Drug Design, Development and Therapy
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ORIGINAL RESEARCH

Mapping Theme Trends and Research Frontiers in Dexmedetomidine Over Past Decade: A Bibliometric Analysis

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Background: Dexmedetomidine, an α_2-adrenergic receptor (α_2-AR) agonist, is extensively used in clinical and animal studies owing to its sedative, analgesic, and anxiolytic effects. The diverse range of research domains associated with dexmedetomidine poses challenges in defining pivotal research directions. Therefore, this study aimed to conduct a qualitative and quantitative bibliometric study in the field of dexmedetomidine over the past decade to establish current research trends and emerging frontiers.
Methods: Relevant publications in the field of dexmedetomidine between 2014 and 2023 were extracted from the Web of Science Core Collection database. The bibliometric analysis, incorporating statistical and visual analyses, was conducted using CiteSpace (6.1.R6) and R (4.3.1).
Results: The present study encompassed a total of 5,482 publications, exhibiting a consistent upward trend over the past decade. The United States and its institutions had the highest centrality. Ji, Fuhai, and Ebert, Thomas J. were identified as the most productive author and the most cited author, respectively. As anticipated, the most cited journal was *Anesthesiology*. Moreover, cluster analysis of cited references and co-occurrence of keywords revealed that recent studies were primarily focused on sedation, delirium, and opioid-free anesthesia. Finally, a timeline view of keywords clusters and keywords burst demonstrated that primary research frontiers were stress response, neuroinflammation, delirium, opioid-free anesthesia, peripheral nerve block, and complications.
Conclusion: Current research trends and directions are focused on sedation, delirium, and opioid-free anesthesia, as evidenced by our results. The frontier of future research is anticipated to encompass basic investigations into dexmedetomidine, including stress response and neuroinflammation, as well as clinical studies focusing on delirium, opioid-free anesthesia, peripheral nerve block, and associated complications.
Keywords: dexmedetomidine, bibliometric analysis, CiteSpace, delirium, opioid-free anesthesia

Introduction

Dexmedetomidine, a dextro-isomer of medetomidine, is an imidazole compound and a highly selective agonist for membrane-bound G-protein-coupled α_2-adrenergic receptors (α_2-AR).[1] It is characterized by its high binding affinity to α_2 and α_1 adrenergic receptors. Moreover, it is potent and highly selective for α_2-AR, with an α_2: α_1 ratio of 1,620:1.[2] This selectivity distinguishes dexmedetomidine from other medications with similar chemical structures, such as clonidine. Additionally, dexmedetomidine can effectively interact with three α_2-AR subtypes (α_{2A}, α_{2B}, and α_{2C}) to induce sedative, analgesic, and anxiolytic effects, making it extensively utilized in both clinical and animal research studies.[3,4]

Received: 13 January 2024
Accepted: 4 July 2024
Published: 16 July 2024

In the clinical setting, dexmedetomidine has been extensively used in intensive care unit (ICU) patients for sedation, hemodynamic stabilization, and as a complement to peripheral nerve block (PNB) and an integral component of opioid-free anesthesia (OFA).[5–15] Several pivotal clinical studies have unveiled its potential effects in mitigating postoperative delirium (POD) and ameliorating postoperative cognitive dysfunction (POCD).[10,16–19] Nevertheless, to date, several large-scale multicenter randomized controlled trials (RCT) have yielded inconclusive or conflicting findings.[20–23] In fundamental research, significant progress has been made in elucidating the impact of dexmedetomidine on vital organs such as the heart, brain, liver, and kidneys.[24–27] Furthermore, a novel formulation referred to as sublingual dexmedetomidine (BXCL501) has demonstrated efficacy in the treatment of acute agitation and relieving opioid withdrawal symptoms.[28–30] Despite numerous investigations into the effects of dexmedetomidine, its underlying mechanism of action remains elusive, and results are inconsistent. Therefore, there is a pressing need to conduct a quantitative analysis of research progress, accomplishments, and future prospects related to dexmedetomidine.

Over the past decade, extensive research has been conducted on dexmedetomidine across various areas. Hence, previous bibliometric analyses of dexmedetomidine primarily focused on its clinical applications and lacked comprehensive coverage.[31] Bibliometrics, as an independent discipline, provides quantitative methods for the investigation of existing literature in a specific field and has been widely applied in literature analysis.[32] In the present study, a comprehensive analysis of dexmedetomidine published over the past 10 years was performed, establishing a visual model to elucidate current research status and trends. This study can inform future developments and serve as a valuable reference for further investigations into dexmedetomidine.

Methods

Data Sources and Search Strategies

The database source for this study was the Web of Science Core Collection (WoSCC), widely acknowledged as a high-quality literature resource library and the most suitable option for conducting bibliometric analyses.[33,34]

The search was conducted within a single day (December 30, 2023) to mitigate potential bias arising from daily database updates. The employed search strategy was as follows: TS = (dexmedetomidine) OR TS = (MPV-1440) OR TS = (MPV 1440) OR TS = (MPV1440) OR TS =(Precedex) OR TS = (BXCL501) OR TS = (Dexmedetomidine Hydrochloride) OR TS = (Hydrochloride, Dexmedetomidine). The publication period ranged between 2014 and 2023.

Inclusion and Exclusion Criteria

Inclusion criteria: (1) Original articles or reviews; (2) Articles published in English; (3) The time span was limited from January 1, 2014, to December 30, 2023.

Exclusion criteria: (1) Studies not related to dexmedetomidine; (2) Dexmedetomidine was not the central focus of the article; (3) Abstracts, editorials, proceeding papers, meetings, letters, book chapters, retracted publications, and expressions of concern; (4) Articles without an abstract or a digital object identifier (DOI) number; (5) Articles unavailable in full text.

All literature retrieval and data downloads were completed on December 30, 2023. Two groups of reviewers (Group 1: ZXZ and XYS; Group 2: YQZ and YYY) independently performed data searches and cleaning after standard training. Disagreements regarding the inclusion of articles between the two groups of reviewers were arbitrated by a third researcher (LZ) until a consensus was reached. Finally, the search yielded a total of 5,482 articles.

Statistical Analysis and Visualization

Data on dexmedetomidine were converted to txt format and exported for bibliometric analysis using CiteSpace (6.1.R6) and R 4.3.1 "bibliometrix" (https://www.bibliometrix.org).

CiteSpace is a visualization software based on the Java platform developed by Professor Chaomei Chen that effectively identifies prominent scientific institutions, authors, and keywords, as well as research trends and directions.[32,35] Each node in the visualization map generated by Citespace represents a country, institution, author, journal, or keyword. The frequency of occurrence or citation is represented by the size of nodes, while the year is indicated by their color. The outermost purple ring in the visualization map denotes the centrality of each node, with thicker rings indicating higher centrality levels. Nodes exhibiting high centrality (> 0.1) are commonly regarded as pivotal or critical points in a field.[36] The modularity (Q value) and mean silhouette scores (S value) were utilized in the cluster analysis to assess the overall structural characteristics of the network, with the cluster quality of the cluster map being satisfactory when $Q > 0.3$ and $S > 0.5$.

"Bibliometrix package" (https://www.bibliometrix.org) is an R-based bibliometrics analysis tool that offers several functions and visualization tools for tracking research themes over time and analyzing journals.[37] The visual network analysis of collaborative efforts between countries and the density visualization map of authors were generated using VOSviewer (1.6.19), SCImago Graphica (1.0.36) (https://graphica.app/, and a bibliometric online webpage (https://bibliometric.com).

Results

Between January 1, 2014, to December 30, 2023, 8,770 publications related to dexmedetomidine were published. After excluding abstracts, editorials, and other document types, a total of 7,524 publications were retained. Next, the two groups of researchers thoroughly reviewed titles and abstracts to exclude studies unrelated to dexmedetomidine or non-English publications. Ultimately, a total of 5,482 papers met the eligibility criteria and were included in the analysis, comprising 4,723 articles and 759 reviews (Figure 1).

Bibliometric Analysis of Publication Outputs

The annual publication volume reflects research achievements and the degree of activity devoted to a specific research field. Figure 2A presents a visual representation of the time distribution of papers published in the field of dexmedetomidine, with a total of 5,482 papers meeting the inclusion criteria between 2014 and 2023. Overall, the number of publications on dexmedetomidine progressively increased. Specifically, it increased by nearly 3-fold from 2014 to 2023 (236 versus 702, respectively). From 2014 to 2018, the overall growth in the number of publications was relatively slow, suggesting a period of difficult exploration. Since 2019, the number of published papers rapidly increased, reaching 866 in 2022. Lastly, the period from 2018 to 2021 was a phase of rapid development, with research maintaining a stable growth rate in recent years.

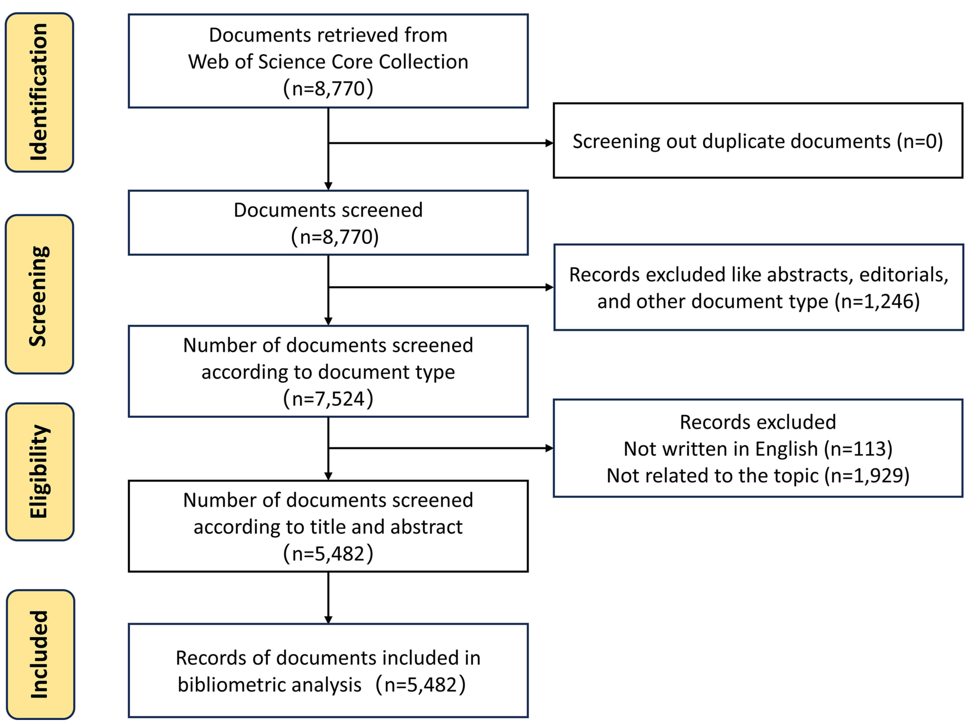

Figure 1 PRISMA flowchart of the study.

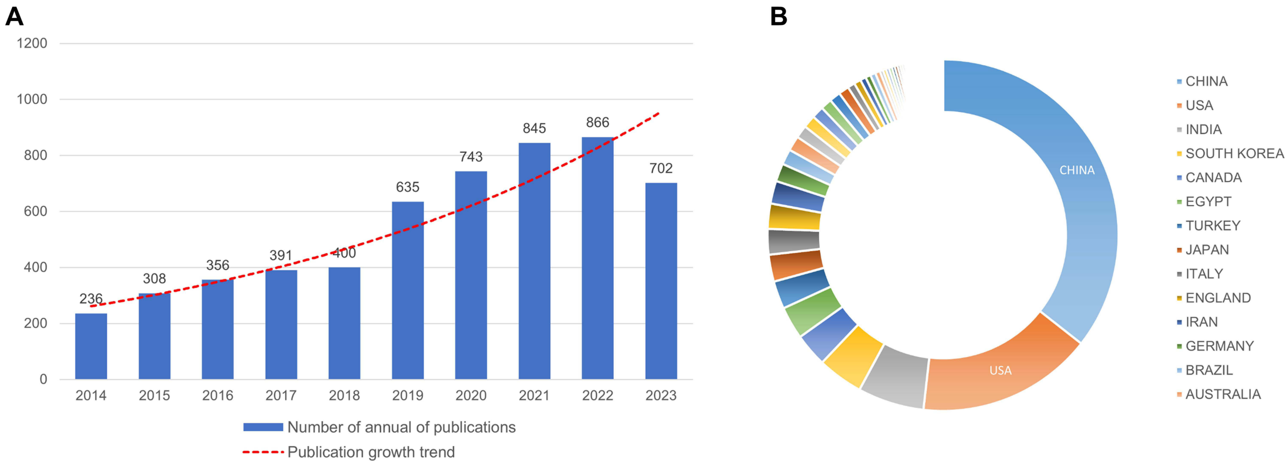

Figure 2 Bibliometric analysis of publication outputs. (**A**) The number of annual publications. (**B**) The distribution of publications by countries/regions.

Studies involving dexmedetomidine were undertaken in 543 different countries/regions, with China being the leading contributor (n = 2,298), followed by the USA (n = 1,047). Indeed, publications from these two countries constituted 61% of the total publications (Figure 2B).

Countries/Regions Distribution Analysis

The top five productive countries were China (n = 2,298), the USA (n = 1,047), India (n = 395), South Korea (n = 271) and Canada (n = 198) (Table 1). Assessment of centrality can provide insights into the significance and impact of nodes within a network. China led in terms of publications in this field, with a total number of publications of 2,298, significantly surpassing that of other nations. Moreover, it exhibited a centrality value of 0.16, indicating a higher frequency of transnational collaboration (Figure 3A and B). The USA exerted a significantly greater influence than any other country (centrality = 0.39), establishing its core position in the research field and its close collaborations with other countries. This highlighted the propensity of researchers in the USA to engage in international cooperation for research endeavors (Figure 3A and C).

Institutions Analysis

To assess the academic impact of each institution in the field, the top 10 institutions with the highest publication counts were compiled, as detailed in Table 1. The leading institutions by publication volume were Shanghai Jiao Tong University (China, n = 94), Sun Yat-Sen University (China, n = 87), Anhui Medical University (China, n = 85), Nanjing Medical University (China, n=79), and Harvard Medical School (USA, n = 78) (Figure 4A and B). In terms

Table 1 The Top 10 Countries/Regions and Institutions Involved in Dexmedetomidine

Rank	Countries/Regions	Count	Centrality	Institutions	Count	Centrality	Country
1	China	2298	0.16	Shanghai Jiao Tong Univ	94	0.11	China
2	USA	1047	0.39	Sun Yat Sen Univ	87	0.14	China
3	India	395	0.07	Anhui Med Univ	85	0.05	China
4	South Korea	271	0	Nanjing Med Univ	79	0.03	China
5	Canada	198	0.11	Harvard Med Sch	78	0.21	USA
6	Egypt	194	0.03	Fudan Univ	74	0.04	China
7	Turkey	166	0.01	Capital Med Univ	66	0.02	China
8	Japan	160	0	Soochow Univ	65	0.03	China
9	Italy	152	0.09	Shandong Univ	62	0.04	China
10	England	150	0.14	China Med Univ	58	0.05	China

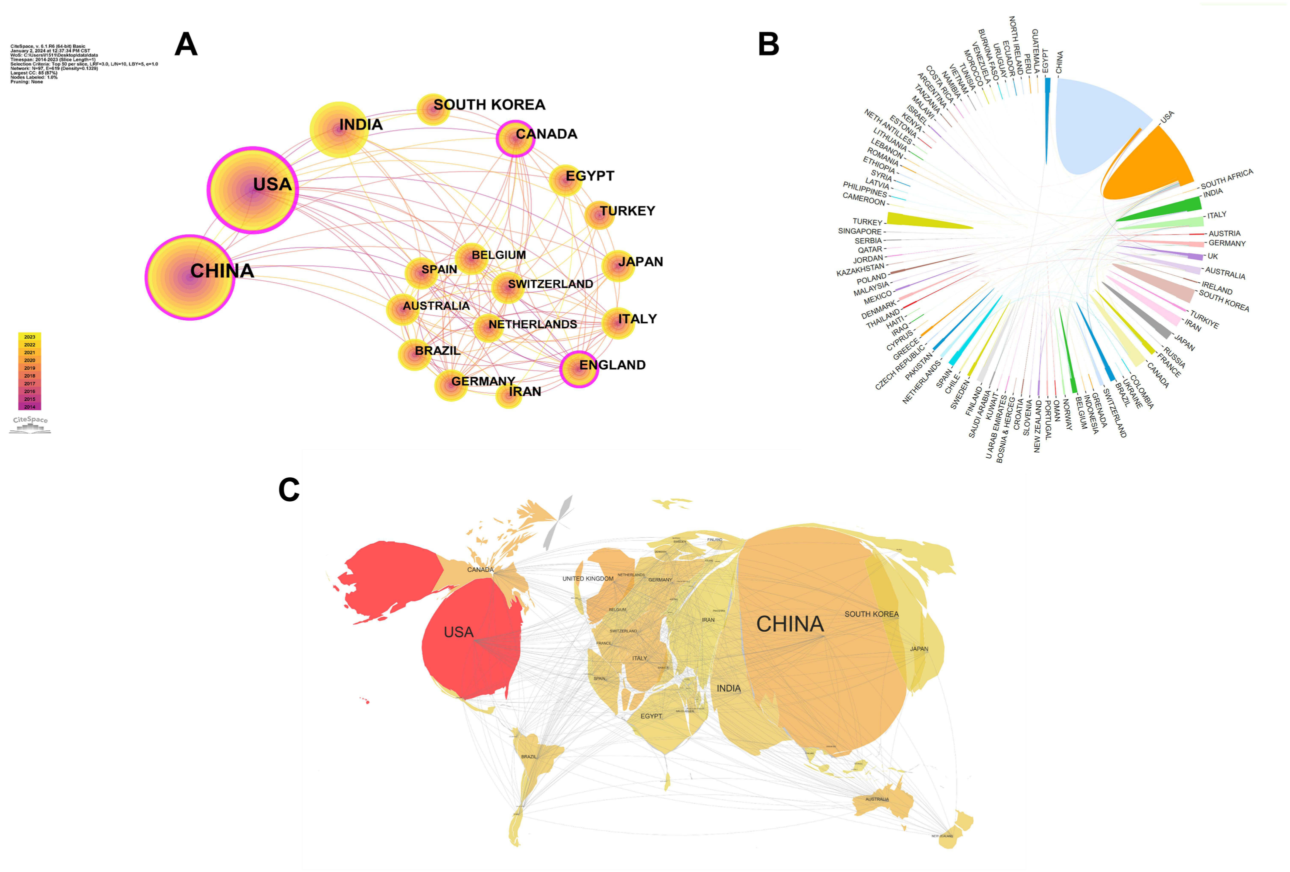

Figure 3 Cooperation between countries/regions on dexmedetomidine. (**A**) The cooperation networks between different countries/regions; (**B**) Countries/regions cross-chord charts; (**C**) Geography map of countries/regions for dexmedetomidine.

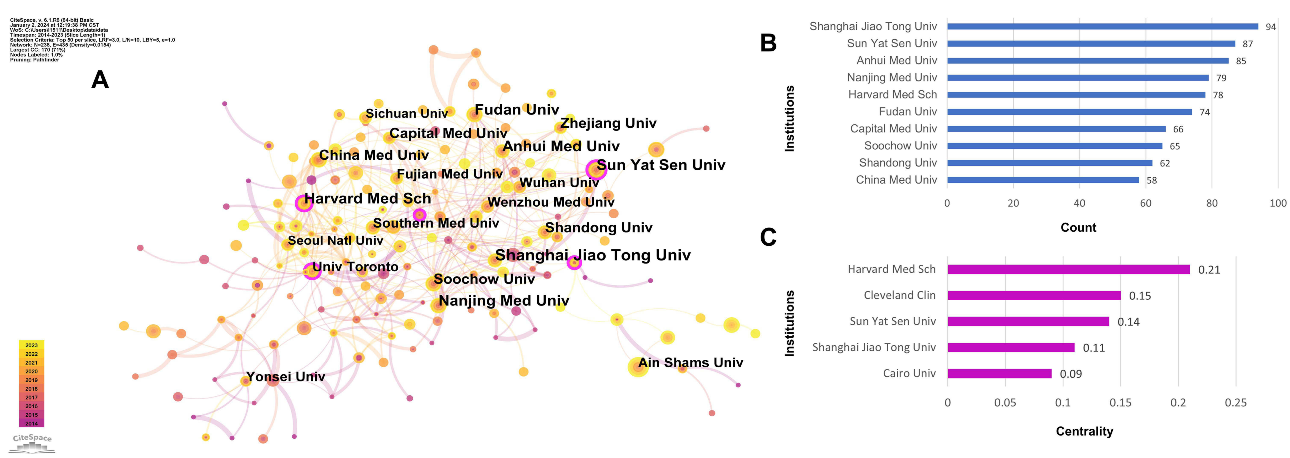

Figure 4 Cooperation between institutions on dexmedetomidine. (**A**) The cooperation networks between different institutions; (**B**) The top 10 institutions in count; (**C**) The top 10 institutions in centrality.

of centrality, Harvard Medical School had the highest centrality among foreign institutions (centrality = 0.21), positioning it as a core institution in the field of foreign research (Figure 4A and C). Among domestic institutions, Sun Yat-sen University had a high degree of centrality, suggesting not only a significant publication frequency but also frequent collaborations with other institutions (centrality = 0.14) (Figure 4C). It has made substantial contributions to pioneering research, and its collaborative efforts have further enhanced research output.

Authors and Cited Authors Analysis

The analysis of Figure 5A revealed a high number of author nodes, indicating a dense network of cooperative relationships among authors in this field. Moreover, the high connection strength observed demonstrated the close collaboration among authors. According to Price's law, the minimum number of publications required for a core author, *N*, was calculated to be 4.68. Rounded up, authors with over 5 publications were considered core authors in the field. A total of 296 core authors were identified, which collectively contributed 2,476 publications, accounting for 45.2% of the total author publications. The top three authors, Ji, Fuhai (n = 39), Peng, Ke (n = 31), and Modir, Hesameddin (n = 25), had centrality values below 0.1, suggesting the absence of prominent authors in this field (Table 2) (Figure 5B). Ma Daqing's relatively high centrality and an H index of 62 implied significant contributions warranting further exploration. The most co-cited author was Ebert, Thomas J. (n = 409), who is widely recognized as an expert in the field of dexmedetomidine (Figure 5C) (Table 2).

Journals Analysis

Figure 6A depicts the top 10 journals ranked by publication numbers, showing significant growth since 2014. Based on Bradford's law, 1,186 journals were categorized into zones 1–3, whereas 31 core source journals fell in zone 1 (Figure 6B) (Table 3).

The co-citation network of journals was mapped using CiteSpace (Figure 7A). The most cited journal was *Anesthesiology* (n = 3,442), followed by *Anesthesia & Analgesia* (n = 3,215) and *British Journal of Anaesthesia* (n = 2,897) (Figure 7B) (Table 4). In terms of centrality, *Anesthesiology* had the highest centrality among journals (centrality = 1.12) (Figure 7C). The aforementioned journals are esteemed publications within the field of anesthesia, renowned for their significant impact and authoritative standing.

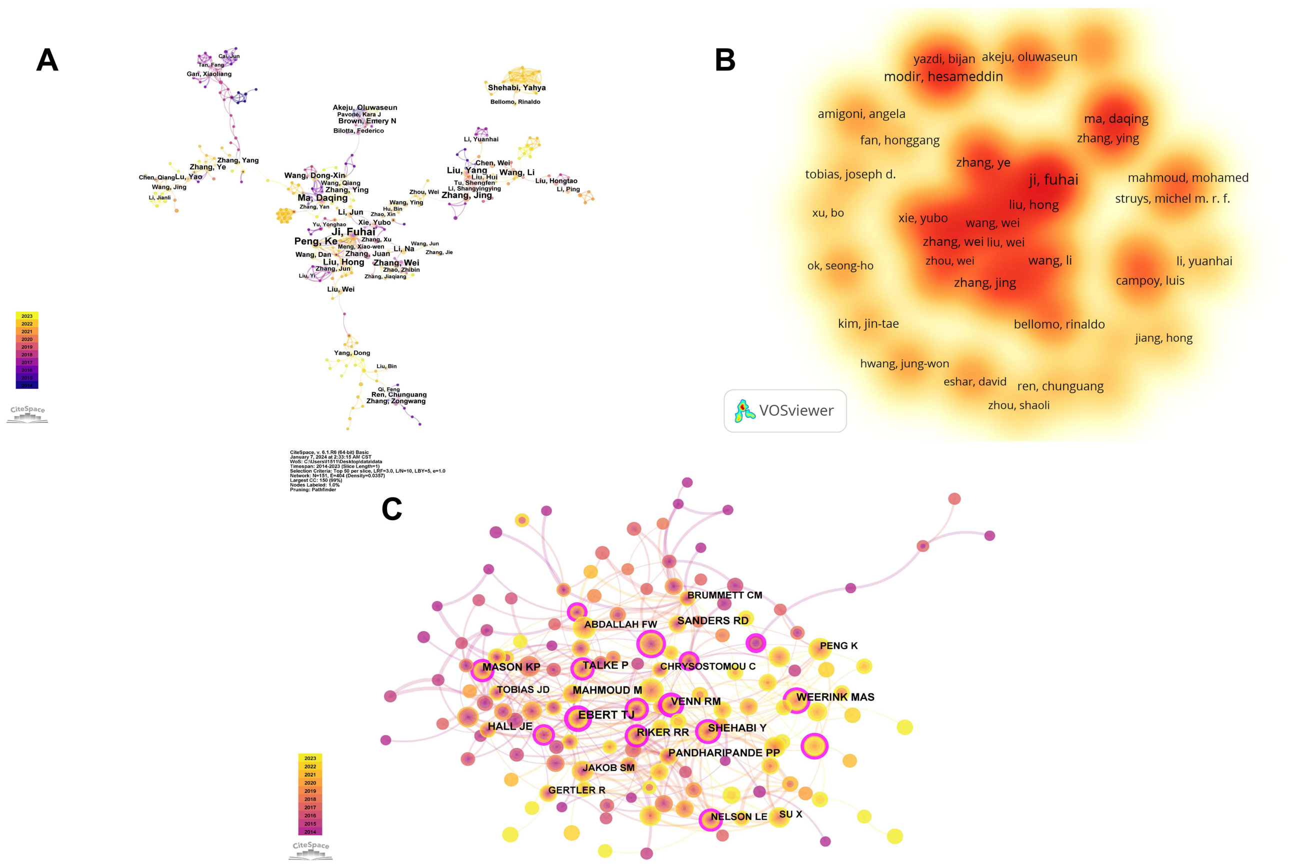

Figure 5 Authors analysis on dexmedetomidine. (**A**) The cooperation networks between different authors; (**B**) The density visualization map of authors based on VOSviewer; (**C**) The cooperation networks between different cited authors.

Table 2 The Top 10 Authors and Cited Authors in Dexmedetomidine

Rank	Author	Count	Centrality	H-index	Cited Author	Count	Centrality
1	Ji, Fuhai	39	0.05	23	Ebert, Thomas J.	409	0.1
2	Peng, Ke	31	0.01	30	Weerink, M. A. S.	398	0.06
3	Modir, Hesameddin	25	0	8	Venn, Robert M.	365	0.12
4	Ma, Daqing	22	0.07	62	Mason, Keira P.	357	0.1
5	Liu, Hong	22	0	29	Riker, Richard R.	310	0.02
6	Zhang, Wei	21	0.01	6	Talke, Pekka	300	0.08
7	Zhang, Jing	20	0.05	4	Pandharipande, Pratik P.	282	0.02
8	Liu, Yang	19	0.01	12	Sanders, Robert D.	279	0.03
9	Kamali, Alireza	19	0	4	Hall, James E.	261	0.03
10	Wang, Li	18	0.02	13	Shehabi, Yahya	258	0.04

In the dual-map overlay illustrating studies focusing on dexmedetomidine (Figure 7D), each data point on the map represents a scientific journal. The map is divided into two sections, with the left side depicting journals used as references and the right side representing journals that have been cited by others. Among them, there were 4 outward citation paths for molecular, medicine, and neurology fields on the left of the figure, highlighting their importance in citations. Simultaneously, utilizing medicine, medical, and clinical as primary sources, disciplines such as health, nursing, and medicine had the highest citation rates (Z value = 7.914).

Cited References Analysis

The analysis of cited references is critical for examining emerging trends and identifying promising research prospects within a specific academic domain. In the current study, a total of 26 articles with centrality above 0.1 were identified. They played a key role or had a transitional significance in the literature, served as foundational classics across various periods, and played a key role in the academic development of this field (Table 5). "Clinical Pharmacokinetics and Pharmacodynamics of Dexmedetomidine", published by Weerink, M. A. S., was the most cited paper, with 307 citations (Figure 8A).

Cluster analysis of cited references unveiled eight major clusters (Q value = 0.707, S value = 0.8799): #0 acute lung injury, #1 chloral hydrate, #2 postoperative delirium, #3 benzodiazepines, #4 hippocampus, #5 opioid-free anesthesia, #6 spinal cord, #7 ischemia-reperfusion injury, #8 nerve block, #9 delirium, #10 children, and #11cardiopulmonary bypass (Figure 8B). The citation frequency of the top 10 cited papers collectively exceeded 80, with a predominant focus on cluster #2 postoperative delirium (n = 4) and #5 opioid-free anesthesia (n = 2).

References that exhibit high burst intensity typically cover a broader spectrum of scientific outputs and exert a more significant influence on future research directions. The top two references in terms of burst strength were "Clinical Pharmacokinetics and Pharmacodynamics of Dexmedetomidine" (strength = 38.51) and "Dexmedetomidine vs Midazolam or Propofol for Sedation During Prolonged Mechanical Ventilation: Two Randomized Controlled Trials" (strength = 32.16) (Figure 8C).

Subject Categories

According to WOS categories, publications on dexmedetomidine were classified into various research topics (Table 6), with "Anesthesiology" (n = 1,245) emerging as the most important research path, followed by "Pharmacology Pharmacy" (n = 806), "Medicine General Internal" (n = 587), and "Medicine Research Experimental" (n = 579).

Research Themes

As delineated in Figure 9, the trend of research topics has evolved over the past decade. From 2014 to 2018, only 5 research topics were related to dexmedetomidine. However, the diversity of research topics progressively expanded over time. In particular, from 2021 to 2023, "delirium" became a research focus (Figure 9). This finding indicates growing interest among researchers in comprehensively exploring delirium-related disorders. In addition to delirium, recent research topics also included "opioid-free anesthesia", "oxidative stress", and other related topics.

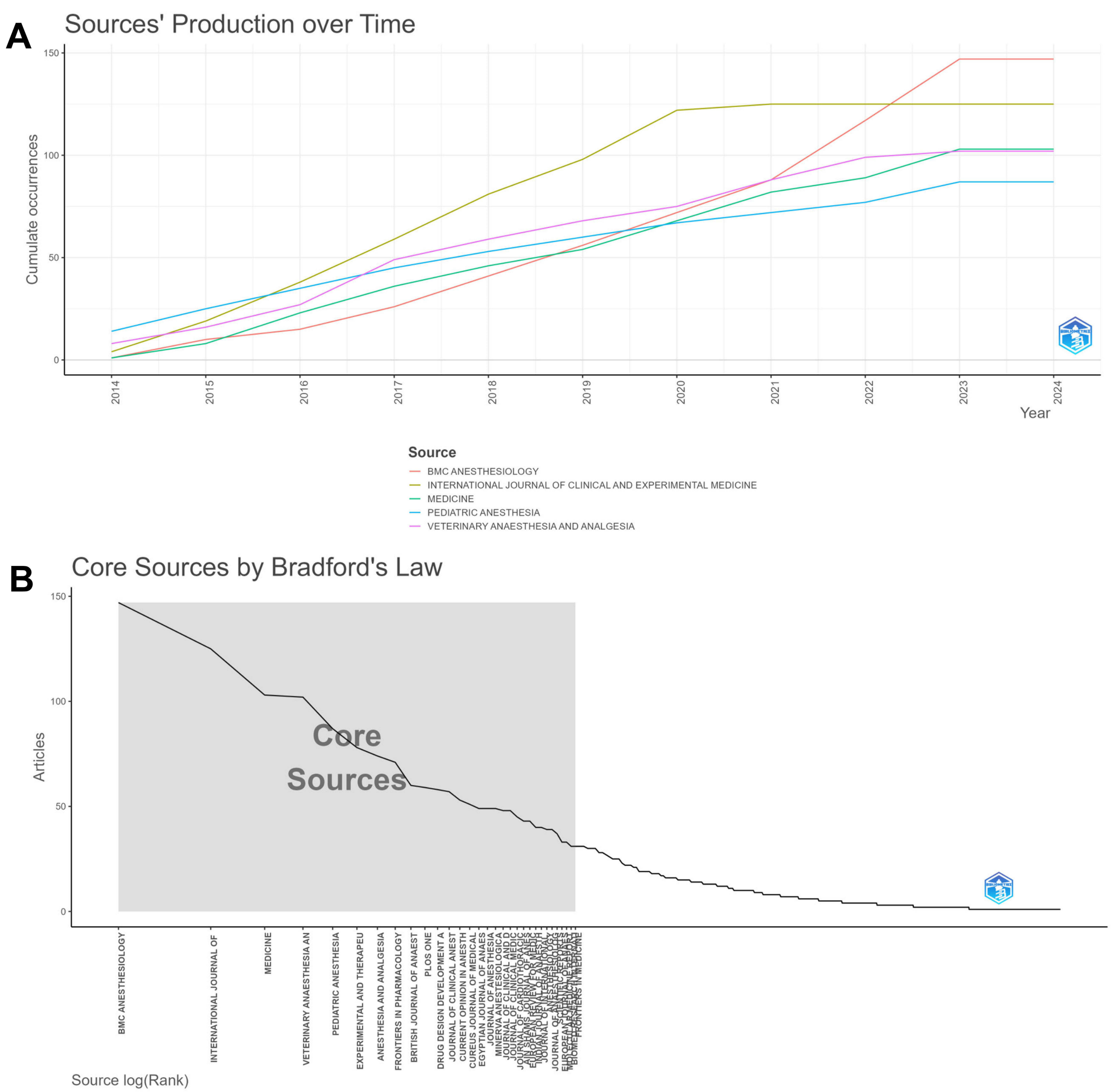

Figure 6 Journals analysis on dexmedetomidine. (**A**) Journals output trends within the top 5 from 2014 to 2023; (**B**) Core journals by Bradford's law.

Keywords Analysis

Keywords Co-Occurrence

The analysis of keyword co-occurrence across the literature allows the effective categorization of high-frequency terms and the evaluation of the strength of their associations. Additionally, this approach enhances our understanding of the internal structure of an academic field and unveils its research frontiers. The keyword co-occurrence mapped by CiteSpace depicted 196 nodes and 708 links (Figure 10A). According to the perspective of knowledge theory, keywords with high frequency and centrality are areas of interest among researchers during a specific period, representing hotspots and frontiers in the field. "anesthesia" (n = 763) emerged as the most frequent keyword in the co-occurrence analysis, with significant attention directed towards "sedation", "propofol", and "dexmedetomidine".

Table 3 According to Bradford's Law, the 1,186 Journals in Dexmedetomidine were Classified into Zones 1–3

Zone	Number of Journals	Number of Publications	Percentage
1	31	1822	33.2%
2	150	1853	33.8%
3	1005	1807	33.0%
Total	1186	5482	100%

Clusters of Keywords

Cluster analysis of keywords displayed that the 196 keywords could be divided into six main clusters (Q value = 0.5581, S value = 0.8586): #0 oxidative stress; #1 medetomidine; #2 delirium; #3 ropivacaine; #4 children and #5 opioid-free anesthesia (Figure 10B). The average year of cluster #5 was 2021, suggesting that relevant research was approaching the frontier. High-frequency keywords in the cluster analysis included "opioid-free anesthesia", "opioid-based anesthesia", "dexmedetomidine", "laparoscopy", and "total intravenous anesthesia". In recent years, opioid-free anesthesia using dexmedetomidine has emerged as a prominent area of research compared to opioid-based anesthesia.

Timeline View Keywords Clusters and Research Hotspot Analysis

The timeline analysis node in CiteSpace was used to generate a keyword time graph, illustrating temporal changes in keywords. The timeline view provides a clearer visualization of historical research results, trends, and internal relationships within each cluster. Each node represents a distinct keyword, with larger nodes indicating a higher frequency of occurrence. The gradual shift in line color from cooler to warmer tones reflects the changing trend in keyword appearance over time.

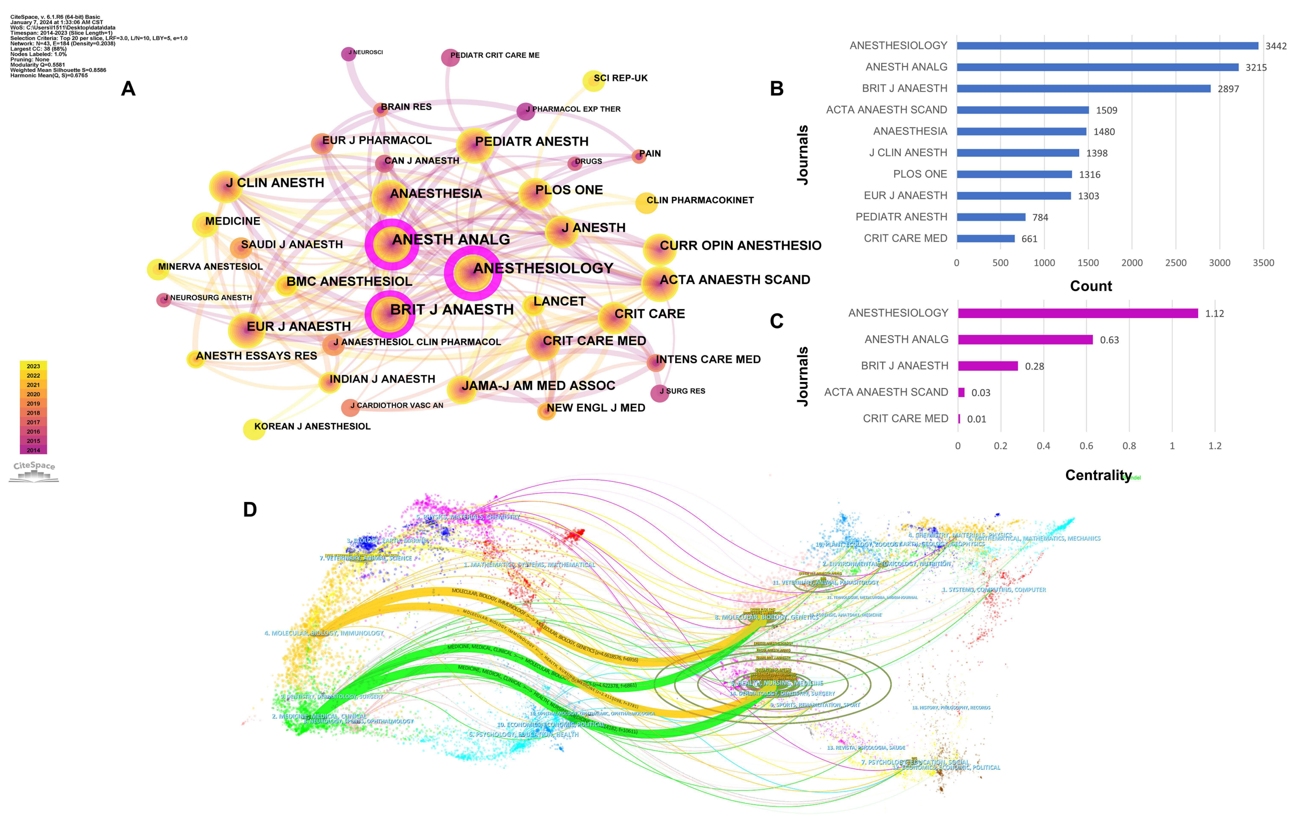

Figure 7 Cited journals analysis on dexmedetomidine. (**A**) The network map of cited journals; (**B**) The top 10 cited journals in count; (**C**) The top 10 cited journals in centrality; (**D**) The dual-map overlay of citing of citation relationship of articles, with citing journal on the left, and the cited journal on the right. The colored path represented the citation relationship.

Table 4 The Top 10 Cited Journals in Dexmedetomidine

Rank	Journal	Count	Centrality	IF (2022)	JCR (2022)
1	Anesthesiology	3442	1.12	8.8	Q1
2	Anesthesia & Analgesia	3215	0.63	5.9	Q1
3	British Journal of Anaesthesia	2897	0.28	9.8	Q1
4	Acta Anaesthesiologica Scandinavica	1509	0.03	2.1	Q4
5	Anaesthesia	1480	0	10.7	Q1
6	Journal of Clinical Anesthesia	1398	0	6.7	Q1
7	PLoS One	1316	0	3.7	Q2
8	European Journal of Anaesthesiology	1303	0	3.6	Q2
9	Pediatric Anesthesia	784	0	1.7	Q4
10	Critical Care Medicine	661	0.01	8.8	Q1

Table 5 The Top 10 Cited References in Dexmedetomidine

Rank	References	Count	Centrality	Publication Year
1	Weerink MAS, Struys MMRF, Hannivoort LN, Barends CRM, Absalom AR, Colin P. Clinical Pharmacokinetics and Pharmacodynamics of Dexmedetomidine. Clin Pharmacokinet. 2017;56(8):893-913. doi:10.1007/s40262-017-0507-7[2]	307	0.17	2017
2	Su X, Meng ZT, Wu XH, et al. Dexmedetomidine for prevention of delirium in elderly patients after non-cardiac surgery: a randomised, double-blind, placebo-controlled trial. Lancet. 2016;388(10054):1893-1902. doi:10.1016/S0140-6736(16)30580-3[10]	146	0.15	2016
3	Wang K, Wu M, Xu J, et al. Effects of dexmedetomidine on perioperative stress, inflammation, and immune function: systematic review and meta-analysis. Br J Anaesth. 2019;123(6):777-794. doi:10.1016/j.bja.2019.07.027[4]	103	0.07	2019
4	Djaiani G, Silverton N, Fedorko L, et al. Dexmedetomidine versus Propofol Sedation Reduces Delirium after Cardiac Surgery: A Randomized Controlled Trial. Anesthesiology. 2016;124(2):362-368. doi:10.1097/ALN.0000000000000951[38]	99	0.12	2016
5	Shehabi Y, Howe BD, Bellomo R, et al. Early Sedation with Dexmedetomidine in Critically Ill Patients. N Engl J Med. 2019;380(26):2506-2517. doi:10.1056/NEJMoa1904710[59]	97	0.05	2019
6	Deiner S, Luo X, Lin HM, et al. Intraoperative Infusion of Dexmedetomidine for Prevention of Postoperative Delirium and Cognitive Dysfunction in Elderly Patients Undergoing Major Elective Noncardiac Surgery: A Randomized Clinical Trial. JAMA Surg. 2017;152(8):e171505. doi:10.1001/jamasurg.2017.1505[20]	96	0.16	2017
7	Barr J, Fraser GL, Puntillo K, et al. Clinical practice guidelines for the management of pain, agitation, and delirium in adult patients in the intensive care unit. Crit Care Med. 2013;41(1):263-306. doi:10.1097/CCM.0b013e3182783b72[39]	92	0.06	2013
8	Mahmoud M, Mason KP. Dexmedetomidine: review, update, and future considerations of paediatric perioperative and periprocedural applications and limitations. Br J Anaesth. 2015;115(2):171-182. doi:10.1093/bja/aev226[40]	91	0.2	2015
9	Lee S. Dexmedetomidine: present and future directions. Korean J Anesthesiol. 2019;72(4):323-330. doi:10.4097/kja.19259[41]	89	0.05	2019
10	Duan X, 2018, BRIT J ANAESTH, V121, P384, DOI 10.1016/j.bja.2018.04.046[42]	80	0.06	2018

In 2014, "anesthesia", "sedation", "propofol", "dexmedetomidine", and "surgery" were pivotal keywords that not only served as the foundation for this study but also remained at the forefront of research throughout its progression. The period from 2015 to 2022 witnessed the emergence of research topics such as "oxidative stress", "postoperative delirium", "apoptosis", "local anesthetics", and "total intravenous anesthesia". In 2023, emerging research areas encompassed "opioid-free anesthesia", "complication", "peripheral nerve block", "abdominis plane block", and "systematic review". These results conjointly suggested that the utilization of dexmedetomidine in combination with peripheral nerve block as an opioid-free anesthesia technique has emerged as a significant focus in future dexmedetomidine research (Figure 10C).

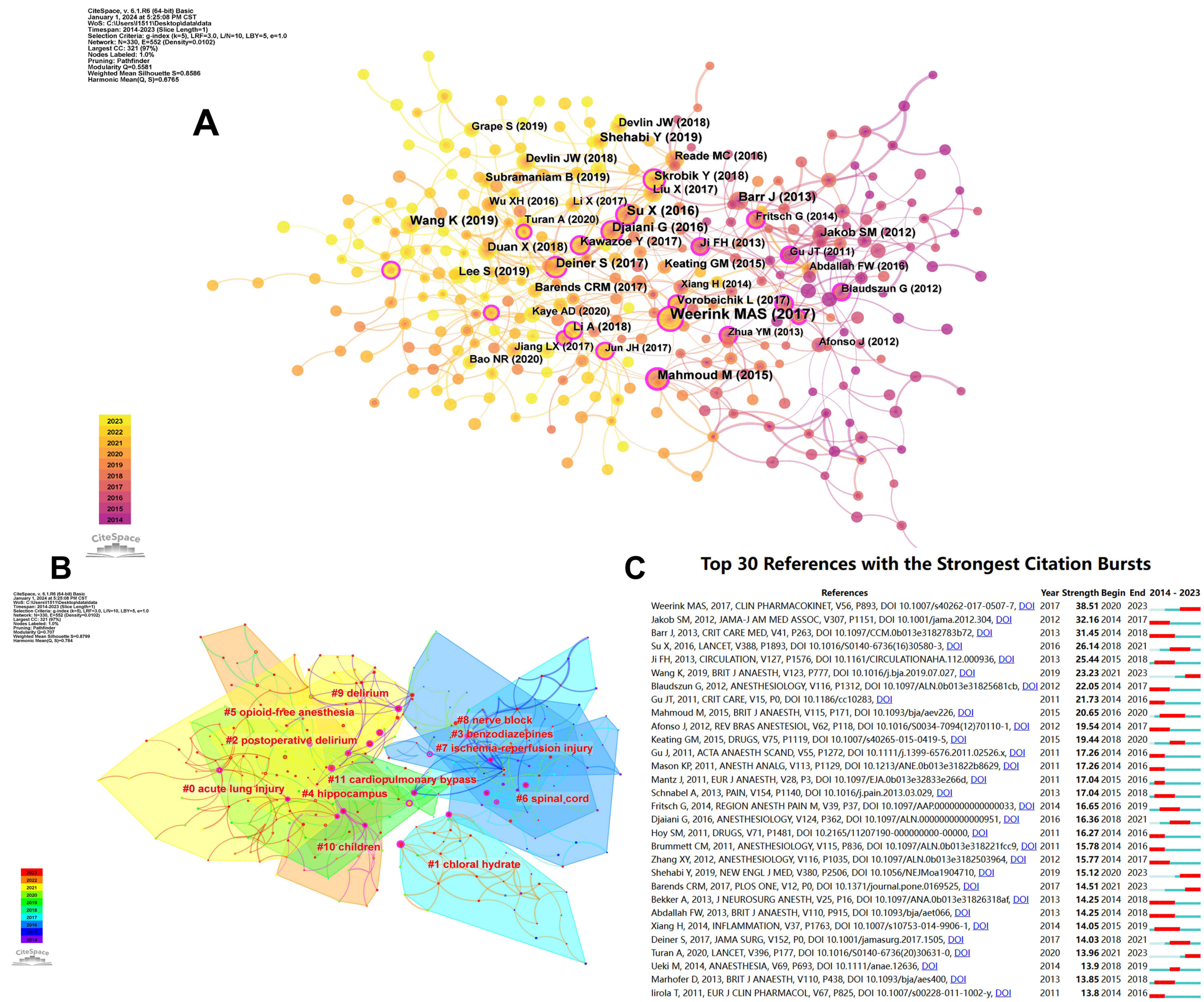

Figure 8 Cited references analysis on dexmedetomidine. (**A**) The network map of cited references; (**B**) The clustering of cited references; (**C**) The top 30 cited references with the strongest citation bursts.

Keyword Bursts

Burst keywords in current research hotspots were identified using CiteSpace. The burst map effectively illustrates the temporal increase in keyword usage, enabling the assessment of research directions and attention levels during specific periods. Over the past decade, "randomized controlled trial" ranked first with the highest burst strength (strength = 21.45). Notably, "stress response", "neuroinflammation", "total intravenous anesthesia", and "emergence delirium" have recently garnered considerable attention, positioning them as current trends and research topics (Figure 10D).

Discussion

Herein, a bibliometric analysis was conducted to visually examine 5,482 articles in the field of dexmedetomidine over the past decade. CiteSpace and R language were employed to reveal current research trends and future prospects for dexmedetomidine, as well as emphasize potential directions for future research.

Basic Information Analysis

According to the results of the qualitative and quantitative analyses obtained from CiteSpace, the number of articles on dexmedetomidine has consistently increased over the past decade. Notably, there has been a remarkable surge in the

Table 6 Top 10 Productive WOS Categories in Dexmedetomidine, Ranked by the Number of Publications

Rank	Web of Science Categories	Record Count
1	Anesthesiology	1245
2	Pharmacology Pharmacy	806
3	Medicine General Internal	587
4	Medicine Research Experimental	579
5	Veterinary Sciences	433
6	Clinical Neurology	293
7	Neurosciences	288
8	Surgery	279
9	Pediatrics	265
10	Critical Care Medicine	229

number of related articles around 2019, which can be attributed to enhanced recognition of the pivotal role of dexmedetomidine.

In terms of countries and institutions, China and its institutions undoubtedly hold a prominent position in this field. However, despite a lower overall publication volume compared to China, the USA and its institutions had the highest centrality, indicating its core role in research and close international collaborations. The dominant position of the USA in this field is likely due to its robust research and development infrastructure, heavy investment in scientific research and innovation, and conducive environment for groundbreaking discoveries.

Importantly, the network of collaborative relationships among authors in the field of dexmedetomidine is relatively dense. The most prolific author was Ji, Fuhai from Soochow University, who conducted numerous clinical trials investigating the perioperative recovery of patients treated with dexmedetomidine, as well as several studies into the mechanisms underlying its anti-inflammatory and organ-protective effects.[43–47] The top most cited author was Ebert, Thomas J. He is recognized as a pivotal figure in the field, and his numerous groundbreaking investigations on dexmedetomidine, encompassing diverse plasma concentrations in human subjects, as well as sedative and analgesic assessments, have garnered significant scholarly attention.[48–50]

The most cited journal was *Anesthesiology*, followed by *Anesthesia & Analgesia* and the *British Journal of Anaesthesia*. The aforementioned three journals hold a prominent position in the field of anesthesiology and exert

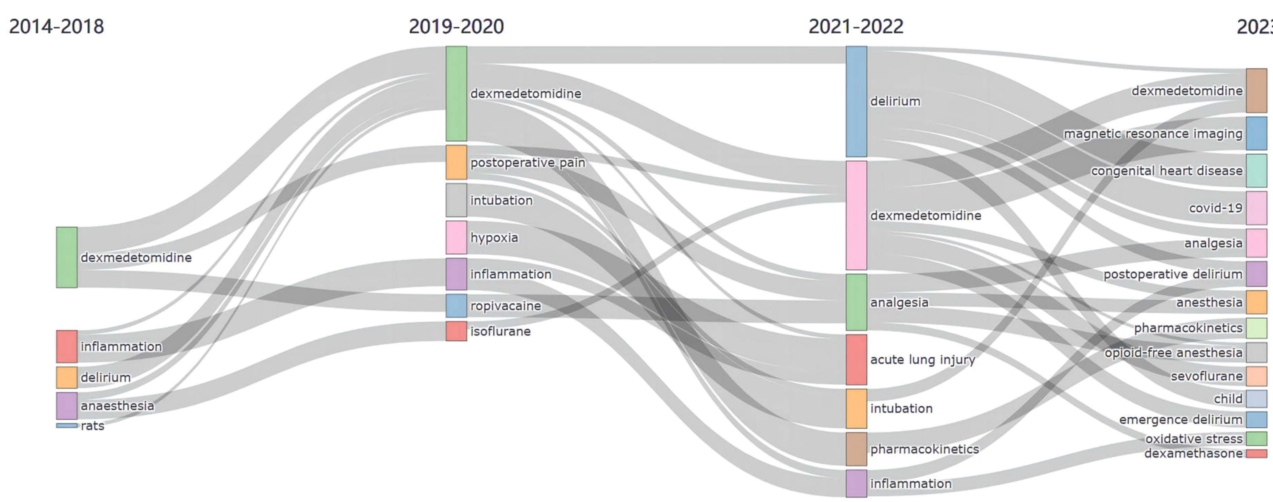

Figure 9 R bibliometrics-thematic evolution tool traces the progression of research themes in the realm of dexmedetomidine, spanning from 2014 to 2023.
Notes: The time segmentation points were established by R in 2018, 2020 and 2022.

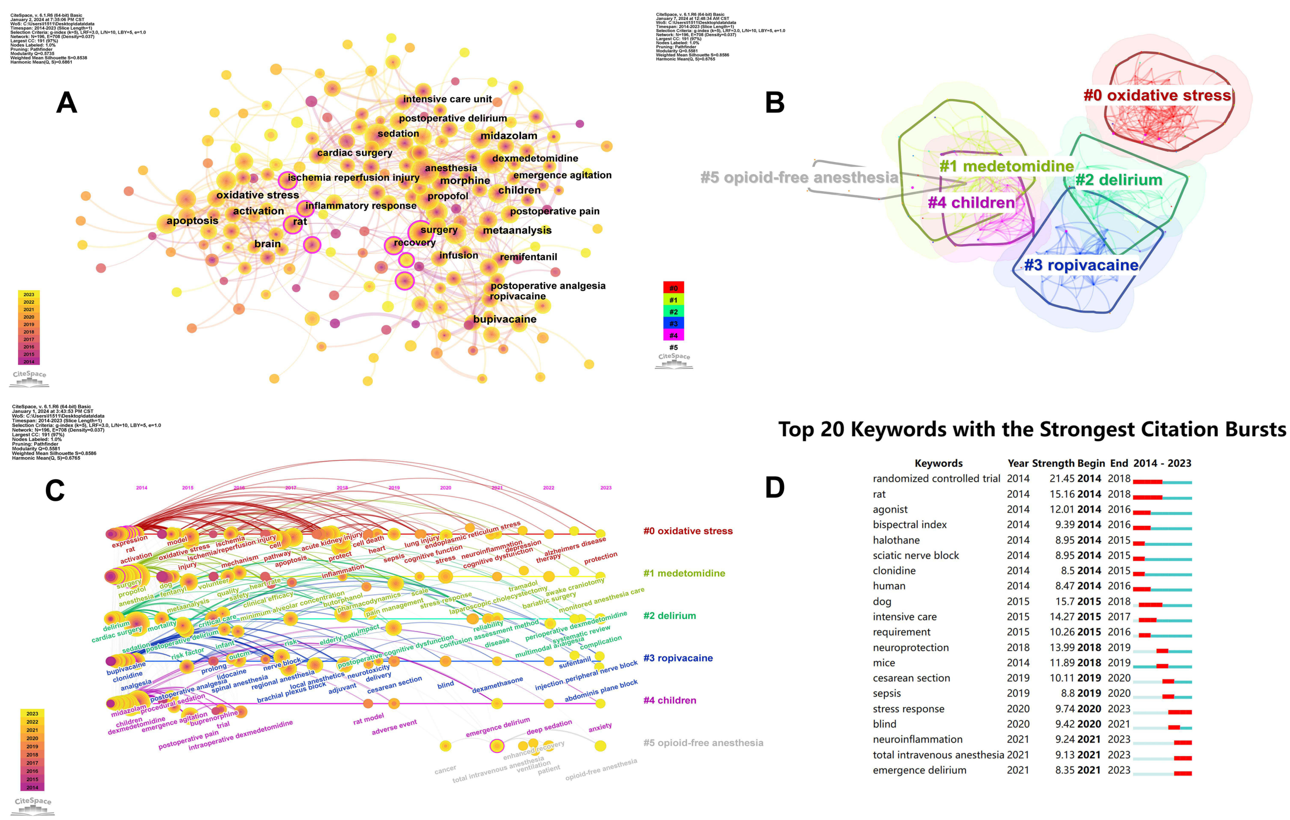

Figure 10 Keywords analysis on dexmedetomidine. (**A**) The network map of the co-occurrence keywords; (**B**) Clusters of keywords; (**C**) Timeline view of keywords analysis; (**D**) The top 20 keywords with the strongest citation bursts.

significant influence. Besides, the most cited reference was "Clinical Pharmacokinetics and Pharmacodynamics of Dexmedetomidine", published by Weerink MAS. This review provides a systematic review of the pharmacology of dexmedetomidine to facilitate a better understanding of its role.[2]

Theme Trends and Hot Topics

Keywords in a research paper are important indicators of its disciplinary structure. These keywords can be combined with highly cited literature within a specific time frame to identify emerging research topics. These trends and research topics represent areas that have garnered substantial attention and interest from the academic community during a specific period.

Sedation

Co-occurrence analysis of keywords identified sedation as a prominent topic in dexmedetomidine research. In other words, one of the focuses of research on dexmedetomidine was sedation. Initially, it was initially approved solely for intravenous sedation of mechanically ventilated adult patients in the ICU, with a maximum duration of 24 hours. Between 2008 and 2011, dexmedetomidine was approved by the US Food and Drug Administration (FDA) and the European Union for use in non-intubated patients, administration during general anesthesia, tracheal intubation and mechanical ventilation procedures, and sedation of patients requiring varying degrees of sedation.[2] In 2022, dexmedetomidine was recommended as a sedative agent for adult ICU patients undergoing invasive mechanical ventilation by the Intensive Care Medicine Rapid Practice Guideline (ICM-RPG).[51]

Several impactful clinical studies have demonstrated the sedative effects of dexmedetomidine. The large, multicenter PRODEX and MIDEX trials conducted by Jakob et al reported that dexmedetomidine was non-inferior to midazolam and propofol in maintaining mild to moderate sedation in ICU patients receiving prolonged mechanical ventilation and could shorten the duration of mechanical ventilation.[7] Nonetheless, it is worthwhile emphasizing that dexmedetomidine increases the risk of adverse reactions such as bradycardia and hypotension.[6,7,52] Another clinical study conducted by Riker et al (SEDCOM trial) documented that dexmedetomidine exerted satisfactory sedative effects and shortened the time to extubation postoperatively.[6] A large number of clinical studies and meta-analyses have also established that dexmedetomidine can reduce the duration of mechanical ventilation post-surgery and does not elicit respiratory depression, positioning it as an effective postoperative sedative and analgesic agent.[53–62]

However, other studies have yielded conflicting results. For instance, an open-label, multicenter randomized clinical trial undertaken by Kawazoe et al (DESIRE trial) in Japan uncovered that dexmedetomidine did not improve the postoperative outcomes of mechanically ventilated patients receiving and did not lower postoperative mortality rates.[63] Similarly, an international, open-label, randomized, controlled trial (SPICE III trial) involving 4,000 patients showed that the sedative effects of dexmedetomidine were weaker than those of other sedatives and did not lower the mortality rate within 90 days after surgery.[64] Furthermore, the results of the MENDS2 trial revealed no difference in mortality rates and mechanical ventilation duration between patients receiving propofol as an anesthetic and those who were administered dexmedetomidine as a sedative.[65]

Recent studies have shown that besides ICU patients, dexmedetomidine has increasingly been considered for pediatric sedation, including intranasal administration. A previous study showed that among 13,072 cases, dexmedetomidine accounted for 5.3% of all pediatric sedation, and intranasal injection of dexmedetomidine was safe and effective in children.[66] Moreover, Yuen et al evinced that intranasal dexmedetomidine was more readily accepted by children, exerted superior sedative effects, and was associated with a lower incidence of nausea and vomiting and fewer significant adverse reactions compared to oral chloral hydrate.[67] Intranasal dexmedetomidine has been widely applied in pediatric magnetic resonance imaging (MRI) and computerized tomography (CT) scans.[68,69] Additionally, in addition to midazolam, intranasal dexmedetomidine can also be used in pediatric surgery, with previous studies describing that preoperative use of intranasal dexmedetomidine can minimize the incidence of respiratory-related adverse reactions following tonsillectomy and adenoidectomy.[70]

The efficacy of dexmedetomidine in inducing sedation remains controversial. Numerous large-scale clinical studies have been conducted and yielded contrasting results, warranting further investigations.

Delirium

Cluster analysis of cited references and research themes pointed out that delirium is a significant topic in the field of dexmedetomidine research. Delirium, featured by acute, fluctuating changes in attention, consciousness, and cognitive function, is a form of acute brain dysfunction and a prevalent neurocognitive complication in elderly patients after surgery. Despite numerous large clinical trials studying the effects of dexmedetomidine on postoperative delirium, the results remain inconclusive.

The SEDCOM trial included delirium as a secondary research endpoint and determined that dexmedetomidine was associated with a lower incidence of postoperative delirium compared to midazolam.[6] In addition to midazolam, intravenous infusion of dexmedetomidine may outperform lorazepam in lowering the risk of postoperative delirium and mortality (MENDS trial).[62] Su et al discovered that prophylactic low-dose intravenous infusion of dexmedetomidine significantly mitigated the risk of delirium within the first 7 days following surgery.[10] Recent clinical studies have also reported that dexmedetomidine can effectively reduce the incidence and duration of delirium episodes compared to other commonly used sedatives.[16–18]

Furthermore, large clinical trials such as DEXACET, DECADE, DESIRE, EXACTUM, and DIRECT trial have yielded conflicting results, demonstrating that dexmedetomidine did not reduce, and even increased, the incidence of postoperative delirium.[19,21,63,71,72] At the same time, Deiner et al[20] conducted a randomized controlled trial involving 404 elderly patients undergoing non-cardiac surgery and found that continuous perioperative and postoperative infusion of dexmedetomidine did not reduce the incidence of postoperative delirium. Likewise, dexmedetomidine did not decrease the risk of postoperative atrial arrhythmias or delirium in patients undergoing cardiac surgery.[21] Overall, the results of clinical studies and meta-analyses have not provided strong support for the use of dexmedetomidine in preventing delirium in patients undergoing cardiac or non-cardiac surgery.[72–75] These findings emphasize the importance of medication timing in dexmedetomidine research.

Opioid-Free Anesthesia

Cluster analysis of cited references and keywords identified OFA as another focus of dexmedetomidine. In recent years, driven by the growing awareness of opioid-related complications and advancements in enhanced recovery after surgery (ERAS), an increasing number of clinical anesthesia procedures are being conducted with minimal or without the administration of opioids. Consequently, a novel method of anesthesia termed OFA has garnered significant attention. Specifically, it is a multimodal anesthesia strategy that integrates various non-opioid drugs and techniques to achieve optimal anesthesia quality while avoiding opioid usage.[76] Several OFA protocols have been published, such as total venous OFA, intravenous OFA combined with inhalation, and OFA with PNB, utilizing a multitude of non-opioid medications, with dexmedetomidine playing a crucial role.[77–83]

Research Frontiers

The global trend in dexmedetomidine research can be explored via the analysis of timeline views, keyword clusters, and keyword bursts.

The investigation of “stress response“ and ”neuroinflammation” is currently at the forefront of scientific research. Notably, clinical research and basic experiments demonstrated that dexmedetomidine alleviates anti-oxidative stress and inflammatory responses, thereby protecting vital organs. These effects primarily involve α_{2A} adrenoceptors in astrocytes, the HMGB1/RAGE/NF-κB signaling pathway, the AMPK/SIRT1 pathway, and the HIF-1a/HO-1 signaling pathway.[84–88] Nevertheless, the protective mechanism of dexmedetomidine on various organs remains underexplored.

Delirium and OFA, as previously described, are not only prominent research areas but also represent promising directions for future investigation. Inconsistency of clinical studies, as well as the normative standardization of OFA, requires larger sample, multi-center studies. The impact of dexmedetomidine in reducing the incidence of postoperative delirium is expected to be addressed in the future.

In addition, the application of dexmedetomidine in PNB is also a trending research topic, which can be regarded as an extension of OFA. Key areas of focus include investigating the impact of dexmedetomidine as an adjuvant on diverse PNB, comparing its efficacy with other adjuvants in PNB, and evaluating the differential effects between perineural and intravenous administration of dexmedetomidine.[12,89–95]

The mechanism of dexmedetomidine as an adjuvant in PNB has been summarized in our previous review; nevertheless, the specific mechanism remains unclear.[89,96] Potential complications associated with dexmedetomidine, such as hypotension and bradycardia, warrant further investigation in future studies.[83,97,98]

Limitations

Notwithstanding, certain limitations of this research should not be overlooked. Firstly, the research exclusively used the WoSCC database as a source of data collection and excluded data from other large databases such as PubMed, Embase, Scope, and Google Scholar. Secondly, despite bibliometrics being a quantitative approach, there is currently no standardized method for assessing the quality of publications, such as the GRADE system. Future studies should include a qualitative analysis of research on dexmedetomidine and provide higher-level evidence-based medicine. Thirdly, certain high-quality studies may have been under-appreciated due to their low citation rates. However, it is important to acknowledge that citations are influenced by multiple factors and do not inherently reflect the scholarly quality of the work. Fourthly, bibliometric analysis has inherent limitations, given that it primarily assesses quantity, citations, and other indicators of scholarly literature while neglecting critical factors such as research design rationality and the rigor of experimental methods, both of which contribute to study quality and impact. Furthermore, bibliometric analysis may reinforce a “rich-get-richer” phenomenon, whereby research fields or institutions that are already influential are more likely to receive citations and attention. This could potentially introduce bias in evaluation outcomes.

Conclusion

Dexmedetomidine is a key drug in the field of anesthesiology. The number of publications has nearly tripled over the past decade, yielding robust outcomes and establishing a solid theoretical reference for dexmedetomidine research. Current trends and research topics are focused on sedation, delirium, and OFA, as revealed by our study. The frontier of future research will encompass basic investigations on dexmedetomidine, including its effect on stress response and neuroinflammation, as well as clinical studies focusing on delirium, OFA, PNB, and associated complications.

Data Sharing Statement

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

Acknowledgments

The authors thank the software of Microsoft Excel, CiteSpace (6.1.R6), SCImago Graphica (1.0.36) (https://graphica.app/, "bibliometrix package" (https://www.bibliometrix.org) in R language (4.3.1), bibliometric online webpage (https://bibliometric.com), VOSviewer (1.6.19) and all the research assistants for their time and efforts in this study. The authors also thank Home for Researchers editorial team (www.home-for-researchers.com) for language editing service.

Author Contributions

All authors made a significant contribution to the work reported, whether that is in the conception, study design, execution, acquisition of data, analysis and interpretation, or in all these areas; took part in drafting, revising or critically reviewing the article; gave final approval of the version to be published; have agreed on the journal to which the article has been submitted; and agree to be accountable for all aspects of the work.

Funding

This work was supported by the Shandong Provincial Key Research and Development Project (No. 2019GSF108193), Shandong Provincial Natural Science Foundation (No. ZR2021MH016), Analgesia and Sedation-Special Foundation for Anesthesia Optimization of Shandong Medical Association (No. YXH2021ZX040) and 2023 Qilu medical characteristics undergraduate education teaching research project-Shandong University (No. qlyxjy-202367).

Disclosure

The authors declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

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