

Original Research

A Bibliometric Analysis of Research on Perioperative Neurocognitive Disorder: A Systematic Review

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Abstract

Background: Perioperative neurocognitive disorder (PND) is a general term for cognitive impairment that negatively affects multiple domains, including memory, concentration, and physical functioning. Numerous articles have been published on PND; however, only a few quantitative analyses covering this disorder have been published. **Methods and Materials:** To clarify PND's developmental history, research foci, and future directions, we conducted a bibliometric analysis using the bibliometric tools VOSviewer and CiteSpace. A total of 4704 publications were obtained from the Web of Science database, including annual publications and trends, keywords, institutions, journals, and collaboration between countries/regions and authors. **Results:** In addition, we found that neuroinflammation is a hotspot in recent studies. **Conclusions:** This bibliometric analysis provides a broad overview of studies in the field of PND.

Keywords: bibliometric analysis; perioperative neurocognitive disorder; research trend; postoperative cognitive dysfunction; neuroinflammation

1. Introduction

Perioperative neurocognitive disorder (PND) is one of the most common central nervous system complications encountered during the perioperative period. It is characterized by hampered social and communication skills, information handling, cognitive performance, and impaired memory. PND can be broadly classified into postoperative cognitive dysfunction (POCD) and postoperative delirium (POD) [1]. POD is an acute disorder that affects attention and cognition [2]. Unlike POD, POCD is defined as a reduction in postoperative cognitive performance and is evaluated by neuropsychological tests, instead of a clinical diagnosis [3]. POD is reported to be a significant risk factor for POCD in the first postoperative month [4]. The prevalence of PND ranges from 5% to 55% within the geriatric population [4], resulting in numerous adverse outcomes, including prolonged hospitalizations, decline in physical functioning and quality of life, and increased incidence of disability and mortality [5–8]. Notably, advanced age is an independent risk factor for the occurrence of PND [9]. A study by Brien HO *et al.* [10] has focused on the risk factors associated with anesthesia and surgery in the senior population, and reported that it might promote cognitive decline and accelerate dementia in this population. Additionally, a large retrospective cohort study has demonstrated that older surgical patients with preoperative cognitive impairment are prone to a higher risk of POD [11]. Patients with a relatively higher level of education are at a reduced risk of

PND [12]. Several preexisting conditions, such as multiple comorbidities, infection, poor vision or hearing, and previous history of cerebrovascular accidents with no residual impairment, have been identified as potential risk factors for POD [13–15]. Due to its rising incidence and debilitating effects, particularly on the geriatric population, PND warrants more attention and research, especially for older patients who suffer overwhelmingly from this condition.

Bibliometrics is a discipline that analyzes academic productivity from a quantitative perspective [16]. Details, including keywords, authors, journals, institutions, countries/regions, and network of visualization can be captured in the analyzing process, enabling researchers to obtain an overall understanding of the hotspots, frontiers, and future trends in a certain field [17]. Thanks to the current developments in technology, bibliometrics has already been widely used [18,19], including hotspots in POD [20] and 100 most-cited articles in delirium [21]. Although numerous reviews on PND have been published in the recent years [22,23], there has been no bibliometric analysis conducted on the subject. In this study, 4704 publications, published until January 18, 2023, were evaluated with the help of bibliometric tools, to outline the overall framework of PND research and further clarify the hotspots and publication trends.



2. Materials and Methods

2.1 Data Retrieval and Collection

To retrieve data comprehensively and precisely, the Web of Science Core Collection (WoSCC) was selected as the data source in this study, and the “citation index” was set as SCI-EXPANDED. The Web of Science, the largest comprehensive academic database, has been broadly accepted among researchers, and is considered as the most suitable database for bibliometric analysis [24]. The retrieval strategy was “TS (topic) = POCD OR (‘postoperative cognitive dysfunction’) OR (‘postoperative delirium’) OR (‘perioperative neurocognitive disorder*’) OR (‘postoperative neuro psychiatric disorder*’).” It needs to be pointed out that an article, also known as original research, is the detailed elaboration of research results, while a review is a reflection of the latest progress of a certain subject or topic in a certain field as well as the latest developments and trends in related issues, which are vital for the research related to this specific field. Compared with other types of literatures, the contents of these two types are more readable and of higher professional value. Therefore, we have restricted the type of literatures to “article OR review”. There were no time or language limitations during this process, only a deadline of the retrieval data (January 18, 2023). All retrieved data were downloaded in “plain text” format, and detailed information was collated for further analysis (Fig. 1).

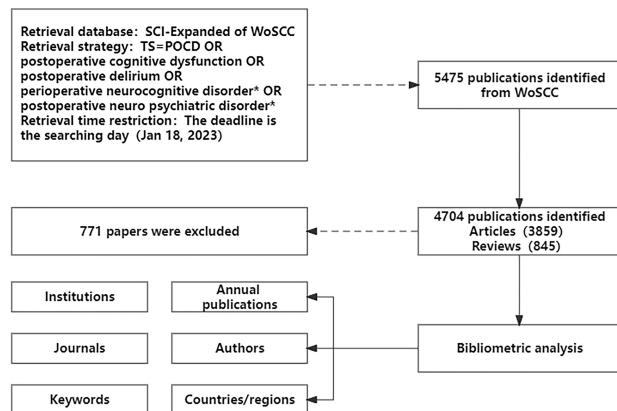


Fig. 1. Flow diagram of the literature retrieval and selection procedure.

2.2 Data Extraction

All data retrieval and extraction were performed by two independent researchers (YY, HL) on separate days to avoid potential bias and improving reliability of the results. Various elements such as the number of annual publications, keywords, journals institutions, authors, countries/regions, etc., were extracted from selected publications for analysis. To assess the academic attainment and scientific output objectively, the H index was designated for

countries/regions, institutions, and authors who had contributed to the field of PND research. Furthermore, the impact factor (IF) and quartile ranks were collected from the Journal Citation Reports (JCR) of 2022 for the top 10 journals.

2.3 Data Analysis and Visualization

CiteSpace 6.1.R2 (Chaomei Chen, Philadelphia, PA, USA) and VOSviewer 1.6.18 (Nees Jan van Eck and Ludo Waltman, Leiden, Netherland) were selected for comprehensive analysis and knowledge mapping. CiteSpace and VOSviewer are the most used bibliometric tools, each having their own advantages [25]. VOSviewer, based on probability theory, provides various visualizations in three dimensions in the fields of countries, authors and co-occurrence of keywords, including overly, density, and network visualizations [26]. CiteSpace, based on set theory, is used to obtain the timeline and time zone views to outline the process of evolution and the historical span of literature, and grasp the trends in this field [27]. Additionally, Microsoft Excel 2019 (Microsoft Corporation, Redmond, WA, USA) was also used for analysis and visualization.

3. Results

Following the above retrieval strategy, a total of 4704 papers on PND, published in 972 journals with 97,048 citations and an average of 20.63 citations per publication were collected from WoSCC (Fig. 1). Of the 4704 papers included in this study, the top 20 highly cited papers were listed in **Supplementary Table 1**. “Article” was the predominant type of content, accounting for 82.04% (3859/4704); meanwhile, English was the predominant language of the literature, among 16 available languages, accounting for 97.13% (4569/4704). Among non-English languages, German was the most common language (1.51%, 71/4704).

3.1 Annual Publications and Trends

As shown in **Supplementary Fig. 1**, the number of publications on our topic of interest, PND, was on the rise, especially since 2010, and the trend showed rapid growth, indicating that PND was receiving increasing attention. The search deadline of January 18, 2023 resulted in a low number of publications in 2023.

3.2 Contributions of Authors

In total, 20,169 authors were noted to have conducted a PND study. According to Price Law, core authors are authors who have published seven or more documents in a particular field. 328 authors met the criterion, accounting for 1.63% of the total (328/20,169) number of authors. The core authors had published 3774 documents, accounting for 80.23% of the total documents (3774/4704). **Supplementary Table 2** lists the top 15 authors.

Edward R. Marcantonio from Harvard Medical School with a total of 88 publications was the most productive author, whereas Sharon K. Inouye from Hebrew Senior Life was the most influential author with an H index of 41 and the maximum citations equaling of 118.69 per paper. Network visualization provides the information regarding representative scholars and collaborations in this field. VOSviewer was applied to demonstrate the coauthored analysis graph, providing information of authors who have published at least 17 works of research on PND. The largest set of connected entries that we could demonstrate consisted of 38 authors. Some authors among the 44 authors in the network were not linked to each other. Among the authors grouped into eight clusters, Edward R. Marcantonio and Sharon K. Inouye showed the highest number of links (Fig. 2).

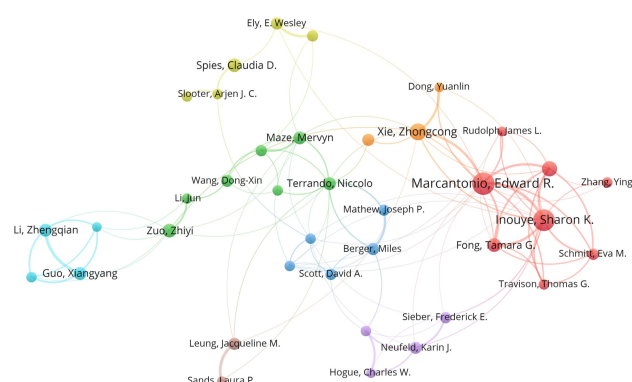


Fig. 2. Contributions of the authors. A map of the coauthored document analysis among the authors who have published at least 17 research articles on perioperative neurocognitive disorder (PND) according to the VOSviewer. Colors of node represent different clusters; sizes of nodes represent the number of documents put out, the larger the node, the more documents put out; and the lines represent the strength of partnership, the thicker the line, the stronger the association between the two authors.

3.3 Contributions of Countries or Regions

Seventy-five countries/regions were altogether incorporated in the study. **Supplementary Fig. 2A** provides a visual analysis of the countries from which at least 17 documents have been published, conducted by the VOSviewer, and the 15 countries/regions with the highest number of published papers have been displayed in **Supplementary Table 3** and Fig. 3A. The contributions of countries/regions were uneven, and the top effect was significantly identified. China was the most productive country with 1507 (32.04%) papers. However, the United States (USA) contributed 1323 (28.13%) papers, second only to China, with 42.87 citations per article, and the highest H index of 199. Interestingly, China and the USA accounted for more than half (55.31%, 2830/5117) of the total of literature published

in the top 15 countries. **Supplementary Fig. 2B** displays the annual number of publications in the top 10 productive countries from 1999 to 2023. China surpassed the USA for the first time in 2016 and has held the top spot almost every year since. It was noteworthy that in spite of publishing only 104 (2.21%) articles, Denmark owned the highest average citations per paper reaching 57.49, which was due to the contribution of Rasmussen Lars Simon at the University of Copenhagen. Besides, international collaboration in this domain has also been demonstrated in Fig. 3B. Notably, the USA was at the center of the field collaborating with China, Canada, Australia, Germany, and the United Kingdom (UK).

3.4 Contributions of Institutions

Until the deadline (January 18, 2023), a total of 4172 institutions had contributed papers dealing with PND. The top 15 institutions are listed in Fig. 4. Nine of these institutes were affiliated with the USA. Harvard Medical School (USA) was the most productive and influential institution with 224 papers and an H index of 63. Papers regarding Hebrew Senior Life (USA), on average, were cited 121.13 times, which was much higher than that of other institutions. Notably, Sharon K. Inouye played a prominent part in this achievement.

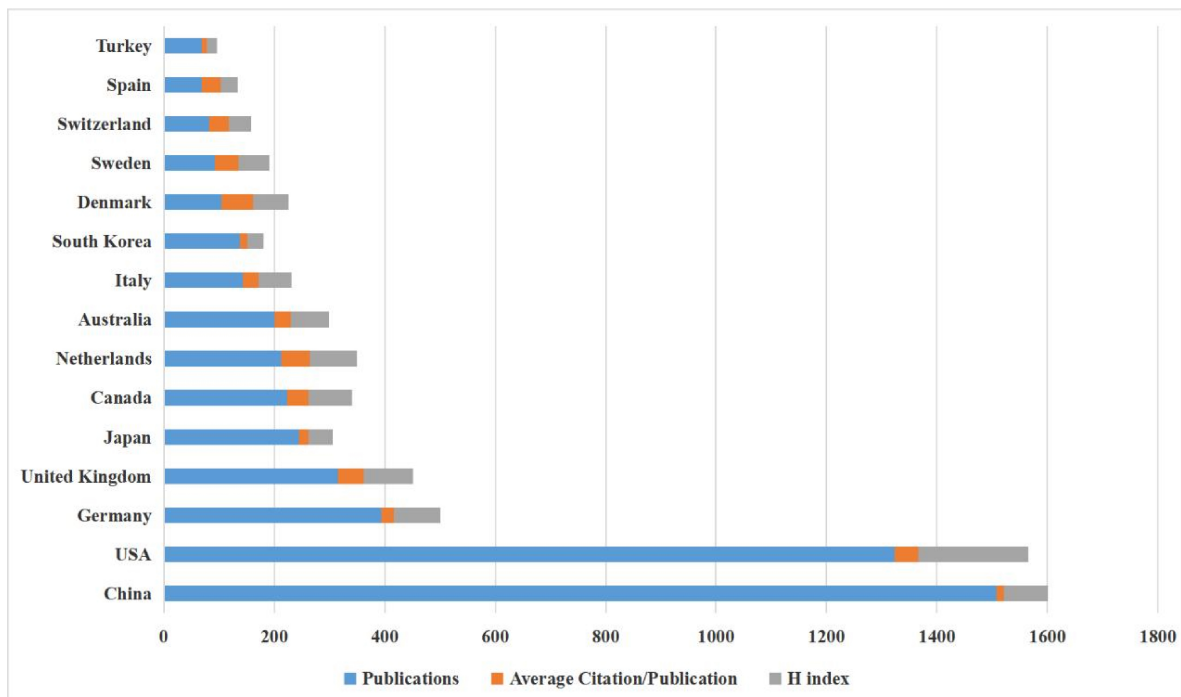
3.5 Analysis of Journals

Over the past 20 years, 972 journals have published papers related to PND. The top ten journals have published 827 papers on PND, accounting for 17.58% of the 4704 publications (Table 1) on the subject. *Anesthesia and Analgesia* (IF: 6.627, Q1) was the most productive journal with 121 papers published. On average, documents from the journal *Anesthesiology* (IF: 8.986, Q1) were cited 86.02 times, making it the most frequently cited journal. Most of the top 10 journals were categorized into Q1 or Q2 according to the JCR 2022 standards, among which *the British Journal of Anaesthesia* (IF: 11.719, Q1) was found to be the journal with the highest IF, with 91 articles and 53.37 citations per article. Notably, all the three journals mentioned above, are journals in the field of anesthesiology, indicating that PND has been receiving increasing attention from researchers in this field.

3.6 Analysis of Keywords

Keywords condense the essence and core of a paper, and thus the co-occurrence analysis of keywords can uncover the evolution of hotspots and further explore the development trends in the field. A map of co-occurrence analysis among 367 PND-related keywords that appeared at least 20 times was obtained with the help of VOSviewer (Fig. 5A). As demonstrated in the mapping of network visualization, all the identified keywords were divided into the five clusters and represented in the mapping by nodes of specific colors as follows: Cluster 1 (postoperative delir-

A



B

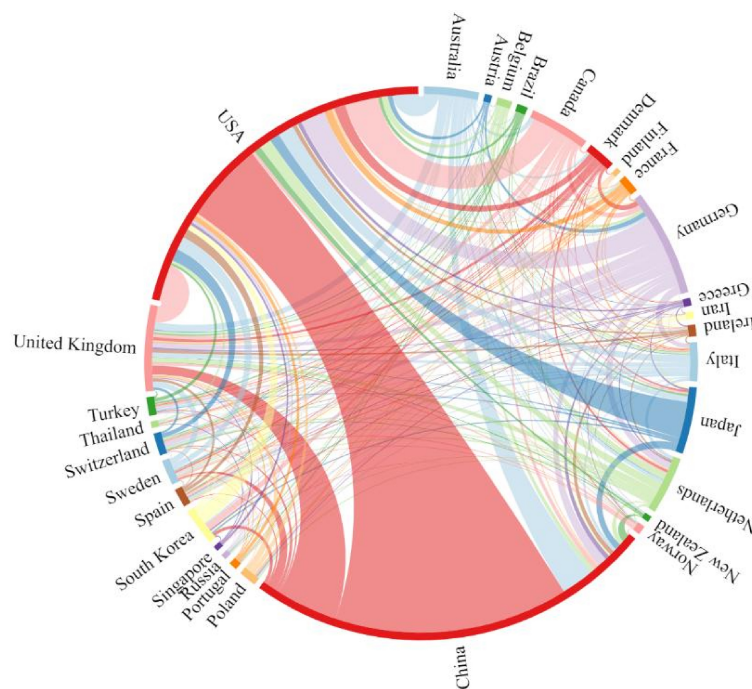


Fig. 3. Contributions of countries or regions. (A) The total publications, average citations per item, and H index of the top 15 countries. (B) International collaboration of countries/regions in this domain. The thickness of the line indicates the frequency of the cooperation, and a thicker line represents a stronger association.

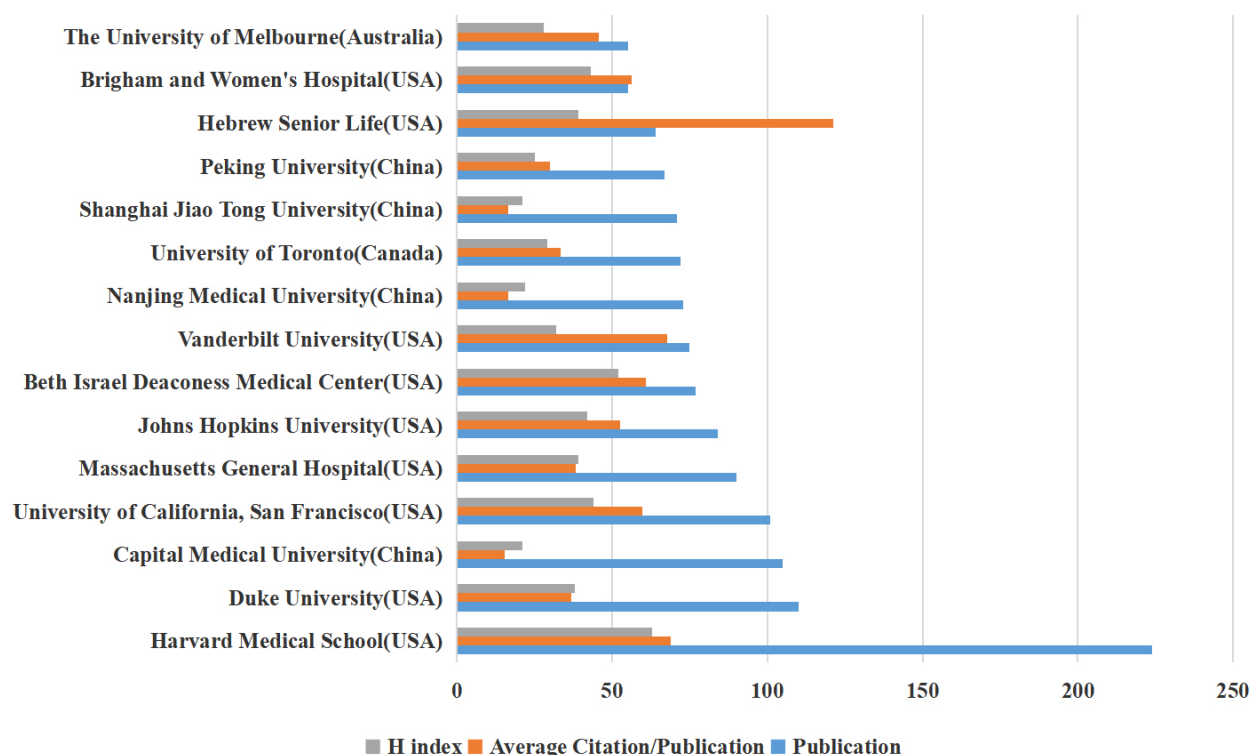


Fig. 4. Contributions of institutions. The H index, average citations per publication, and total number of publications of the top 15 institutions.

ium, green nodes); Cluster 2 (impairment, red nodes); Cluster 3 (prognosis, blue nodes); Cluster 4 (anesthesia, purple nodes); and Cluster 5 (operation, yellow nodes).

To trace the progress of PND research with regards to time dimension, CiteSpace provided a time zone view depicting the evolution of keywords over the past 20 years, as shown in Fig. 5B. Keywords, such as cardiac surgery, older patients, and intensive care unit, were prominently searched for before 2010. Few keywords, such as neuroinflammation and neurocognition, have gained prominence in recent years.

Furthermore, the top 15 keywords related to PND with maximum citation bursts have been listed in **Supplementary Fig. 3**. Through burst detection and co-citation analysis, we identified burst keywords emerging frequently in a certain time period, which may indicate the future direction in the field. From the figure, it is evident that prior to 2018, research on PND focused on anesthetic methods and intraoperative procedures, and exploration of its mechanisms using mouse models. However, after 2018, the focus shifted on the new keyword, perioperative neurocognitive disorder. Notably in November 2018, the latest definition of PND was simultaneously published in six leading journals focusing on the field of anesthesiology. It recommended that “perioperative neurocognitive disorders” be used as the primary term for cognitive disorders diagnosed before or after surgery, attracting increasing attention to perioperative neurocognitive disorder [1].

4. Discussion

PND, referring to significant perioperative complications, especially in the aged population, has been attracting increasing attention over the past two decades. In this study, we collected and analyzed 4704 documents from the field of PND published in the WoSCC database and carried out a detailed analysis with respect to factors, such as, annual outputs and global trends; the most influential and productive institutions; countries/regions, authors, and journals with maximum contribution in the field of PND; hotspots; and keywords; thereby providing a comprehensive summary of the happenings in the field of PND.

According to the change of annual output, the development progress of PND research could be divided into two stages: “Fluctuation (before 2010)” and “Stable growth (since 2010)”. This indicates that PND research has attracted increasing attention in recent years and is likely to continue in the future. This is presumably due to current interest in PND and newer discoveries regarding the related mechanisms due to ongoing research.

Edward R. Marcantonio from Harvard Medical School and Sharon K. Inouye from Hebrew Senior Life are the two authors with the largest number of published papers related to PND. The H index, which is a bibliometric indicator, simultaneously evaluates the quantity (number of papers) and quality (largely dependent on citations) of authors, journals, or national publications [28]. This analysis demonstrated that, Sharon K. Inouye has a higher H index,

Table 1. The top 10 journals for PND research.

Rank	Journal	Publication count	Impact Factor TM (2022)	Journal Citation Reports TM (2022)	Total citations	Average citations
1	Anesthesia and Analgesia	121	6.627	Q1	5443	44.98
2	British Journal of Anaesthesia	91	11.719	Q1	4857	53.37
3	Journal of The American Geriatrics Society	88	7.538	Q1	6461	73.42
4	Anesthesiology	86	8.986	Q1	7398	86.02
5	Plos One	84	3.752	Q2	2332	27.76
6	Frontiers in Aging Neuroscience	83	5.702	Q1	589	7.1
7	Journal of Cardiothoracic and Vascular Anesthesia	74	2.894	Q3	1452	19.62
8	BMJ Open	72	3.006	Q2	806	11.19
9	BMC Anesthesiology	69	2.376	Q3	876	12.7
10	Medicine	59	1.817	Q3	420	7.12

indicating that she is the most influential author in this field. It should be noted that the literature published by Sharon K. Inouye has the highest average frequency of citations, indicating that her papers reflect high quality and are worth learning. One of the highly cited articles authored by Inouye has provided a state-of-the-art and comprehensive review of delirium in the aged population as of 2014 that can guide clinical practice and extensively educate the public about the significance of delirium [2].

In terms of national/regional contributions toward PND research, China and the USA are the top two productive countries, and the USA has the highest H index, while Denmark, the country from where article regarding the effect of POCD on long-term prognosis has been published [29], has the highest average frequency of citations. There is active international collaboration between different countries/regions, the USA being the main collaborating center. The partnership between China and the USA is strongest among all the cooperative relationships.

Harvard Medical School in the USA has published the maximum literature on PND and has the highest H index among all institutions, making it the most influential and productive institution on this topic. However, the average number of citations received by the Hebrew Senior Life in the USA was the highest; indicating that the literature published was of high quality and was widely recognized. It is of noteworthy that 9 of the top 15 institutions are from the USA, and it can be considered that the USA is a pioneer in this field. Analysis of the correspondence between authors and institutions indicated that Prof. Edward R. Marcantonio, the most productive author, and his working institution Harvard Medical School, ranked highest in terms of the number of documents published.

Anesthesiology (IF: 8.986, Q1), *Journal of The American Geriatrics Society* (IF: 7.538, Q1), *British Journal of Anaesthesia* (IF: 11.719, Q1), and *Anesthesia and Analgesia* (IF: 6.627, Q1) were the four journals with the highest average frequency of citations and the highest number of published articles. Journals with high JCR categories and impact factor (IF) have a greater chance of attracting high-

quality literature, and the publication of outstanding papers. And that, in turn, can improve the academic quality and impact of these journals.

Keyword co-occurrence analysis helps estimate hotspots in a scientific field, and the time zone view presents the trends in a more graphical manner and makes them easier to visualize, while burst keywords (keywords with a burst in citations), to some extent, can help understand future trends in this field. “Elderly patients” was one of the most frequently encountered keywords, which is in accordance with the high morbidity rate associated with PND in the aged population. Other high-frequency keywords included “risk factor”, “anesthesia”, “cardiac surgery”, and “assessment method”. We speculate that future research would be closely related to neuroinflammation and other pathogenic mechanisms.

Generally, PND may share several common pathways with neuropsychiatric disorders [30], such as Alzheimer’s disease [31] and depression [32]. Various hypotheses have been proposed to shed light on the mechanisms of PND, including impaired synaptic function [33], oxidative stress [34], and blood-brain barrier (BBB) dysfunction [35]. Neuroinflammation is one of the primary pathogenesis of PND [36]. Surgery and anesthetic exposure can trigger neuroinflammation and induce the onset of PND [37]. As pivotal mediators of neuroinflammation, microglial cells are activated for producing an exaggerated immune response, triggering the release of inflammatory cytokines [38], such as IL-1, IL-1 β and tumor necrosis factor (TNF)- α [39,40]. Moreover, preexisting inflammation has been observed to increase the severity and morbidity of PND in rats [41]. Recent findings by Glumac *et al.* [42,43] have demonstrated that prophylactic administration of dexamethasone can ameliorate the inflammatory response induced by cardiac surgery, which has a short-term and long-term beneficial effect on cognitive function postoperatively.

Prediction and early recognition of high-risk patients with PND are of great significance in clinical settings. Currently, the diagnosis of PND is mainly based on neuropsychological tests, traditional scales, and biomark-

delirium

confusion assessment method

alzheimers disease

risk factor

pain

dementia

mortality

critically ill patient

cardiopulmonary bypa

general anesthesia

anesthesia

propofol

depression

surgery

intensive care unit

analgesia

dysfunction

elderly patient

hip fracture

cardiac surgery

complication

postoperative delirium

coronary artery bypa

noncardiac surgery

impairment

neurocognitive function

neuroinflammation

isoflurane

postoperative cognitive dysfunction



ers, which includes Mini Emotional State Examination (MESE), Mini Mental State Examination (MMSE), Modified Mini Mental State Examination (3MS), Wechsler Adult Intelligence Scale-Fourth Edition (WAIS-IV), Montreal Cognitive Assessment (MoCA), confusion assessment method (CAM), CAM-ICU, CAM-S, 4 A's test (4AT), Intensive Care Delirium Screening Checklist (ICDSC), brain-derived neurotrophic factor (BDNF), serum uric acid (SUA) and so on [44–49]. Early detection of at-risk patients and timely targeted prevention can reduce the incidence of PND. Feasible interventions mainly consist of pharmacologic agents and nonpharmacologic approaches. Various pharmacologic agents include drug candidates targeting systemic inflammation, on signaling pathways regulating immune response (NLRP3, HMGB1, and toll-like receptors), microbial-based treatments (short-chain fatty acids and prebiotics), and dexmedetomidine. The main non-pharmacologic approaches are preoperative multidisciplinary evaluation, the guidance of bispectral index (BIS), electroacupuncture (EA) and so on [50,51]. However, the pathogenesis of PND has not been deduced and requires further elucidation, and there is no standard prevention and treatment strategy for PND currently available. Further research must identify early predictors and potential therapeutic targets.

The limitations of this study are as follows: first, WoSCC was selected as the data source, and the “citation index” was set as SCI-EXPANDED, with data retrieval from 1999, which inevitably raises the issue of data omission. Second, due to the rapid update of WoSCC database, bibliometric analysis results usually lag behind the actual research situation, for factors such as H index, the number of publications and citations. Furthermore, high-quality bibliometric analysis requires a thorough and in-depth understanding of this field.

5. Conclusions

In this study, 4704 publications were collected and bibliometric analysis was conducted to identify the hotspots, frontier areas, and future tendencies on PND research. Overall, the PND research is in the rapid development phase, and this is likely to continue. The USA, undoubtedly, is in a leading position as well as the collaborating center in global research. In recent years, “neuroinflammation” has become a hotspot in this field showing that neuroinflammation plays a vital role in the mechanism of PND. However, further studies are needed to illustrate pathogenesis of PND and identify potential therapeutic targets.

Abbreviations

3MS, Modified Mini Mental State Examination; 4AT, 4 A's test; BBB, blood-brain barrier; BDNF, brain-derived neurotrophic factor; BIS, bispectral index; CAM, confusion assessment method; EA, electroacupuncture; ICDSC, Intensive Care Delirium Screening Checklist; IF, Impact Fac-

tor; IL, interleukin; JCR, Journal Citation Reports; MESE, Mini Emotional State Examination; MMSE, Mini Mental State Examination; MoCA, Montreal Cognitive Assessment; PND, perioperative neurocognitive disorders; POCD, postoperative cognitive dysfunction; POD, postoperative delirium; SUA, serum uric acid; TNF, tumor necrosis factor; TS, topic; UK, the United Kingdom; USA, United States; WAIS-IV, Wechsler Adult Intelligence Scale-Fourth Edition; WoSCC, Web of Science Core Collection.

Availability of Data and Materials

The datasets used and/or analyzed during the current study are available from the corresponding author on reasonable request.

Author Contributions

YY and HL: Data curation, writing original draft. YY and TH: visualization. TH: Methodology. YY, WW and TH: Formal analysis. CL, CY and CH: Conceptualization. QZ, DW, ZW, SH: Figure design. QZ, DW, ZW, SH, CL, CY, TH and CH: Writing, review and editing. All authors contributed to editorial changes in the manuscript. All authors read and approved the final manuscript. All authors have participated sufficiently in the work and agreed to be accountable for all aspects of the work.

Ethics Approval and Consent to Participate

Not applicable.

Acknowledgment

Not applicable.

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Conflict of Interest

The authors declare no conflict of interest.

Supplementary Material

Supplementary material associated with this article can be found, in the online version, at <https://doi.org/10.31083/j.jin2206140>.

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