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Global Research and Scientific Publications on Dexmedetomidine Use in Adults for Anesthesia Care between 2001 and 2021: A Bibliometric Analysis

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ARTICLE INFO

Article history:

Received 14 February 2022

Accepted 9 June 2022

Key words:

Adults
anesthesia
bibliometric analysis
dexmedetomidine

ABSTRACT

Background: An increasing number of studies on dexmedetomidine use in adults have been published, but the effectiveness of dexmedetomidine remains contentious.

Objective: This study aimed to describe the changing trends and structural relationships of scientific achievements regarding dexmedetomidine over the past 2 decades and provide researchers with information to help them explore better research opportunities.

Methods: Quantitative data of publications were retrieved from the Scopus database. Analyses of co-occurrence and collaboration among authors, countries, and key words were conducted using VOSviewer 1.6.17 software. Weighted occurrence and average publications per year were calculated.

Results: The 1868 publications retrieved showed an increasing trend of annual publications on dexmedetomidine use in adults between 2001 and 2021. China accounted for the largest contribution to publications in the world ($n=577$ [30.89%]). Four key word clusters indicating research hotspots were identified using VOSviewer. The number of articles published in the top 10% of journals in the United States was the highest among all publications from the country (97 out of 201 [48.26%]). Journals from the United Kingdom obtained the highest CiteScore (16.56). *Journal of Anaesthesiology Clinical Pharmacology* published the highest number of articles on this topic ($n=56$). Wang authored the highest number of published articles ($n=42$). Recent publications focused on the theme of cytokines and immunomodulation. *Sufentanil* attracted particular interest as a drug-related key word. Moreover, meta-analysis is becoming an increasingly popular research method in this field.

Conclusions: The increasing number of publications on dexmedetomidine use reflects growing interest in this topic. Future research should focus on meta-analyses to identify the most effective therapeutic methods. The immunomodulatory effect of dexmedetomidine on health and disease is of particular interest.

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Introduction

Dexmedetomidine is an α_2 -adrenoceptor agonist that has a 7-fold higher selectivity for α_2 -adrenoceptor ($\alpha_2:\alpha_1$, 1,600:1) and a substantially shorter context-sensitive half-life than clonidine.¹ It is effective for the purpose of sedation, amnesia, and analgesia in operating rooms and intensive care units with/without mild respiratory depression. It can also reduce the need for anesthetics during general, neuraxial, and regional anesthesia. Although it

has some side effects, such as causing the heart rate, arterial pressure, and plasma catecholamine concentration to decrease, it has subtle cardiovascular effects when used in the form of therapeutic doses. Therefore, this has become a popular drug for clinicians to administer. Compared with propofol, dexmedetomidine has been shown to provide better sedation levels with good hemodynamic stability.²⁻⁴ A study demonstrated that intraoperative intravenous dexmedetomidine and acetaminophen during primary palatoplasty provided safe and effective perioperative pain control, resulting in a significantly decreased need for postoperative pain relief.⁵ Dexmedetomidine can also aid in suppressing bleeding after thyroidectomy by reducing coughing and emergence agitation.⁶ Additionally, it can reduce shivering⁷ and also prevent shivering during spinal anesthesia.⁸ A recent meta-analysis also showed that it

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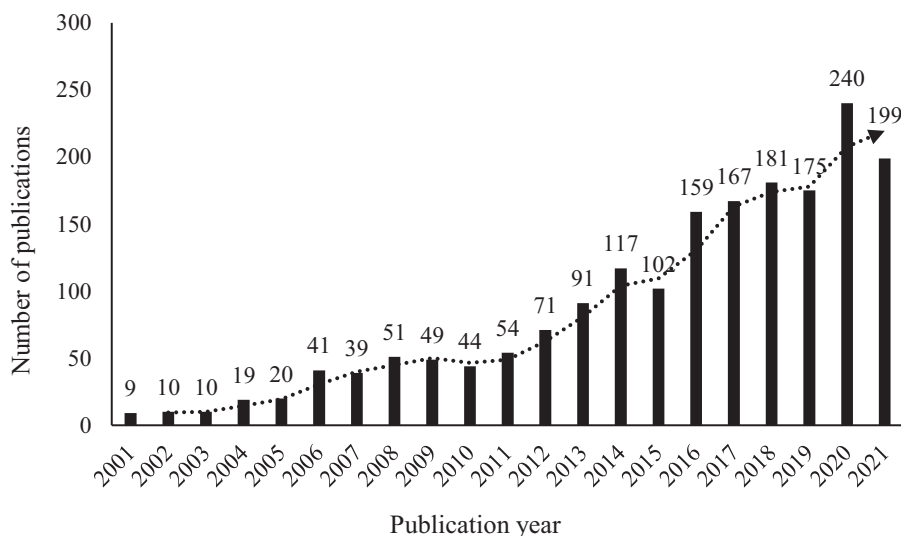


Figure 1. Number of articles published in each year (2001–2021).

effectively decreased the incidence of emergence agitation and reduced postoperative analgesic requirements in adults.⁹

Besides its sedative and analgesic effects, dexmedetomidine can suppress neuroapoptosis and neurodegeneration. It has beneficial effects against ischemia-reperfusion injuries.¹⁰ Available data also suggest that dexmedetomidine exerts anti-inflammatory effects and prevents ventilator-induced lung injury. Many recent pre-clinical studies have shown that dexmedetomidine can suppress neuroinflammation.^{11–15}

This brief overview of the obtained findings shows that dexmedetomidine research encompasses a wide range of topics and dimensions. Many researchers predict that more individuals will become interested in performing research on dexmedetomidine in the future. The amount of related data in databases will also increase. Additionally, using data mining of big data, search tools are now available to analyze patterns and explanations for unstructured knowledge. Bibliometrics involves the statistical analysis of bibliographic data with the goal of determining the level of scientific activity in a certain topic, research area, journal, country, or other variable of interest.¹⁶ Bibliometrics can help researchers understand the developments in a field within the worldwide research community. VOSviewer is a free Java-based software (Centre for Science and Technology Studies, Leiden University, the Netherlands). It allows researchers to construct and visualize bibliometric networks from data obtained from bibliometric searches of important databases to create a citation map.¹⁷

Against this background, this study aimed to explore the current status of big data on dexmedetomidine use in adults through visualization analysis on journal articles in a major database. The bibliometric analysis was implemented in this study.

Materials and Methods

Data source and search strategy

The Scopus database (Elsevier, Amsterdam, the Netherlands) was used to search for literature on dexmedetomidine use in adults in November 2021. The search focused on literature published during 2001–2021. The search strategy used the following key words: AFFIL (anesthesia OR anesthesiology OR anaesthesia OR anaesthesiology OR anesthetic OR anaesthetic OR anesthetization OR anaesthetization OR autoanesthesia OR autoanaesthesia OR neuroanesthesia OR neuroanaesthesia OR narcosis) AND TITLE

(dexmedetomidine OR cepedex OR dexamedetomidine OR dexdomitor OR dexdor OR “mpv 1440” OR mpv1440 OR precedex OR primadex OR sedadex OR sileo) AND NOT ALL (neonatal OR newborn OR “newly born” OR baby OR babies OR infant OR infants OR child OR children OR pediatric OR paediatric OR pediatrics OR paediatrics) AND PUBYEAR >2000. In total, 1868 publications from 562 scientific journals were identified. Retrieval work was performed in the same week to avoid variations due to daily updates. Because all data were secondary and contained no personal information, informed consent was not required.

Data extraction and bibliometric analysis

The data extracted from the Scopus database were imported into Microsoft Excel 2019 (Redmond, Washington). Two authors performed this procedure independently, and disagreements were discussed until a consensus was reached. The recorded information included the following: publication year, country, affiliation, publisher, journal title, author, topic of publication, citation count, author key words, and index key words. The authors extracted all journal titles (source titles) from the downloaded data to find the CiteScore 2020 version (Elsevier). The “VLOOKUP” function in Microsoft Excel 2019 was used to match the journal title and CiteScore.

The authors used VOSviewer version 1.6.17 (<https://www.vosviewer.com>) to analyze weighted total link strength, weighted occurrence, and average publication year. The authors exported the list of publications from Scopus in a “.csv” file and performed the visualization of coauthorship, key word co-occurrence, and creation of a citation map. VOSviewer 1.6.17 is free Java-based software designed for creating maps based on bibliographic data and for visualizing and exploring such maps.

Results

Overview of publications on dexmedetomidine use in adults

A total of 1868 publications were extracted from the Scopus database. The number of publications on this topic per year increased over time and more than tripled in 10 years (from 71 publications during 2012 to 219 publications during 2021). In terms of the article types, only reviews and articles were published. The largest number of articles was published in 2020 (n = 240 [12.85%]) (see Figure 1).

Table 1
Number of articles published in the top 10% of journals in the Scopus database (NTOP10%)*, CiteScore,† and SCImago journal rank (SJR),‡ ranked by number of publications.

No.	Country	No. of publications	NTOP10%	NTOP10% per all publications (%)	CiteScore 2020	SJR
1	China	577	56	9.71	3.17	0.65
2	India	246	5	2.03	2.15	0.46
3	United States	201	97	48.26	7.10	1.48
4	Japan	155	32	20.65	4.73	0.97
5	Turkey	139	19	13.67	3.02	0.67
6	South Korea	117	11	9.40	3.77	0.75
7	Egypt	72	8	11.11	2.10	0.45
8	Iran	59	0	0.00	1.70	0.36
9	Canada	28	12	42.86	9.38	1.73
10	Italy	24	4	16.67	8.03	1.26
11	Finland	22	11	50.00	7.57	1.61
12	United Kingdom	21	11	52.38	16.56	3.01
13	Spain	17	8	47.06	5.06	1.05
14	Germany	15	5	33.33	7.58	1.59
15	Saudi Arabia	15	3	20.00	4.04	0.89
16	France	14	4	28.57	4.75	1.05
17	Switzerland	13	3	23.08	4.64	1.10
18	Republic of China (Taiwan)	12	4	33.33	5.39	1.04
19	Australia	11	4	36.36	6.51	1.39
20	Brazil	11	2	18.18	3.48	0.82

* Scopus abstract and citation database; Elsevier, Amsterdam, the Netherlands.

† CiteScore 2020 version; Elsevier, Amsterdam, the Netherlands.

‡ The SCImago Journal & Country Rank; Elsevier, Amsterdam, the Netherlands.

Table 2
List of the top 20 most published journals in descending order.

Journal title	Country	Main text Language	Open access offered	No. of publications				
				China	India	United States	Other countries	All
<i>Journal of Anaesthesiology Clinical Pharmacology</i>	India	English	No	0	51	0	5	56
<i>Journal of Clinical Anesthesia</i>	United States	English	Yes	12	2	21	21	56
<i>Anesthesia and Analgesia</i>	United States	English	Yes	1	0	23	26	50
<i>Indian Journal of Anaesthesia</i>	India	English	No	0	43	1	2	46
<i>Journal of Anesthesia</i>	Japan	English	Yes	6	2	1	28	37
<i>Anesthesiology</i>	United States	English	Yes	1	0	18	15	34
<i>Saudi Journal of Anaesthesia</i>	India	English	No	1	16	1	12	30
<i>BMC Anesthesiology</i>	United Kingdom	English	Yes	13	0	2	15	30
<i>British Journal of Anaesthesia</i>	United Kingdom	English	Yes	4	0	5	21	30
<i>Chinese Journal of Anesthesiology</i>	China	Chinese	No	26	0	0	0	26
<i>Minerva Anestesiologica</i>	Italy	Italian, English	No	3	0	3	17	23
<i>Nan fang yi ke da xue xue bao*</i>	China	Chinese, English	No	22	0	0	0	22
<i>Journal of Neurosurgical Anesthesiology</i>	United States	English	Yes	1	3	11	4	19
<i>Journal of Cardiothoracic and Vascular Anesthesia</i>	United Kingdom	English	Yes	5	0	9	5	19
<i>Anaesthesia, Pain and Intensive Care</i>	Pakistan	English	No	0	12	1	6	19
<i>Journal of Clinical and Diagnostic Research</i>	India	English	No	0	18	0	0	18
<i>International Journal of Clinical and Experimental Medicine</i>	United States	English	No	14	0	0	4	18
<i>Medicine (United States)</i>	United States	English	Yes	10	0	0	8	18
<i>National Medical Journal of China</i>	China	Chinese	No	14	0	0	0	14
<i>Experimental and Therapeutic Medicine</i>	Greece	English	No	13	0	0	0	13

* English translation: *Journal of Southern Medical University*.

Countries/regions of publications

The country from which the largest proportion of articles were published was China (n = 577 [30.89%]), followed by India (n = 246 [13.17%]) and the United States (n = 201 [10.76%]). The number of articles published in the top 10% of journals was 97 in the United States, followed by 56 in China and 32 in Japan. The proportion of articles published in the top 10% of journals among all publications was highest in the United States (97 out of 201 [48.26%]). Articles published in the United Kingdom obtained the highest CiteScore (n = 16.56) (see Table 1).

Table 2 lists the top 20 most published journals in descending order. The majority of journals publish articles in English. As indicated in Table 1, China had the highest number of publications among countries. Articles published by Chinese researchers were published in journals across different regions of the world, and most of them were in English. Researchers from China no longer

publish only in Chinese journals. Moreover, Chinese is not used as the main language for publication by many Chinese researchers. Researchers from India still mainly published in Indian journals and those of neighboring countries such as Pakistan. However, on the basis of the SCImago journal rank index (Elsevier) and total citations of the top-3 Indian journals (*Journal of Anaesthesiology Clinical Pharmacology*, *Indian Journal of Anaesthesia*, and *Saudi Journal of Anaesthesia*), the slope values continued to increase in the most recent 5 to 6 years. This indicates that Indian journals are gaining popularity.

Bibliometric maps of co-citations

The bibliometric data were input into VOSviewer 1.6.17. To analyze coauthorship, a search with a minimum number of articles of an author of 5 and a minimum number of citations of an author of 0 resulted in hits on 202 authors from a total of 6567 au-

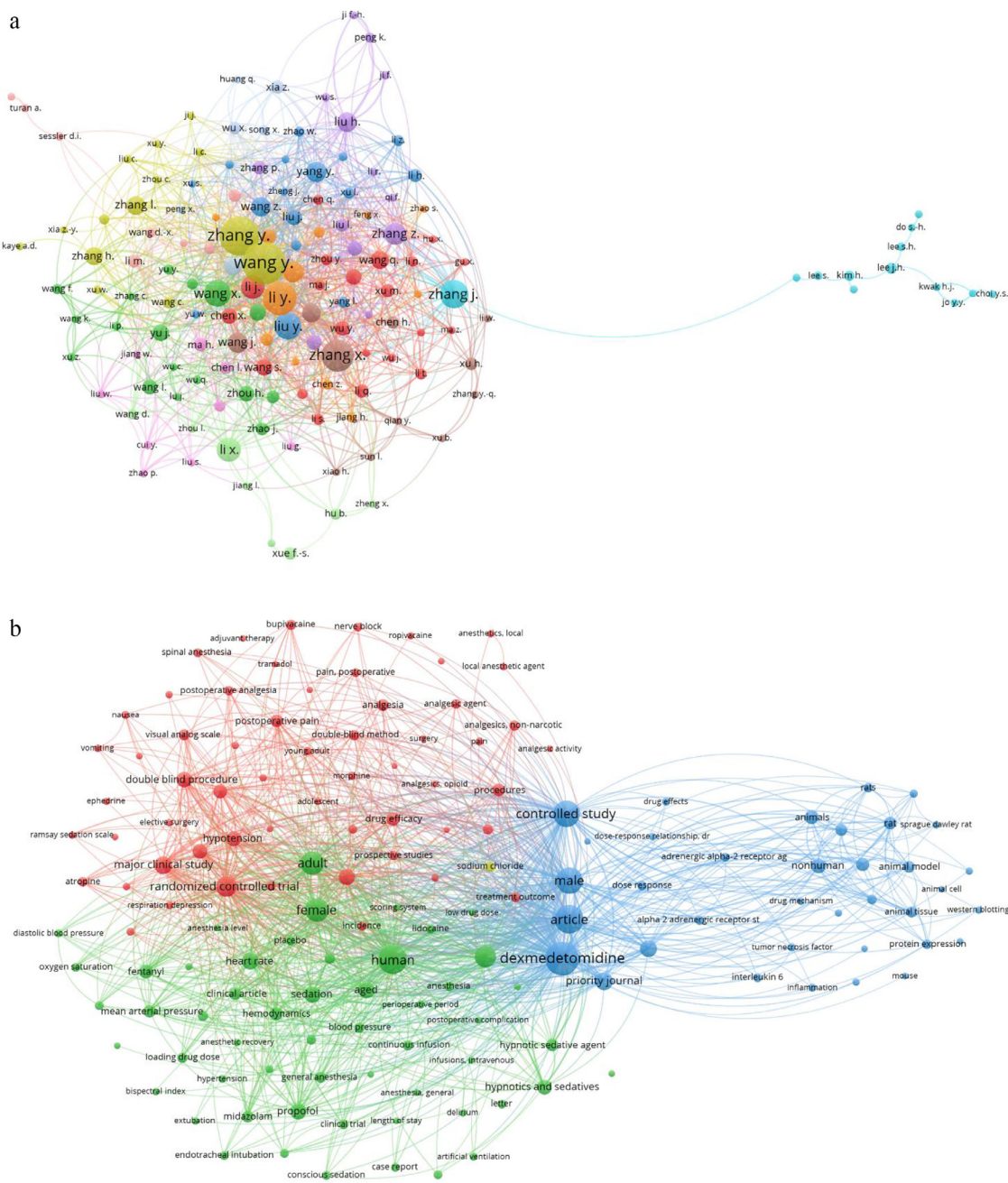


Figure 2. (A) Visualization of coauthorship of articles related to dexmedetomidine use in adults. (B) Visualization of co-occurrence of key words related to dexmedetomidine use in adults.

thors. Wang et al authored the highest number of published articles ($n=42$) and had the highest total link strength with others (89), followed by Zhang et al ($n=37$; total link strength: 78) and Li et al ($n=31$; total link strength: 55). The lines connecting researchers from South Korea appeared to be separated from the others (Figure 2).

To analyze co-occurrence, a search with a minimum number of occurrences of a key word of 66 resulted in hits on 150 key words from a total of 8402 key words. Using VOSviewer, 4 clusters of key words related to dexmedetomidine use in adults were identified. The first cluster included 58 key words and focused mainly on “regional anesthesia” (C1). The second cluster included 55 key words and focused mainly on “sedation and general anesthesia” (C2). The third cluster included 36 key words and mainly focused on “cytokines and immunomodulation” (C3). The fourth cluster included

1 key word: *sodium chloride* (C4). The authors ranked all 150 key words by average publication year and obtained the top-10 key words, reflecting the issues receiving the most attention in recent years. Table 3 shows that most of the top-10 key words were in the third cluster (C3). The other key words were *meta analysis*, *sufentanil*, and *randomized controlled trial* (topic).

Table 3 shows that, among the top-10 key words ranked by average publication year, there were a large number of key words from C3 (7 out of 10 key words). The authors then grouped the words that fit in the cytokines and immunomodulation category in the C3 cluster (eg, “Tumor necrosis factor,” “Interleukin 1 β ,” and “Western blotting”). Ten words fit in this theme. The authors plotted a line graph to determine which country among the top-3 countries was the most interested in the C3 cluster. From this, the trend by which dexmedetomidine research has de-

Table 3
Top-10 key words extracted from VOSviewer* ranked by average publications per year.

Key word	Cluster	Weight (links)	Weight (total link strength)	Weight (occurrences)	Score (average publication year)
Tumor necrosis factor	C3	137	2193	115	2018.9652
Interleukin 1 β	C3	129	1473	80	2018.475
Western blotting	C3	72	1499	92	2018.2826
Apoptosis	C3	79	1108	69	2018.2319
Meta analysis	C1	126	1115	66	2018.1364
Sufentanil	C1	131	1643	69	2018.029
Signal transduction	C3	77	1566	88	2017.9773
Randomized controlled trial (topic)	C1	125	1449	90	2017.9333
Interleukin 6	C3	143	2481	130	2017.8846
Pathology	C3	122	1617	85	2017.8118

C1 = the first cluster or “regional anesthesia” publications; C3 = the third cluster or “cytokines and immunomodulation” publications.

* VOSviewer 1.6.17. Centre for Science and Technology Studies, Leiden University, the Netherlands; 2009.

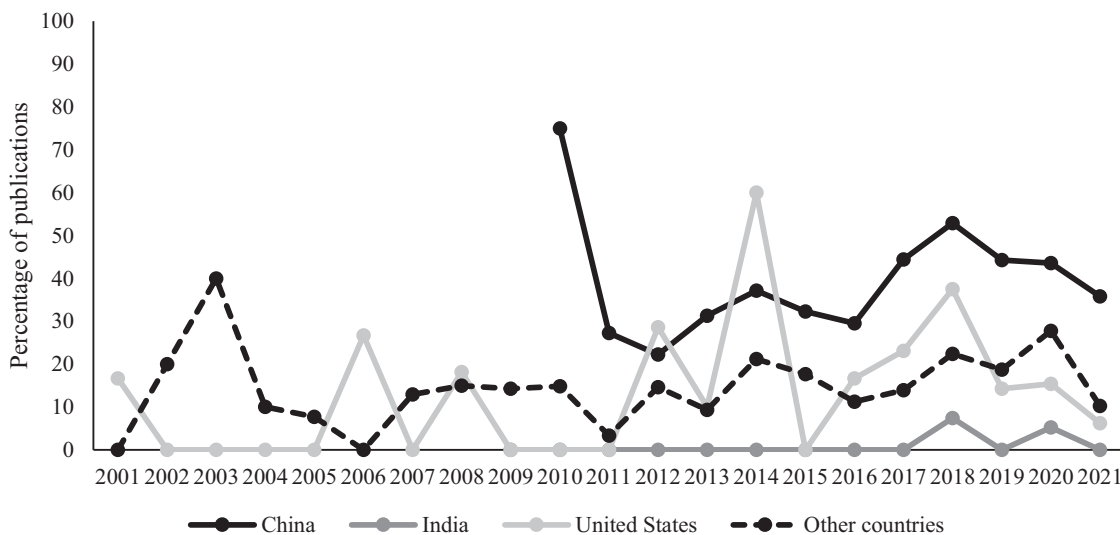


Figure 3. Proportion of publications containing key words in the cytokines and immunomodulation (C3) category among all publications per year.

veloped was delineated. When the authors constructed a graph of the percentage of C3 studies divided among the 3 leading countries in this field and others, the authors found that researchers in China had become more interested in “cytokines and immunomodulation” than those from any other country since 2010 (Figure 3).

Researchers had also become more interested in the topic of “cytokines and immunomodulation” in recent years (Figure 4). Additionally, the graph on drug names showed that the drug focused on most in recent studies was sufentanil (Figure 5). Table 3 also shows that sufentanil has been an attractive topic of research and publications in recent years.

Our findings also showed that meta-analysis has become an increasingly interesting research method for those researching dexmedetomidine use in adults. Meta-analyses on this issue were initiated approximately 10 years ago (2012–2021).

Discussion

Trends of publications related to dexmedetomidine use in adults

Dexmedetomidine is a highly selective $\alpha 2$ adrenergic agonist that has analgesic as well as sedative properties. Although minimal respiratory depression is a significant benefit of dexmedetomidine, it can lead to bradycardia and hypotension. During the past 20 years, there has been growing interest in dexmedetomidine use in terms of both published articles and overall research interest. China ranks first in terms of the number of publications among all countries/regions, suggesting that China dominates research on

dexmedetomidine use in adults. However, journals from the United Kingdom had the highest CiteScore, much higher than those from the second-ranked country. This indicates a high level of citations of nonoriginal research articles.

Although dexmedetomidine has attracted increasing attention from researchers in recent years, it has been used in adults since its approval in December 1999 by the US Food and Drug Administration as a short-term medication (<24 hours) for analgesia and sedation for critically ill patients on mechanical ventilation in the intensive care unit.¹⁸ During early 1999, 119 patients admitted postoperatively to general or cardiothoracic intensive care units at 4 teaching hospitals in the United Kingdom were enrolled in a multicenter, randomized, placebo-controlled trial to determine whether or not dexmedetomidine was useful for the provision of postoperative analgesia and sedation. This article was cited by 410 publications.¹⁹

The use of dexmedetomidine for sedation was of great interest for reducing opioid use, but many issues related to adverse cardiovascular effects were identified. Because the key word *dexmedetomidine* has strong links to *major clinical study*, *human*, *hypotension*, and *heart rate*, the authors may assume that, in early years, focus was often on the clinical characteristics, hemodynamics, and vitality outcomes of this drug.

This study found an increasing amount of recent dexmedetomidine-related data on cytokines and immunomodulation, most of which were from preclinical studies or studies performed on rats. In the “cytokines and immunomodulation” cluster, the article titled “Dose- and time-related effects of dexmedetomidine on mortality and inflammatory responses to

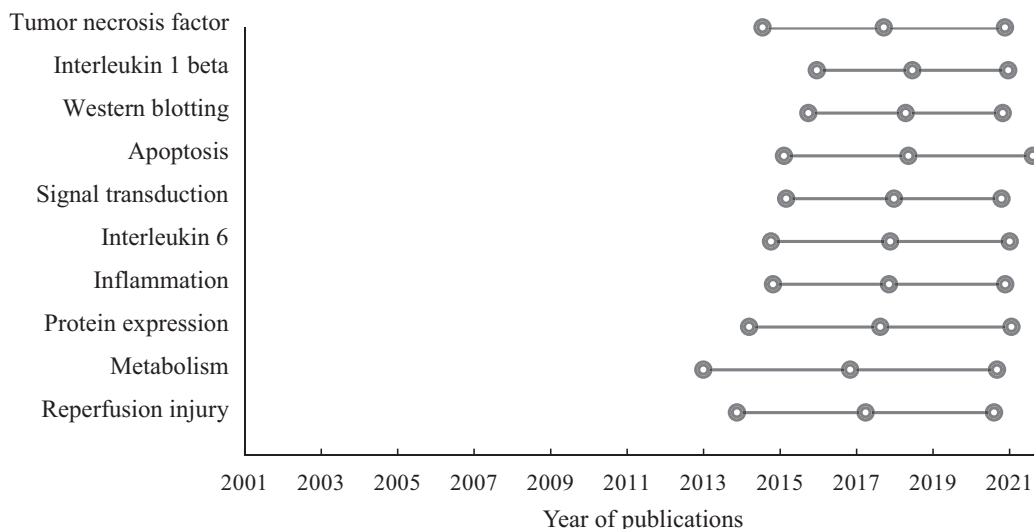


Figure 4. Average year of publications that used the “cytokines and immunomodulation” cluster of key words.

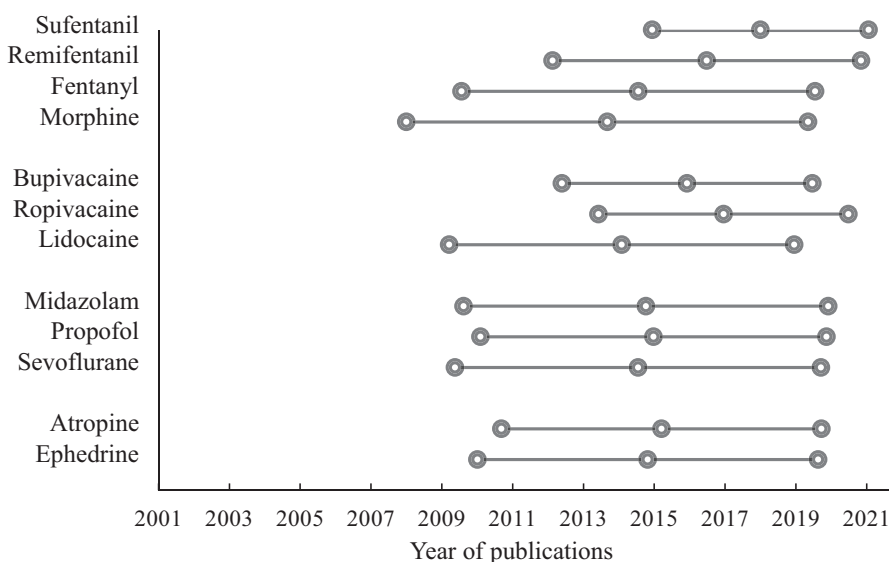


Figure 5. Average year of publications that included the drug name as a key word.

endotoxin-induced shock in rats” was the most-cited article (125 times), which was published in *Journal of Anesthesia* in 2008 by Taniguchi et al.²⁰ This study proposed a new method for considering the anti-inflammatory effects of dexmedetomidine and the therapeutic dose and timing of administration.²⁰ The bibliometric analysis showed that cytokines and immunomodulation associated with dexmedetomidine may be a new research target in this field.

In the “regional anesthesia” cluster, an article titled “Perineural administration of dexmedetomidine in combination with bupivacaine enhances sensory and motor blockade in sciatic nerve block without inducing neurotoxicity in rat” was the most-cited article (204 times), and was published in the journal *Anesthesiology* in 2008 by Brummett et al.²¹ This study proposed a new method for studying the safety of the drug in regional anesthesia because it did not affect the nervous system. Intravenous injection was mainly used previously. This study demonstrated the importance of histopathology of cells that were affected by dexmedetomidine and paved the way for more human trials.²¹

In the “sedation and general anesthesia” cluster, an article titled “Dexmedetomidine vs midazolam or propofol for sedation during prolonged mechanical ventilation: Two randomized controlled tri-

als” was the most-cited article (551 times), which was published in *Journal of the American Medical Association* in 2012 by Jakob et al.²² The study proposed a new method for studying the safety and efficacy of dexmedetomidine in critical patients under mechanical ventilation. The results of this study showed that dexmedetomidine was not inferior to midazolam and propofol and that it can reduce the duration of mechanical ventilation and improve patients’ ability to communicate their pain symptoms. This was a multicenter study with a large sample size.²²

Sodium chloride is the only key word in the last cluster. The authors found that it was mainly used as a placebo control in many trials.

Journal of Anaesthesiology Clinical Pharmacology, Journal of Clinical Anesthesia, Anesthesia and Analgesia, Indian Journal of Anaesthesia, and Journal of Anesthesia are the top-5 journals for publications on dexmedetomidine use in adults, which suggests that more studies on this topic will continue to be published in these journals. Authors who are interested in dexmedetomidine use in adults should focus particularly on these journals.

Many articles with trial-related key words, such as *randomized controlled trial* and *controlled study*, suggested that numerous

drugs that possess the ability to compete with dexmedetomidine are currently in the trial phase. A large network meta-analysis included several of these articles.²³ These types of key words were also strongly linked to dexmedetomidine in this study. Furthermore, meta-analysis is becoming a particularly interesting research method in this field.

Limitations of this study

This study presented bibliometric and graphic data related to articles on dexmedetomidine use in adults extracted from the Scopus database. Although it is relatively objective and comprehensive, this study has some limitations. First, several excellent publications not written in English are absent from the Scopus database, so they were not considered in this study. Because numerous reports from China have been published on dexmedetomidine, it is believed that there are still many Chinese-language articles that have not yet been indexed in this database. Second, this study only investigated the effects of the drug on anesthesia care, so this may not cover all uses. Third, bibliometric analysis might not accurately reflect the current data. For instance, some excellent recent publications are not cited frequently, but the total number of citations will increase in the future. Finally, because bibliometric data evolve over time, various conclusions may emerge with time.

Conclusions

This bibliometric study showed that there is an increasing trend in both published articles related to dexmedetomidine use in adults and interest in related research during the past 20 years. China dominates research on dexmedetomidine use in adults, whereas studies from the United Kingdom lead in terms of most citations. Many authors are interested in publishing articles on this topic in Indian journals. Finally, cytokines and immunomodulation associated with dexmedetomidine use in adults may be a new focus of research in this field.

Author contributions

RK and NR were equally involved in: Conceptualization; Data curation; Formal analysis; Methodology; Project administration; Resources; Software; Validation; Visualization; Roles/Writing - original draft; Writing - review & editing.

Disclosure of funding support

This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors.

Declaration of Competing Interest

The authors have indicated that they have no conflicts of interest regarding the content of this article.

Acknowledgments

The authors thank all those who provided intellectual assistance and technical help (including writing and language editing) and the developer of VOSviewer 1.6.17 software. The authors also thank Edanz (www.edanz.com/ac) for editing a draft of this manuscript.

R. Komonhirun and N. Ruananukun were equally involved in conceptualization; data curation, formal analysis; methodology; project administration, resources, and software; validation; visualization; and writing of the original draft, review, and editing.

Supplementary materials

Supplementary material associated with this article can be found, in the online version, at doi:[10.1016/j.curtheres.2022.100677](https://doi.org/10.1016/j.curtheres.2022.100677).

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