all the data supporting the findings of this study are available within the article and its supplementary information files.

Ethics approval and consent to participate

Not applicable

Consent for publication

Not applicable

Competing interests

The authors declare that they have no competing interests.

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Figures

Figure 1

Forecast graph of growth trend of publications

a

b

Figure 2

Country distribution. a The top 10 countries that published the largest number of articles are listed. b Distribution of PJI research in world map

a

b

c

Figure 3

the quality of publications. a The top 10 countries of the H-index of publications. b The top 10 countries of the Average citations per item. c The top 100 countries of total cited frequency

b

d

c

e

Figure 4

Characteristic of publications. a The top 10 institutions of the number of their publications. b The high impact authors in the world. c The 10 major research orientations. d The top 10 journals with most publications related to the PJI. e The main contribution funds in the world

a

b

c

Figure 5

The bibliographic coupling analysis of worldwide research on PJI. a Network map showing the relations between 48 countries in the PJI field. b Network map on 181 institutions on PJI. c Network map on 181 journals on PJI.

bozic kj, 2012, j bone joint surg

namba rs, 2013, j bone joint surg

ong kl, 2009, j arthroplasty, v24

kurtz s, 2007, j bone joint surg

kurtz sm, 2008, j arthroplasty, v

wilson mg, 1990, j bone joint sur

zimmerli w, 2004, new engl j med,

marculescu ce, 2006, clin infect

tsukayama dt, 1996, j bone joint

mortazavi smj, 2011, clin orthop

kilgus dj, 2002, clin orthop rela

aligh ja, 2012, j shoulder elb su

dodson cc, 2010, j shoulder elb s

butler-wu sm, 2011, j clin microb

deirmengian c, 2014, clin orthop

parvizi j, 2011, j bone joint sur

trampuz a, 2006, j clin microbiol

schinsky mf, 2008, j bone joint s

della valle cj, 2007, j arthropla

spangehl mj, 1999, j bone joint s

feldman ds, 1995, j bone joint su

athanasou na, 1995, j bone joint

The co-citation analysis on PJI. a Network map of co-cited journals related to PJI. b Network map of co-cited references related to PJI

a

b

c

Figure 7

The co-authorship analysis of PJI. a Network map of the 43 countries nodes of PJI. b Network map of 118 institutions nodes of PJI. c Network map of 316 author nodes of PJI.

3

Figure 8

The co-authorship analysis of PJI. a Network map of the 43 countries nodes of PJI. b Network map of 118 institutions nodes of PJI. c Network map of 316 author nodes of PJI.