


Research Trends and Knowledge Mapping of Opioid-Free Anesthesia: A Global Bibliometric Analysis

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Purpose: Opioid-free anesthesia (OFA), as a potential anesthetic strategy, can provide better clinical outcomes for surgical patients while avoiding opioid-related adverse side effects. However, the current knowledge framework and research progress in OFA have not yet been systematically reviewed or comprehensively analyzed. This study aims to employ bibliometric methods to thoroughly explore research trends, hotspots, and developmental directions in this field.

Methods: This study retrieved opioid-free anesthesia-related literature published between 1980 and 2024 from the Web of Science Core Collection database. Through systematic analysis of publications, countries, institutions, authors, journals, references, and keywords, combined with bibliometric visualization using software such as Citespace, VOSviewer, and Bibliometrix, this study comprehensively reveals the research status and developmental trends in this field.

Results: OFA research demonstrates a significant growth trend, with a sharp increase in publications over the past decade, reaching 2,219 citations in 2024 alone. The United States leads globally with 291 publications (7,896 citations) yet exhibits low international collaboration network density (0.008). Research hotspots evolve into three phases: early-stage focus on basic anesthetic protocols, mid-stage shift toward perioperative management optimization, and recent emphasis on clinical outcome improvement. Keyword analysis identified four core themes: anesthetic agents and protocols, perioperative management, and analgesic strategy optimization.

Conclusion: OFA research is in a phase of rapid development but requires enhanced international collaboration and clinical translation. Future efforts should focus on developing personalized OFA protocols, investigating long-term outcomes, and establishing multicenter research networks to provide higher-quality evidence for clinical practice.

Keywords: opioid-free anesthesia, pain, opioid, bibliometrics

Introduction

Opioids have long served as fundamental elements in general anesthesia practice. The clinical application of opioids has evolved from initial morphine to pethidine and subsequently to the fentanyl family. However, opioid-related adverse effects and complications, such as respiratory depression, nausea and vomiting, persist. Recent studies indicate that opioids may not only interfere with immune processes but also induce postoperative hyperalgesia and tolerance.^{1–3} Opioid dependence has become a global public health concern. The prescription opioid crisis has resulted in profound social, medical, and economic consequences that persist today.⁴ Given these risks, OFA has gained increasing attention and research interest as an alternative strategy in recent years.

OFA refers to a technique that completely avoids any opioids during the perioperative period while achieving adequate analgesia and anesthesia management through multimodal analgesic strategies.⁵ In 1993, Friedberg first introduced an opioid-free combination of ketamine and propofol.⁶ OFA can reduce the incidence of postoperative nausea

and vomiting while providing adequate analgesia without interfering with postoperative recovery.⁷ In clinical practice, various non-opioid intravenous analgesics are widely used, including non-steroidal anti-inflammatory drugs (NSAIDs), α 2-adrenergic receptor agonists, N-methyl-D-aspartate (NMDA) receptor antagonists, gabapentinoids, sodium channel blockers, corticosteroids, and magnesium sulfate. Unlike opioids, which act primarily through central mu-opioid receptor agonism—posing risks such as respiratory depression and dependence—key non-opioid agents exert their effects through distinct mechanisms. Local anesthetics block sodium channels to inhibit nerve conduction; NSAIDs and acetaminophen inhibit cyclooxygenase enzymes to reduce inflammatory pain; ketamine antagonizes NMDA receptors, modulating central sensitization; and dexmedetomidine activates alpha-2 adrenergic receptors to produce both analgesia and sedation. This multimodal strategy enables effective pain control while minimizing opioid-related adverse effects.

Perioperative pain management is a critical component of surgical practice, directly affecting patient satisfaction, length of hospital stays, surgical costs, readmission rates, and complication incidence. OFA can optimize anesthesia management by reducing doses of hypnotic agents, maintaining hemodynamic stability, and improving perioperative clinical outcomes. These strategies align well with the evolution of enhanced recovery after surgery (ERAS) protocols, jointly promoting optimization and innovation in perioperative management.

OFA has gained increasing relevance in modern clinical practice, particularly for patients with opioid use disorder or those undergoing chronic opioid therapy. These populations often exhibit altered opioid receptor sensitivity and a heightened risk of opioid-induced hyperalgesia, tolerance, and dependency.⁸ OFA offers a multimodal approach that minimizes these risks and supports safer perioperative care. Recent studies support its use in reducing postoperative opioid requirements and improving recovery outcomes in high-risk patients.⁹

Bibliometrics refers to the quantitative analysis of academic literature, using statistical and network-based methods to examine publication patterns, research hotspots, and collaboration structures. In the context of OFA, bibliometric analysis offers an objective lens to trace the field's development—particularly its response to the opioid crisis and advancements in anesthetic techniques. This approach enables the identification of knowledge gaps, emerging research trends, and influential contributors, thereby providing a data-driven foundation for understanding OFA's rapid growth and informing future clinical and research priorities.

Methods

Data Collection and Retrieval Strategy

This study conducted a retrospective bibliometric analysis of OFA literature published between 1980 and 2024. Data were extracted from the Web of Science Core Collection (WOSCC) using the following search strategy: (((TS= (opioid-free anesthesia)) OR TS= (opioid free anesthesia)) OR TS= (opioid-free anaesthesia)) OR TS= (opioid free anaesthesia)). The search strategy was developed and finalized in December 2024. To avoid the influence of ongoing database updates and ensure reproducibility, we completed all literature retrieval and data downloads on December 31, 2024. This date represents the definitive cut-off point for data inclusion in this study.

Inclusion and Exclusion Criteria

This study systematically searched for original research articles and reviews on OFA published between January 1980 and December 2024. All searches were completed by December 30, 2024, to avoid bias from database updates. Two researchers independently performed literature screening, including initial screening (based on title and abstract), full-text evaluation (for uncertain records), and final determination of included studies. The initial screening showed 95% agreement between the two researchers. A third researcher participated in the discussion for disputed records until a consensus was reached. Exclusion criteria included letters, meeting abstracts, book reviews, and other non-research publication types.

Data Analysis and Visualization

This study systematically extracted metadata from the search results, including publication year, journal name, country/region, research institution, author information, keywords, and references. Data analysis was comprehensively processed

using multiple bibliometric software tools. First, Bibliometrix in R was used for fundamental bibliometric analysis, including journal source statistics of citations and references. Core journal identification based on Bradford's law, construction of international collaboration networks, and highly cited literature analysis were performed. To thoroughly demonstrate research collaboration networks and knowledge evolution pathways, Citespace was employed to generate country collaboration networks, author and institutional collaboration networks, and reference and keyword burst detection maps. In the network maps, node size corresponds to publication quantity, while node centrality reflects its importance level. This study employed VOSviewer for keyword co-occurrence analysis to further reveal research hotspots. The analysis selected the "All Keywords" mode, merged synonyms, and ultimately presented results through network visualization and density visualization modes. All analyses were based on the final search dataset completed on December 30, 2024, to ensure result reproducibility.

Results

Publication Output and Citation Impact

Eight hundred sixty-one publications on OFA were included from 1980 to 2024 (Figure 1A), showing a clear temporal growth trend with particularly significant increases in the last decade. This growth trend stems from multiple interacting factors: primarily the opioid abuse crisis in the United States and associated societal issues (including addiction and overdose deaths) that prompted strict opioid prescription regulations worldwide; secondly, the rapid development of clinical alternatives, including innovations in regional anesthesia techniques, development of novel non-opioid analgesics, and clinical application of target-specific drugs; furthermore, international clinical guidelines recommending perioperative opioid reduction have further propelled research advancements in this field. Bibliometric analysis reveals substantially enhanced research impact in the recent five years, with total citations exceeding 1,000, including 2,219 citations in 2024 alone (Figure 1B), fully demonstrating the growing academic importance and attention of OFA research.

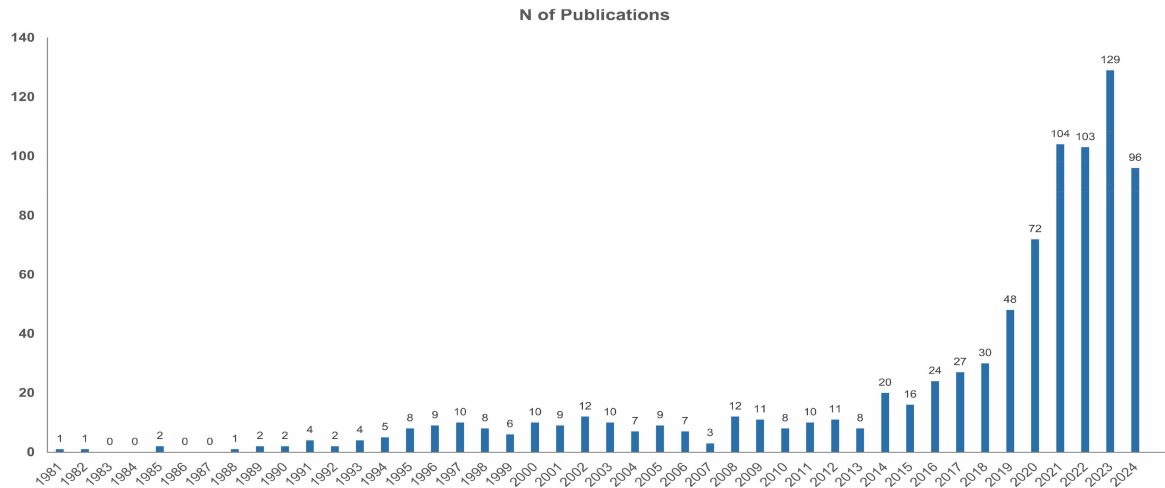
Journal Analysis

Journal distribution analysis of OFA research (Figure 2A) shows BRITISH JOURNAL OF ANAESTHESIA ranked first with 39 publications (4.53%). Bradford's law analysis (Figure 2B) identified a core zone comprising 18 journals (Table 1) collectively publishing 289 articles (33.57%), where ANESTHESIOLOGY, with an impact factor of 9.3 emerged as the highest-IF journal in the core zone, and 66.67% (12/18) of core journals belonged to JCR Q1 category. Cited journal analysis (Figure 2C) indicates ANESTHESIOLOGY, ANESTHESIA AND ANALGESIA, and BRITISH JOURNAL OF ANAESTHESIA formed the top three most-cited journal clusters.

Countries and Institutions Analysis

Country analysis of OFA research reveals significant geographical disparities (Figure 3A). The United States leads globally with 291 publications and 7,896 citations, likely attributable to the Centers for Disease Control and Prevention's opioid prescription restrictions and promotion of alternative analgesic strategies. Although China ranks second with 84 publications, its 843 citations suggest room for improvement in international influence. In contrast, England's modest output (68 publications) achieved 2,722 citations, highlighting the high-quality nature of its research. International collaboration analysis (Figure 3B) shows active participation from Chinese, British, and Italian authors. The country collaboration network (Figure 4A) includes 65 nations with 233 links, featuring strong partnerships between England, Germany, Australia, and Japan. Institutional analysis (Table 2) shows that the United States institutions claimed 6 top 10 positions, France 2, Egypt, and Germany 1 each, led by the University of Texas System (33 publications). The institutional network (Figure 4B) comprises 278 institutions with 335 links, showing relatively loose collaboration (density=0.008) with small-group clustering. Notably, Assistance Publique Hopitaux Paris emerges as the most central hub (centrality=0.14), reflecting its academic leadership in this field.

A



B

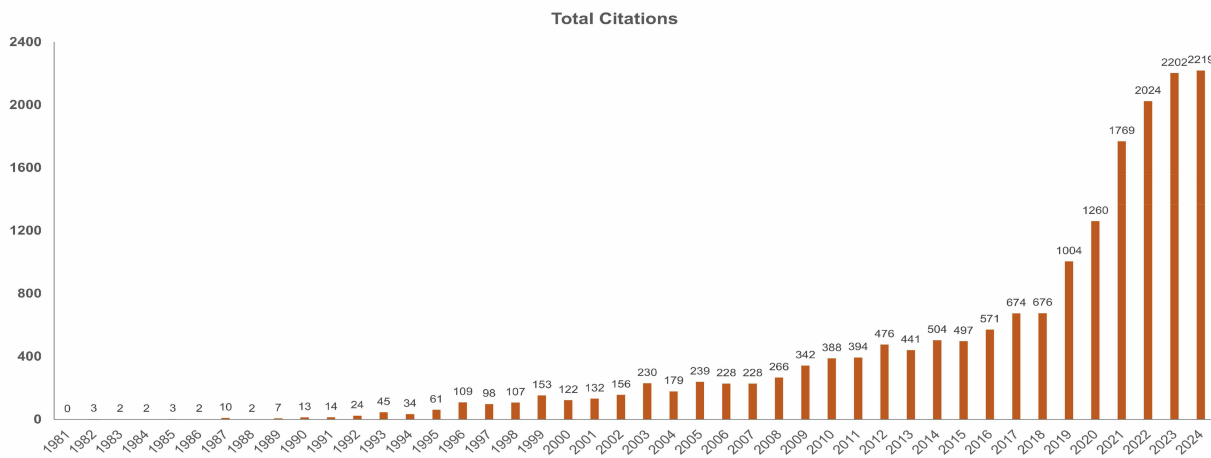


Figure 1 The number of annual publications (A) and citations (B) for OFA from 1981 to 2024.

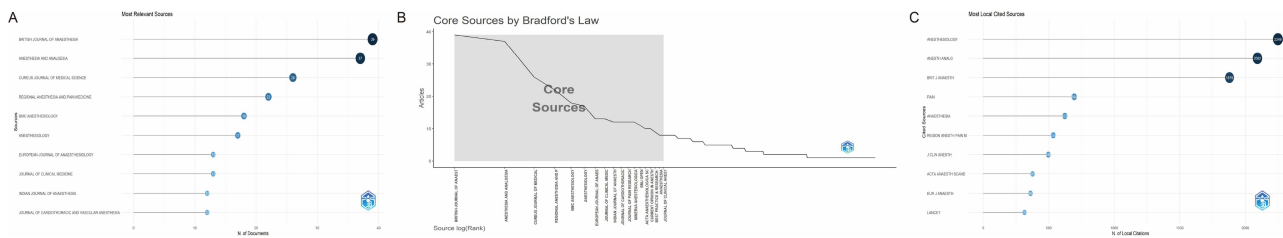


Figure 2 Bibliometric analysis of sources in the field of opioid-free anesthesia. (A) The top 10 most relevant sources. (B) Core sources by Bradford's Law. (C) The top 10 most local cited sources.

Authors Analysis

Analysis of prolific authors (Table 3) reveals Juan P. Cata as the most productive scholar in this field with 10 publications. This researcher has specialized in OFA studies since 2014. According to Price's Law, we defined authors with ≥ 3 publications as prolific, identifying 18 core researchers meeting this criterion. Collaboration network analysis

Table 1 Top 18 Journals of the Most Publications Related to Opioid-Free Anesthesia

Rank	Journal	Count	Percentage (%)	Cumulative Percentage (%)	IF	Quartile in Category
1	BRITISH JOURNAL OF ANAESTHESIA	39	4.53	4.53	9.1	Q1
2	ANESTHESIA AND ANALGESIA	37	4.30	8.83	4.6	Q1
3	CUREUS JOURNAL OF MEDICAL SCIENCE	26	3.02	11.85	1.0	Q3
4	REGIONAL ANESTHESIA AND PAIN MEDICINE	22	2.56	14.41	5.1	Q1
5	BMC ANESTHESIOLOGY	18	2.09	16.50	2.3	Q2
6	ANESTHESIOLOGY	17	1.97	18.47	9.3	Q1
7	EUROPEAN JOURNAL OF ANAESTHESIOLOGY	13	1.51	19.98	4.2	Q1
8	JOURNAL OF CLINICAL MEDICINE	13	1.51	21.49	3.0	Q1
9	INDIAN JOURNAL OF ANAESTHESIA	12	1.39	22.88	2.9	Q1
10	JOURNAL OF CARDIOTHORACIC AND VASCULAR ANESTHESIA	12	1.39	24.27	2.3	Q2
11	JOURNAL OF PAIN RESEARCH	12	1.39	25.66	2.5	Q2
12	MINERVA ANESTESIOLOGICA	12	1.39	27.05	2.9	Q1
13	BMJ OPEN	11	1.28	28.33	2.4	Q1
14	ACTA ANAESTHESIOLOGICA SCANDINAVICA	10	1.16	29.49	1.9	Q2
15	CURRENT OPINION IN ANESTHESIOLOGY	10	1.16	30.65	2.3	Q2
16	BEST PRACTICE & RESEARCH-CLINICAL ANAESTHESIOLOGY	9	1.04	31.69	4.7	Q1
17	ANAESTHESIA	8	0.94	32.63	7.5	Q1
18	JOURNAL OF CLINICAL ANESTHESIA	8	0.93	33.56	5.0	Q1

(Figure 4C) shows Juan P. Cata, Changhong Miao, and Wankun Chen have formed a relatively stable research team. Still, the network contains numerous isolated nodes and lacks effective connectivity between research groups, reflecting significant deficiencies in academic collaboration among researchers. This fragmented collaboration pattern may hinder cross-team knowledge exchange.

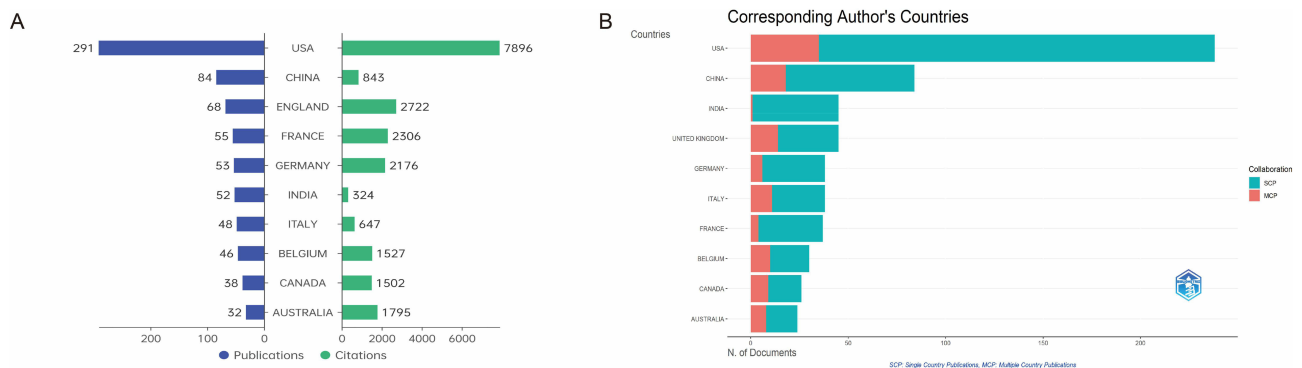


Figure 3 Bibliometric analysis of countries in the field of opioid-free anesthesia. (A) The top 10 countries by number of publications and citations. (B) Top 10 corresponding author's countries.

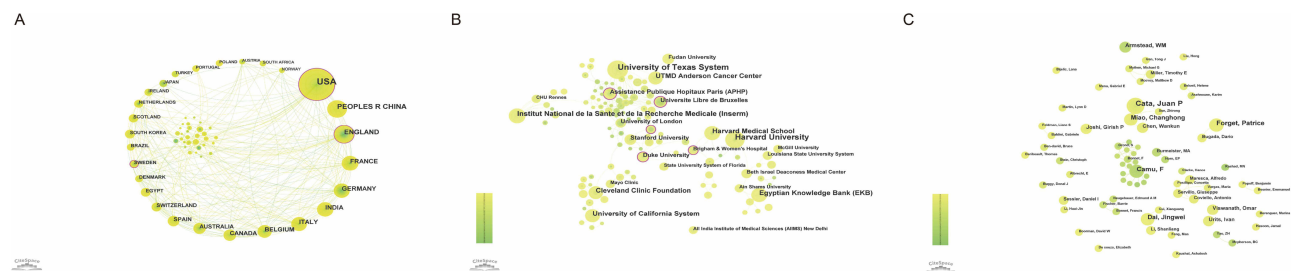


Figure 4 Cooperation network among (A) countries, (B) institutions, and (C) authors.

Table 2 Top 10 Institutions According to the Total Number of Publications

Rank	Institutions	Country	Count	Centrality
1	University of Texas System	USA	33	0.03
2	Harvard University	USA	29	0.07
3	Institut National de la santé et de la Recherche Médicale (Inserm)	France	19	0.04
4	Harvard Medical School	USA	18	0
5	Egyptian Knowledge Bank (EKB)	Egyptian	18	0
6	University of California System	USA	17	0.02
7	UT MD Anderson Cancer Center	USA	16	0.01
8	Cleveland Clinic Foundation	USA	16	0.07
9	Assistance Publique Hopitaux Paris (APHP)	France	13	0.14
10	Free University of Berlin	Germany	12	0

Table 3 Top 10 Most Productive Authors According to the Total Number of Publications

Rank	Authors	Year	Count
1	Cata, Juan P	2014	10
2	Camu, F	1991	7
3	Forget, Patrice	2023	7
4	Dai, Jingwei	2023	6
5	Miao, Changhong	2020	6
6	Armstead, WM	1996	5
7	Chen, Wankun	2020	4
8	Joshi, Girish P	2019	4
9	Urits, Ivan	2020	4
10	Viswanath, Omar	2020	4

Research Directions and Hotspot Analysis

The two most-cited pivotal studies in OFA research demonstrate (Figure 5A) that the top-cited study by Ziemann-Gimmel et al (2014, Br J Anaesth) demonstrated that opioid-free total intravenous anesthesia in bariatric surgery significantly reduced the relative risk of postoperative nausea and vomiting (PONV) by 46.4% (absolute risk reduction 17.3%); The second most-cited systematic review by Frauenknecht et al (2019, Anesthesia) further confirmed that while no significant difference existed in postoperative pain scores, OFA significantly reduced PONV risk. These two high-impact studies collectively established the clinical advantage of OFA in PONV reduction, providing evidence-based guidance for anesthetic protocol selection.

The evolution of OFA research demonstrates distinct developmental phases (Figure 5B and C). Early studies by the Biki B team primarily investigated the relationship between anesthetic techniques and oncological outcomes, revealing that opioids may suppress immune function and consequently affect cancer recurrence, highlighting the potential value of regional anesthesia in oncologic surgery. These groundbreaking studies provided crucial theoretical foundations for OFA applications in oncologic surgery. Subsequent research by the Bakan M team through prospective randomized controlled trials confirmed that dexmedetomidine-based OFA protocols significantly reduced early postoperative opioid requirements and PONV incidence, though without demonstrating superior analgesic efficacy compared to traditional opioid-containing regimens. In the most recent phase, the Salomé A team conducted evidence-based, comprehensive evaluations of OFA's clinical benefits and limitations. This evolutionary trajectory reflects the scientific pathway from basic research to clinical validation and demonstrates the sustained contributions from diverse research teams.

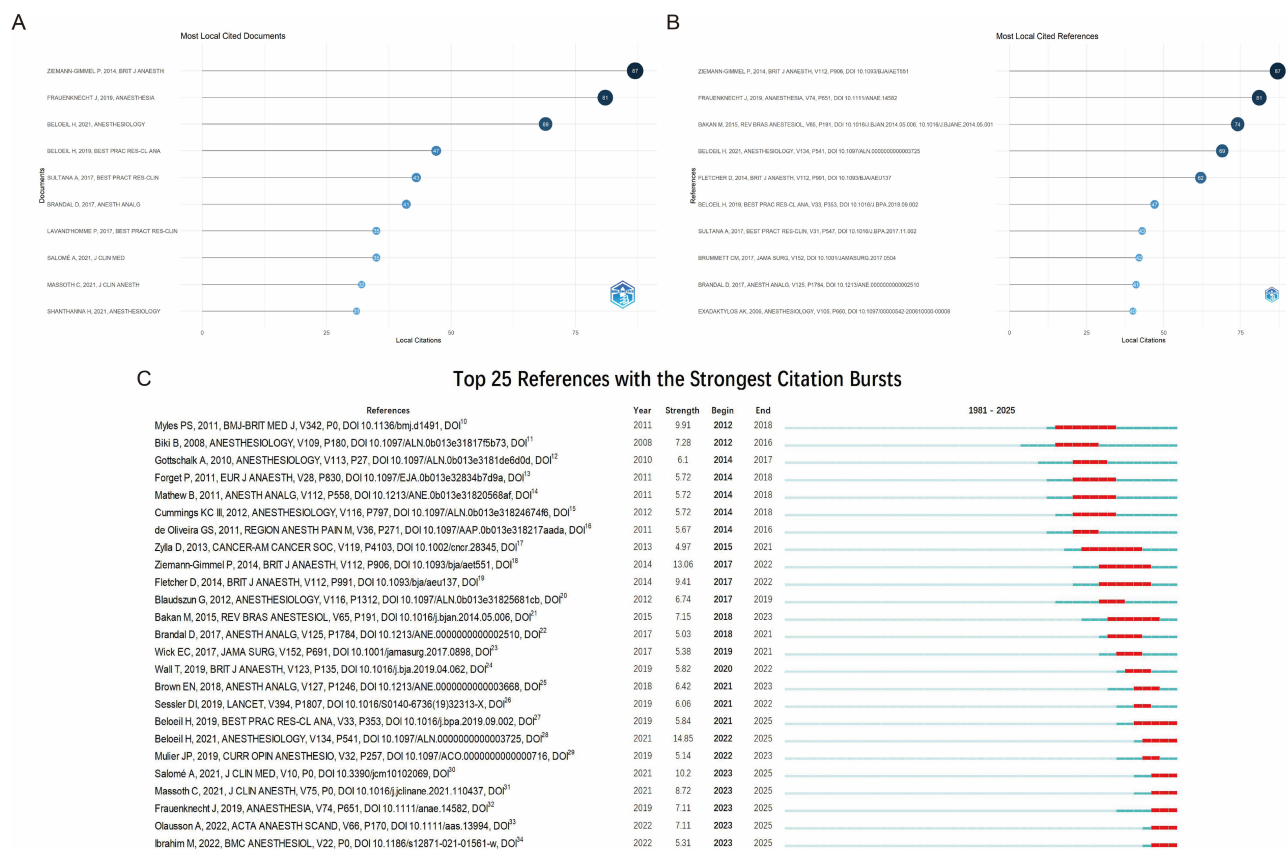


Figure 5 Bibliometric analysis of documents and references in the field of opioid-free anesthesia. (A) Most local cited documents, (B) Most local cited references and (C) Top 25 References with the Strongest Citation Bursts.

Keyword Analysis

Keyword co-occurrence analysis (Figure 6A) revealed four core themes in OFA research. The red cluster primarily focuses on OFA, containing 22 keywords, including opioid-free anesthesia (182), dexmedetomidine (125), and ketamine (66). The green cluster concentrates on anesthesia with 22 keywords like analgesia (194), morphine (86), and fentanyl (56). The blue cluster features perioperative management, highlighting 20 keywords such as surgery (180), postoperative pain (158), and opioids (135). The yellow cluster represents analgesia, covering 16 keywords, including pain (192), anesthesia (167), and management (94). These thematic clusters maintain relative independence while exhibiting intrinsic connections, forming a comprehensive research framework.

Temporal keyword analysis (Figure 6B) demonstrates distinct evolutionary characteristics in OFA research: Early-stage research (dark nodes) primarily focused on basic anesthetic protocols (morphine, fentanyl); Mid-term studies

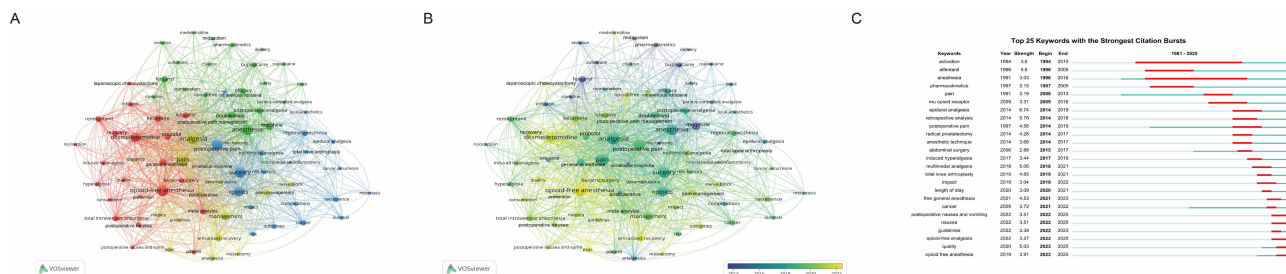


Figure 6 Bibliometric analysis of the keywords in the field of opioid-free anesthesia. (A) Co-occurrence analysis of keywords in the field of opioid-free anesthesia, (B) Timeline distribution of keywords in the field of opioid-free anesthesia, (C) Top 25 Keywords with the Strongest Citation Bursts.

gradually shifted toward perioperative management optimization (surgery, postoperative pain); Recent studies (light nodes) have emphasized clinical outcome improvement (OFA, ERAS, enhanced recovery). Burst detection analysis (Figure 6C) further identifies three persistently active research directions: Prevention and management strategies for PONV, Technical optimization of opioid-free analgesia, And evaluation frameworks for patient quality of life. These findings provide clear directional guidance for future research in this field.

Discussion

General Information

This study systematically elucidates the global development trends of OFA research from 1980 to 2024 through bibliometric analysis. The results demonstrate a significant temporal growth pattern, with particularly exponential increases in publications over the past decade and 2,219 citations recorded in 2024 alone, reflecting sustained academic attention to OFA research. Geographically, the United States dominates with 291 publications and 7,896 citations, demonstrating its leadership in policy guidance and scientific innovation. China shows comparable output but significantly fewer citations. England demonstrates quality-over-quantity with 2,722 citations from 68 publications. International collaborations show fragmented cluster patterns.

Knowledge Structure

The evolution of research hotspots demonstrates distinct phases: initial focus on basic anesthetic protocols, transitional emphasis on perioperative management optimization, and recent prioritization of clinical outcome enhancement. Keyword analysis identified four core themes: OFA pharmacological agents/regimens, perioperative management, and analgesic strategies, with PONV prevention/management, personalized OFA, and quality-of-life assessment representing the most active current frontiers.

Balanced anesthesia effectively controls surgical nociception and postoperative pain through combined pharmacological agents targeting distinct sites in the nociceptive system. The current practice of balanced anesthesia typically relies on opioid medications. However, accumulating evidence suggests opioids are suboptimal analgesics, mainly when used as monotherapy. Strictly speaking, “analgesia” is more precisely defined as “antinociception” - a complex physiological phenomenon involving multiple mechanisms and pathways that cannot be achieved solely through opioid receptor modulation. Opioid analgesic efficacy varies by pain type, demonstrating potency against visceral and inflammatory pain but limited effectiveness for A δ fiber-mediated dynamic pain and central sensitization-associated neuropathic pain. This differential efficacy underscores the clinical necessity for mechanism-based multimodal analgesic strategies.³⁵

OFA can effectively meet analgesic requirements for mild-to-moderate pain. OFA delivers sufficient analgesia for mild-pain surgeries (inguinal herniorrhaphy, varicose vein ligation, and laparoscopic procedures). Furthermore, OFA demonstrates comparable efficacy in moderate-pain surgeries such as knee/distal leg procedures, shoulder/back operations, hysterectomies, and maxillofacial surgeries.³⁶ However, OFA exhibits limitations in high-pain surgeries (thoracotomy, laparotomy, total joint arthroplasties, and major vascular procedures). Thus, multimodal analgesia combining non-opioid agents with opioids or enhanced analgesic protocols is recommended for optimized pain control and patient comfort.³⁷ Substantial evidence confirms multimodal analgesia significantly reduces postoperative opioid requirements while improving pain management.^{38,39}

Common multimodal analgesic agents include acetaminophen, NSAIDs, α 2-adrenergic agonists, (NMDA) receptor antagonists, gabapentinoids, and local anesthetics. By suppressing noradrenergic neurotransmission, α 2-adrenergic agonists effectively modulate central nervous system hyperexcitability. Choi et al demonstrated that although α 2-adrenergic agonists provide weaker direct analgesia than opioids, they reduce opioid requirements by 30–50%.⁴⁰ Research evidence indicates that incorporating dexmedetomidine into OFA protocols significantly improves postoperative pain scores, reduces opioid consumption, and decreases the incidence of PONV. However, these studies also identified extended extubation times, prolonged PACU stays, and increased bradycardia rates in OFA patients.^{41,42}

Grounded in multimodal analgesia principles, opioid-free patient-controlled intravenous analgesia (OF-PCIA) has emerged as a significant pain management strategy. This approach achieves postoperative analgesia through synergistic

combinations of two or more non-opioid analgesics. Studies confirm the feasibility of purely OF-PCIA in selected cases, effectively controlling surgical inflammation while reducing adverse effects like respiratory depression, nausea, vomiting, and hyperalgesia. Furthermore, this method decreases postoperative opioid dependence and may mitigate risks of tumor recurrence and metastasis.⁴³ Particularly for elderly, frail, or critically ill patients, OF-PCIA demonstrates less impact on consciousness and respiratory function, offering superior safety compared to conventional opioid-based PCIA. A clinical trial in thyroidectomy patients confirmed that the dexmedetomidine-flurbiprofen combination significantly enhances post-anesthesia pain control, reduces emergence agitation, mitigates cognitive impairment, and improves immune function/wound healing.⁴⁴ In total joint arthroplasty analgesia, studies reveal that NSAIDs-gabapentin PCIA regimens achieve comparable pain scores to opioid-only analgesia while significantly reducing opioid consumption and postoperative pulmonary complications.⁴⁵ Furthermore, evidence indicates NSAIDs-ketamine combinations produce synergistic analgesia via multiple mechanisms: elevating pain thresholds, modulating pain perception, and suppressing inflammatory responses, thereby alleviating hyperalgesia.⁴⁶ Notably, NSAIDs-tramadol coadministration counteracts tramadol-induced constipation and enhances cellular immunity by stimulating macrophage release of proinflammatory cytokines.⁴⁷ Concurrently, OF-PCIA demonstrates significant clinical advantages in ambulatory and ERAS settings.⁴⁸ However, OF-PCIA presents certain limitations in clinical practice. Compared to opioids, non-opioid analgesics have a relatively narrow therapeutic window and are prone to ceiling effects. Yet, with advancements in multimodal analgesia and nerve block techniques, OF-PCIA combined with regional anesthesia now adequately serves some severe postoperative pain cases.

Cancer is an inflammatory disease that often involves some degree of immune suppression. Studies have documented opioid-mediated immunosuppression that promotes tumor dissemination.⁴⁹ This raises concerns about opioids potentially influencing cancer recurrence and tumor progression. Opioids have been shown to modulate the activity of various immune cells, including NK cells. Rodent studies indicate chronic high-dose opioid exposure may inhibit tumor progression, whereas acute/low-dose perioperative opioids could promote tumor growth.⁵⁰ Existing studies have associated opioids with poorer oncological outcomes.^{51,52} Compared to traditional opioids, OFA protocols typically combine α 2-agonists, lidocaine, regional techniques, and ketamine, which synergistically mitigate surgical stress and maintain immune-inflammatory homeostasis.^{53,54} However, randomized controlled trial data remain scarce for cancer surgery populations. Significant knowledge gaps persist regarding OFA in cancer surgery, with marked methodological heterogeneity in existing studies precluding definitive conclusions about its impact on early postoperative outcomes.⁵⁵ Although preliminary findings suggest potential advantages of OFA in perioperative immediate outcomes, higher-quality clinical trials are needed to validate its superiority in cancer surgery patients.

Despite the growing interest in OFA, current protocols face several limitations that restrict their universal applicability. A key concern is the ceiling effect of many non-opioid analgesics, such as NSAIDs and acetaminophen, which limits their efficacy in managing moderate-to-severe postoperative pain. Additionally, agents like dexmedetomidine and ketamine may cause hemodynamic instability or delayed emergence. To address these challenges, future research should explore novel multimodal drug combinations that synergistically enhance analgesia without increasing adverse effects. Promising strategies include pairing α 2-agonists with NMDA antagonists or integrating anti-inflammatory agents with regional anesthesia techniques. Personalized OFA regimens based on surgical type and patient comorbidities may also improve safety and effectiveness in diverse clinical settings.^{28,42}

The Frontiers

PONV

Our bibliometric analysis identified PONV as one of the most frequently cited and persistently active research hotspots in the field of OFA. This reflects not only the academic interest but also the growing clinical relevance of PONV in perioperative care. The consistent emergence of this theme across high-impact studies suggests a strong translational potential, with implications for refining anesthesia protocols and enhancing guideline recommendations—particularly within ERAS pathways.

PONV has long been recognized as a critical outcome measure in ERAS protocols. Recent studies show that while OFA demonstrates comparable pain control and opioid consumption to conventional anesthesia, it significantly reduces

PONV incidence, albeit with higher bradycardia rates in OFA patients.^{8,30,33} Frauenknecht et al compared opioid-based versus OFA regarding immediate postoperative pain and PONV. Analysis of 23 RCTs demonstrated that intraoperative opioids failed to improve 2-hour resting pain scores compared to OFA but were significantly associated with increased PONV rates.³² Notably, for cancer patients with potential chemotherapy-induced nausea preoperatively, anesthetic strategies reducing both opioid use and PONV are particularly valuable. However, the specific effect of OFA on PONV reduction remains unconfirmed in the oncologic population.

Personalized OFA

Although evidence supports OFA's efficacy and clinical feasibility, the lack of high-quality data on optimal non-opioid combinations and personalized dosing precludes definitive recommendations for universal OFA adoption. Current evidence suggests implementing multidimensional preoperative screening (genetic testing, standardized questionnaires, and advanced imaging) to identify high-risk patients for opioid-related complications. This personalized risk assessment strategy facilitates optimized anesthesia selection and enhances perioperative safety.

Patients with preexisting respiratory depression risk factors, particularly obese patients with obstructive sleep apnea, should avoid medications that may exacerbate respiratory depression. Given the substantially increased risk of opioid-related adverse events in obese patients, evidence has accumulated supporting OFA use in this population. A systematic review and meta-analysis confirmed that opioid-sparing strategies significantly reduce opioid-induced respiratory depression incidence.⁵⁶ α 2-adrenergic agonists like clonidine and dexmedetomidine may provide safer analgesic alternatives for obese patients.

Studies reveal that 10% of cardiothoracic surgery patients continue opioid use at 90 days postoperatively, suggesting opioid-based anesthesia may promote chronic opioid consumption.⁵⁷ This prevalence may be higher in reality due to underreported opioid-related complications in cardiac surgery populations. Research shows cardiac surgery patients receiving dexmedetomidine-based OFA require significantly fewer postoperative IV opioids than conventional opioid anesthesia. OFA patients experience reduced cough-associated pain and lower atrial fibrillation rates.⁵⁸

Future research should prioritize the development of more targeted OFA with improved receptor specificity while optimizing surgery-tailored OFA protocols based on procedural invasiveness and patient risk profiles. International multicenter collaborations will be essential to overcome sample size limitations and standardize outcome measures. Particular emphasis should be placed on investigating OFA's long-term immunological impacts, especially its potential to modulate cancer-related immunity and influence recurrence risks through well-designed longitudinal studies with oncology-specific endpoints.

Strengths and Limitations

The rapid advancement of computer science has driven a transition from traditional laboratory-based research to digital and networked paradigms, significantly increasing attention to bibliometric analysis. Bibliometrics is valuable for assessing research outputs, identifying disciplinary trends, and enhancing study quality. This study's significance lies in conducting the first systematic bibliometric analysis of OFA while providing valuable references and insights to guide future research directions for scientists and clinicians. However, several limitations should be acknowledged. First, the relatively small sample size of OFA studies and our exclusive use of the Web of Science Core Collection may have resulted in incomplete literature coverage. The exclusive use of the Web of Science may introduce selection bias, as it predominantly indexes high-impact journals, potentially overlooking relevant studies from other sources. Additionally, excluding non-English publications limits geographic representation and may omit regionally significant findings, particularly from non-Western research communities. As a retrospective study, there is an inevitable time lag between data collection and publication. Although data were retrieved on December 31, 2024, the conclusions remain consistent with the current trajectory of the field. Given the rapid development of OFA research, periodic updates will be essential to ensure continued relevance. While bibliometric analysis reveals macro-level research trends, it cannot replace systematic reviews when evaluating clinical efficacy. Future work may combine our findings with meta-analyses to bridge knowledge mapping and evidence synthesis.

Conclusions

This bibliometric analysis highlights the rapid development of OFA research, driven by the opioid crisis and innovations in alternative analgesia. Over the past decade, the field has shown exponential growth, with major focuses including OFA protocol development, perioperative optimization, PONV prevention, and integration into ERAS pathways. However, clinical adoption remains variable, and high-quality evidence on long-term outcomes—such as chronic pain, opioid dependence, and cancer prognosis—is still lacking. These limitations, along with the exclusive use of a single database and heterogeneity in included studies, may affect the generalizability of our findings. Future research should prioritize the development of individualized, evidence-based OFA protocols and assess their efficacy through multicenter randomized controlled trials in cancer surgery populations, as well as comparative trials with conventional opioid-based regimens. Such studies will be essential to bridge current knowledge gaps, support clinical translation, and improve patient outcomes across diverse surgical contexts.

Abbreviations

OFA, opioid-free anesthesia; NSAIDs, non-steroidal anti-inflammatory drugs; NMDA, N-methyl-D-aspartate; ERAS, enhanced recovery after surgery; OF-PCIA, opioid-free patient-controlled intravenous analgesia.

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Disclosure

The authors declare no conflicts of interest in this work.

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