Journal of Acute Disease

Original Article

jadweb.org

doi: 10.4103/jad.jad_115_24

Sepsis-associated acute kidney injury: A bibliometric analysis of the global research output and collaboration network (2013-2023)

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ABSTRACT

Objective: To explore the current status of sepsis-associated acute kidney injury (SA-AKI) research and predict its future research directions.

Methods: The bibliometric overview of publications was conducted in the field of SA-AKI based on Web of Science Core Collection database from January 2013 to August 2023. This study employed software such as CiteSpace and VOSviewer to conduct bibliometric and visualization analysis of the included literature, including publication trends, geographic distribution characteristics, author contributions, citations, funding sources characteristics, and keyword clustering.

Results: A total of 6509 articles were analyzed, and the number of publications and citations increased from 2013 to 2022. The United States had the highest number of publications in SA-AKI, while France was the country with the highest number of citations per publication. Keyword clustering analysis showed that the pathophysiology and definition of SA-AKI were the research focus, and the research hotspots were "machine learning", "vitamin C", "kinase", "hemodynamics", "renal microcirculation" and "mitochondria". Literature coupling analysis indicated that exploring the management and treatment of SA-AKI was the research frontier.

Conclusions: Over the past decade, SA-AKI research has shown a upward trend in terms of the number of publication. Research primarily focuses on exploring mechanisms and improving early warning systems. Mechanisms involve microcirculatory dysfunction, inflammation, and other pathophysiological factors. Future recommendations include continuing basic research, achieving clinical application of novel biomarkers, and prioritizing renal recovery mechanisms in treatment strategies.

KEYWORDS: Sepsis; Kidney injury; Research trends; Visual analysis; Bibliometrics

1. Introduction

Sepsis associated acute kidney injury (SA-AKI) is a serious condition that affects the kidneys when the body has an overwhelming infection[1]. Sepsis is defined as organ dysfunction resulting from the host's deleterious response to infection[2].

Summary

Question: What is the current research status and future research trends of sepsis associated acute kidney injury (SA-AKI)?

Findings: The research on SA-AKI has gradually become a hotspot, with a sharp increase in publication volume and citation frequency from 2019 to 2021. The United States, China, and European countries are the main contributors to SA-AKI research. The current research focuses on exploring the mechanism of SA-AKI and improving its early warning mechanism.

Meaning: The research elucidates the trends in SA-AKI research, thereby facilitating the direction of future studies. Understanding the complex pathophysiological mechanism of SA-AKI is crucial for further research.

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How to cite this article: Yin MH, Hou QL, Zhu CL, Zhao SP. Sepsis-associated acute kidney injury: A bibliometric analysis of the global research output and collaboration network (2013-2023). J Acute Dis 2025; 14; 10.

Article history: Received 3 November 2024; Revision 13 January 2025; Accepted 22 May 2025; Available online 26 May 2025

One of the most common organs affected is the kidneys, resulting in SA-AKI that contributes to the morbidity and mortality of sepsis[3]. The prognosis of SA-AKI is poor, with a high mortality rate ranging from 40% to 70%[4]. The survivors of SA-AKI may have an increased risk of developing chronic kidney disease (CKD) or end-stage renal disease (ESRD), as well as cardiovascular complications and impaired quality of life[5].

Bibliometrics is the use of statistical methods to analyse books, articles and other publications, especially in scientific contents[6]. Bibliometrics can help answer questions about a field based on data about publications, such as authors, topics, funding, citations, downloads, and impact. Bibliometrics can also show the relationships between published works, such as co-authorship, co-citation, bibliographic coupling, and keyword co-occurrence[7].

There is a lack of bibliometric analysis on the research trends, development, and future prospects of SA-AKI in the existing literature. Therefore, this study aims to summarize the research progress and trends in the field of SA-AKI from 2013 to 2023 through bibliometric analysis, and to glimpse new insights into the future direction of SA-AKI progress from it.

2. Materials and methods

2.1. Inclusion and exclusion criteria

This study screened the literature according to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA statement)[8]. The SA-AKI related studies were included, including clinical and basic research; the language was English; the literature type was original articles, excluding reviews, letters, conference abstracts, editorial materials, book chapters and other types of articles.

2.2. Literature source and search strategy

The search was completed on August 1, 2023, in the Web of Science Core Collection database as the data sample source. The search expression was as follows: [TS=(Sepsis OR Bloodstream Infection OR Bloodstream Infections OR Infection, Bloodstream OR Pyemia OR Pyemias OR Pyohemia OR Pyohemias OR Pyaemia OR Pyaemias OR Septicemia OR Septicemias OR Poisoning, Blood OR Blood Poisoning OR Blood Poisonings OR Poisonings, Blood OR Severe Sepsis OR Sepsis, Severe) AND TS=(Acute Kidney Injury OR Acute Kidney Injuries OR Injury Kidney Injuries, Acute OR Kidney Injury, Acute OR Acute Renal Injury OR Acute Renal Injuries OR Renal Injuries, Acute OR Renal Injury, Acute OR Renal Insufficiency, Acute OR Acute Renal Insufficiencies OR Renal Insufficiencies, Acute OR Acute Renal Insufficiency OR Kidney Insufficiency, Acute OR Acute Kidney Insufficiencies OR Kidney Insufficiencies, Acute OR Acute Kidney Insufficiency OR Kidney Failure, Acute OR Acute Kidney Failures OR Kidney Failures, Acute OR Acute Renal Failure OR Acute Renal Failures OR Renal Failures, Acute OR Renal Failure, Acute OR Acute Kidney Failure)] OR TS=(Sepsis associated Acute Kidney Injury OR Septic Acute Kidney Injury OR Septic AKI OR Sepsis induced Acute Kidney Injury), publication date from January 1, 2013 to August 1, 2023, language as "English", literature type as "article".

2.3. Literature screening and data extraction

Literature was screened by two authors according to the inclusion and exclusion criteria. The retrieved results were exported in plain text and tab-delimited file format, with the record content as "full record and cited references". Each record included literature-related information, such as title, author, abstract, keywords, nationality, research institution and citation.

2.4. Statistical methods

Microsoft Office Excel 2013 software was employed to draw line charts, analyzing the trends of publication volume and citation over the years. CiteSpace 6.2.2 software was applied to conduct cluster analysis of co-occurring keywords and burst word analysis. VOSviewer 1.6.19 software was usded to analyze co-cited articles, keywords, countries/regions, institutions, journals, authors and references. H-index (the maximum value of h such that the author has published h papers that have each been cited at least h times) and impact factor (the average number of citations received by articles published in a journal during a two-year period) were collected from Web of Science Citation Database.

3. Results

3.1. Literature search strategy

Based on the Web of Science citation database, this study retrieved 7041 English articles in the field of SA-AKI research, and finally included 6509 articles for analysis. The flowchart is shown in Figure 1.

3.2. Publication and citation trends

As shown in Figure 2, the annual publication volume and annual citation frequency showed a relatively stable upward trend from 2013 to 2022 (due to the cut-off time of the search, the data for 2023 was not included for the whole year), indicating a growing interest and research activity in this field. From 2019 to 2021, the annual citation frequency and publication volume showed a sharp

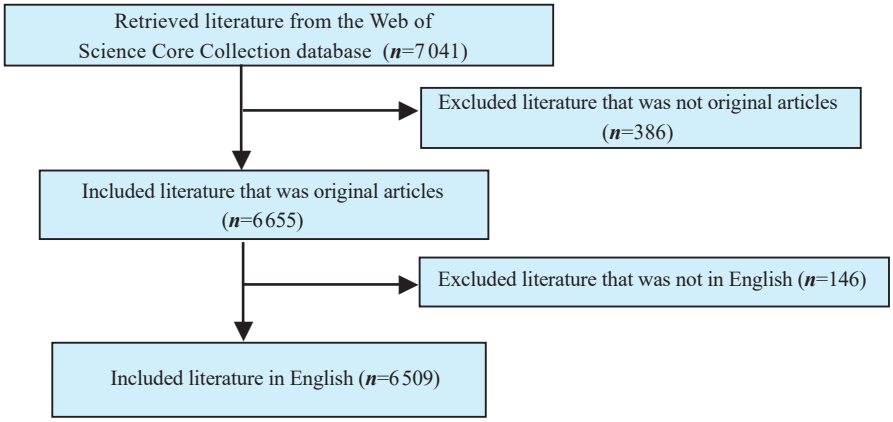


Figure 1. Literature screening process.

upward trend, indicating that SA-AKI related research gradually became a research hotspot. The highest number of publications was in 2021, with 980 articles, while the highest number of citations was in 2022, with 30258 citations. This suggests that the recent publications have received more attention and recognition from the scientific community. We believe that there are two main reasons for this trend. Firstly, the Third International Consensus (Sepsis-3) Definitions published in 2016 mark a refinement of the definition of sepsis[9,10]. And the definition of sepsis-associated AKI has also changed accordingly, which may have aroused the interest of a large number of relevant researchers. Meanwhile, the surge in AKI related research from 2019 to 2021 can be attributed to COVID-19 becoming a pandemic worldwide. In the initial stage of the COVID-19 outbreak, research focused on the clinical symptoms of COVID-19-infected patients with AKI, while in a later stage, the associations between SARS-CoV-2 infection and AKI, as well as the negative effects of multiple factors such as sepsis or nephrotoxic drugs on the kidney, gained more attention[11]. However, the impact of these two reasons will weaken over time, which is why there is a slight downward trend in 2023. The figure also shows that the citation frequency is generally higher than the publication frequency, indicating that the SA-AKI related articles have a high impact and quality.

3.3. Geographic distribution characteristics

The articles were distributed in 137 countries/regions, with the United States (1925, 25.9%) having the highest number of publications, followed by China (1505, 23.1%), Germany (407, 6.2%), Italy (377, 5.7%) and the United Kingdom (368, 5.6%), as shown in Table 1. The top three countries/regions with the highest average citation frequency were France (78.0), Canada (75.5) and Australia (71.3). Using CiteSpace software to calculate the intermediary centrality (nodes with more than 0.10 are called key nodes), the United Kingdom (0.12) and Canada (0.12) occupied the core position in the SA-AKI research field.

3.4. Institutional distribution characteristics

The top five institutions with the highest number of publications were the University of Pittsburgh in the United States (193, 2.9%), the University of California in the United States (176, 2.7%), Harvard University in the United States (173, 2.6%), the University of London in the United Kingdom (142, 2.1%) and the Mayo Clinic in the United States (113, 1.7%), as shown in Table 2. The University of Pittsburgh had the highest number of publications and average citation frequency, while the University of California had the highest intermediary centrality, indicating their authoritative status in the SA-AKI research field. In addition, institutions such as the Royal Brisbane and Women's Hospital in Australia (with an average citation frequency of 31.4), Monash University in Australia (42.6), and the University of Melbourne in Australia (22.2) also had high average citation frequencies. Institutions with high intermediary centrality also included the University of Pennsylvania in the United States (0.58) and Ohio State University in the United States (0.35). Average citation frequency and betweenness centrality are among the key indicators used to measure the impact of an institution's research output. Although some institutions are not directly listed in the top 10 based on the number of publications, their high average citation frequency and betweenness centrality still demonstrate their significant influence in the relevant field.

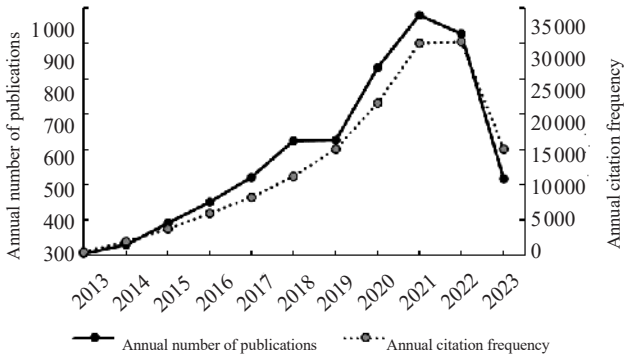


Figure 2. Temporal trends in of SA-AKI related articles publication.

3.5. Authors' contribution

The most productive author in the field of SA-AKI research is John A. Kellum from the University of Pittsburgh in the United States, who published 92 articles. He is followed by Rinaldo Bellomo from the Monash University School of Medicine in Australia (82) and Claudio Ronco from the San Bortolo Hospital in Vicenza, Italy (74) (Table 3). The author collaboration network graph (Figure 3A) shows that they are also the top three authors in terms of collaboration frequency, with different colors indicating different clusters, *i.e.*, small research groups formed by multiple authors. The collaboration among researchers is mainly within their own countries/regions, although some international collaborations are evident. The author with the highest average citation frequency is Sean M. Bagshaw from the University of Alberta in Canada (102.1), followed by Jean-Louis Vincent from the Free University of Brussels in Belgium (91.3).Notably, Jean-Louis Vincent also has the highest H-index (150), indicating a significant impact in the field. Rinaldo Bellomo, with an H-index of 123, also demonstrates substantial influence.

3.6. Co–occurrence keyword cluster analysis

We used VOSviewer to create a map with 184 terms (Figure 4A), with 6 clusters. "Inflammation", "oxidative stress", "mechanism", "expression" and "activation" occupy the core part. The red cluster #1 consists of 54 terms, including "inflammation", "oxidative stress", "mechanism", "expression", "activation" and "apoptosis". It mainly focuses on the pathophysiological mechanism of SA-AKI, and highlights the role of inflammatory response. The green cluster #2 consists of 38 terms, including "mortality", "outcome", "epidemiology" and "management". It mainly focuses on the

Table 1. Top 10 countries/areas ranked by number of publications.

Rank	Country/region	Publications	Total citation frequency	Average frequency of citations	Betweenness centrality
1	The United States	1925	63377	32.9	0.07
2	China	1505	25485	16.9	0.00
3	Germany	407	23637	58.0	0.08
4	Italy	377	22275	59.0	0.06
5	The United Kingdom	368	24302	66.0	0.12
6	France	335	26133	78.0	0.06
7	India	296	10735	36.2	0.04
8	Canada	275	20773	75.5	0.12
9	Australia	261	18633	71.3	0.09
10	Japan	259	12288	47.4	0.04

Table 2. The top 10 institutions ranked by number of publications.

Rank	Institution	Country/region	Publications	Total citation frequency	Average frequency of citations	Betweenness centrality
1	University of Pittsburgh	The United States	193	10735	55.6	0.10
2	University of California	The United States	176	5306	30.1	0.65
3	Harvard University	The United States	173	2255	13.0	0.09
4	University of London	The United Kingdom	142	919	6.4	0.06
5	Mayo Clinic	The United States	113	2870	25.3	0.02
6	Ohio State University	The United States	109	498	4.5	0.35
7	Shanghai Jiao Tong University	China	83	1221	14.7	0.00
8	Monash University	Australia	79	3367	42.6	0.08
9	University of Toronto	Canada	74	3805	51.4	0.00
10	Capital Medical University	China	72	724	10.0	0.01

Table 3. Top 10 authors ranked by number of publications.

Rank	Author	Publications	Total citation frequency	Average frequency of citations	H-index
1	John A. Kellum	92	6571	71.4	110
2	Rinaldo Bellomo	82	4289	52.3	123
3	Claudio Ronco	74	4115	55.6	97
4	Kent Doi	38	659	17.3	45
5	Jean-Louis Vincent	34	3105	91.3	150
6	Peter Pickkers	34	1751	51.5	73
7	Suvi T. Vaara	28	818	29.2	20
8	Michael Joannidis	28	1067	38.1	50
9	Sean M. Bagshaw	27	2757	102.1	81
10	Ville Pettila	27	833	30.8	64
11	Marlies Ostermann	26	734	28.2	54

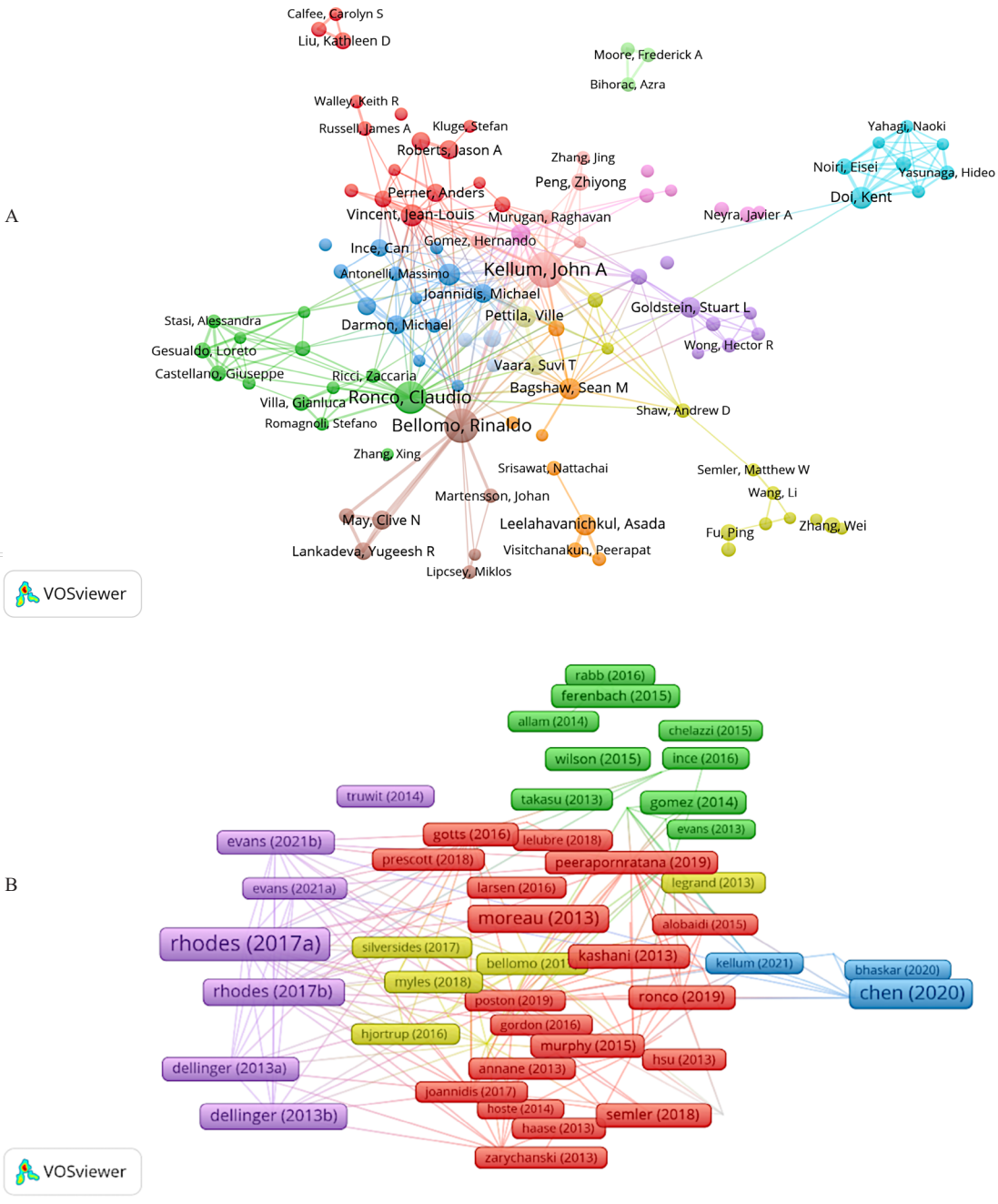


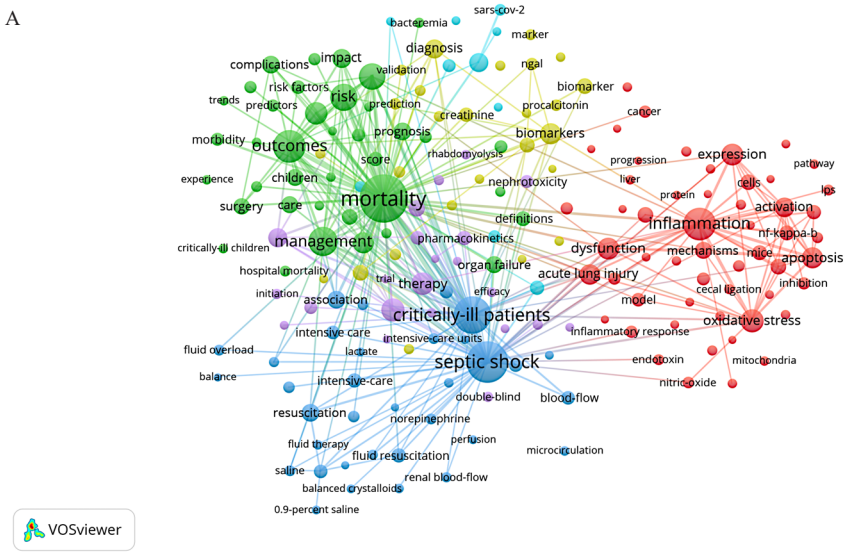
Figure 3. Collaboration and coupling analysis in SA-AKI research. A) Author cooperation network diagram. B) Literature coupling analysis network diagram.

prognosis of SA-AKI. The blue cluster #3 consists of 34 terms, including "critically ill patients", "septic shock" and "resuscitation". It focuses on the circulatory resuscitation of severe SA-AKI. The yellow cluster #4 consists of 26 terms, including "biomarkers", "neutrophil gelatinase-associated lipocalin", "diagnosis" "creatinine" and "cardiac surgery". It focuses on the early diagnosis of SA-AKI using biomarkers. The purple cluster #5 consists of 29 terms, including "treatment", "blood purification" and "antibiotics". It focuses on the treatment of SA-AKI. The cyan cluster #6 consists of 26 terms, including "COVID-19", "acute respiratory distress syndrome" and "mechanical ventilation". It focuses on the SA-AKI in COVID-19 patients. Using CiteSpace software to visualize the timeline and burst co-occurrence of keywords (Figure 4b), it shows that "infection", "guidelines", "score" and "definitions" dominate the recent research. Notably, "definitions" and "score" exhibit strong citation bursts from 2019 to 2023, while "infection" and "guidelines" have been consistently prominent since 2013.

3.7. Highly cited and co-cited literature analysis

The top 10 highly cited studies on SA-AKI research are shown in Table 4. The most cited work is The Third International Consensus Definitions for Sepsis and Septic Shock (Sepsis-3) (651 citations, 2016), published in JAMA, which redefined diagnostic criteria for sepsis and septic shock, profoundly influencing subsequent research. Other highly cited studies focus on various aspects of SA-AKI, including its current concepts, epidemiology, pathophysiology, prevention, treatment, and a unified theory encompassing inflammation, microcirculatory dysfunction, bioenergetics, and tubular cell adaptation. A literature co-citation analysis map (Figure 3B) was made using VOSviewer. We screened out some noteworthy papers published in recent years from the co-citation burst figure (Figure 4C) as follows: Peerapornratana *et al.* (2019) (burst strength: 84.06, 2021-2023), which advanced biomarker-driven strategies for early SA-AKI detection, underscoring the role of mitochondrial dysfunction in disease progression[12].

A



B

Keywords	Year	Strength	Begin	End	2013 - 2023
hydroxyethyl starch	2013	25.84	2013	2017	
continuous venovenous hemofiltration	2013	23.79	2013	2017	
replacement therapy	2013	22.08	2013	2017	
acute renal failure	2013	18.33	2013	2015	
gelatinase associated lipocalin	2013	18.13	2013	2017	
fluid resuscitation	2013	17.11	2013	2016	
nitric oxide	2013	15.36	2013	2015	
united states	2013	15.36	2013	2015	
renal function	2013	14.15	2013	2016	
organ failure	2013	12.96	2013	2016	
dialysis	2013	10.38	2013	2017	
blood flow	2014	16.21	2014	2016	
severe sepsis	2013	14.34	2014	2015	
mice	2014	13.15	2014	2016	
cardiac surgery	2013	11.6	2015	2017	
complications	2017	17.27	2017	2020	
renal failure	2013	13.28	2017	2019	
nf kappa b	2017	10.9	2017	2019	
surgery	2015	13.37	2018	2019	
international consensus definitions	2018	11.55	2018	2021	
definitions	2019	20.26	2019	2023	
score	2019	17.13	2019	2023	
protects	2019	12.8	2019	2020	
guidelines	2013	9.86	2019	2023	
infection	2013	10.93	2020	2023	

C

References	Year	Strength	Begin	End	2013 - 2023
Dellinger R, 2013, INTENS CARE MED, V41, P580, DOI 10.1007/s00134-012-2769-8, DOI	2013	67.69	2013	2018	
Perner A, 2012, NEW ENGL J MED, V367, P124, DOI 10.1056/NEJMoa1204242, DOI	2012	46.46	2013	2018	
Eckardt KU, 2012, KIDNEY INT SUPPL, V2, P7, DOI 10.1038/kisup.2012.8, DOI	2012	44.75	2013	2018	
Myburgh JA, 2012, NEW ENGL J MED, V367, P1901, DOI 10.1056/NEJMoa1209759, DOI	2012	42	2013	2018	
Zarjou A, 2011, J AM SOC NEPHROL, V22, P999, DOI 10.1681/ASN.2010050484, DOI	2011	31.24	2013	2016	
Yunos NM, 2012, JAMA-J AM MED ASSOC, V308, P1566, DOI 10.1001/jama.2012.13356, DOI	2012	28.05	2013	2018	
Bellomo R, 2009, NEW ENGL J MED, V361, P1627, DOI 10.1056/NEJMoa0902413, DOI	2009	23.92	2013	2014	
Boyd JH, 2011, CRIT CARE MED, V39, P259, DOI 10.1097/CCM.0b013e3181feeb15, DOI	2011	22.92	2013	2016	
Gomez H, 2014, SHOCK, V41, P3, DOI 10.1097/SHK.0000000000000052, DOI	2014	38.55	2015	2020	
Young P, 2015, JAMA-J AM MED ASSOC, V314, P1701, DOI 10.1001/jama.2015.12334, DOI	2015	23.69	2015	2020	
Kellum JA, 2013, CRIT CARE, V17, P0, DOI 10.1186/cc11454, DOI	2013	22.51	2015	2018	
Caironi P, 2014, NEW ENGL J MED, V370, P1412, DOI 10.1056/NEJMoa1305727, DOI	2014	22.3	2015	2020	
Asfar P, 2014, NEW ENGL J MED, V370, P1583, DOI 10.1056/NEJMoa1312173, DOI	2014	21.43	2015	2018	
Hoste E, 2015, INTENS CARE MED, V41, P1411, DOI 10.1007/s00134-015-3934-7, DOI	2015	42.42	2017	2020	
Rhodes A, 2017, CRIT CARE MED, V45, P486, DOI 10.1097/CCM.0000000000002255, DOI	2017	26.12	2017	2023	
Alobaidi R, 2015, SEMIN NEPHROL, V35, P2, DOI 10.1016/j.semnephrol.2015.01.002, DOI	2015	21.36	2017	2020	
Singer M, 2016, JAMA-J AM MED ASSOC, V315, P801, DOI 10.1001/jama.2016.0287, DOI	2016	116.33	2019	2022	
Zhou F, 2020, LANCET, V395, P1054, DOI 10.1016/S0140-6736(20)30566-3, DOI	2020	29.44	2020	2022	
Cheng YC, 2020, KIDNEY INT, V97, P829, DOI 10.1016/j.kint.2020.03.005, DOI	2020	20.61	2020	2023	
Peerapornratana S, 2019, KIDNEY INT, V96, P1083, DOI 10.1016/j.kint.2019.05.026, DOI	2019	84.06	2021	2023	
Poston JT, 2019, BMJ-BRIT MED J, V364, P0, DOI 10.1136/bmj.k4891, DOI	2019	55.44	2021	2023	
Rudd KE, 2020, LANCET, V395, P200, DOI 10.1016/S0140-6736(19)32989-7, DOI	2020	46.76	2021	2023	
Bellomo R, 2017, INTENS CARE MED, V43, P816, DOI 10.1007/s00134-017-4755-7, DOI	2017	36.87	2021	2023	
Ronco C, 2019, LANCET, V394, P1949, DOI 10.1016/S0140-6736(19)32563-2, DOI	2019	35.17	2021	2023	
Cecconi M, 2018, LANCET, V392, P75, DOI 10.1016/S0140-6736(18)30696-2, DOI	2018	31.83	2021	2023	

Figure 4. Keyword dynamics and influential literature. A) Visualization of co-occurrence keyword clusters. B) Temporal evolution of keyword citation bursts. C) List of co-cited literature with strongest citation bursts.

Zhou *et al.* (2020) (burst strength: 29.44, 2020-2022), which delineated COVID-19's impact on renal outcomes, demonstrating the pandemic's impact on research priorities[13]. The figure also reflects evolving trends, with Hoste *et al.* (2015) (burst strength: 42.42, 2017-2020) emphasizing risk stratification models[14]. Collectively, these bursts illustrate shifting research priorities, from mechanistic insights to translational innovations, driving SA-AKI's interdisciplinary advancement.

3.8. Funding agency analysis

The top five funding sources with the most publications were the US Department of Health and Human Services, the US National Institutes of Health, the National Natural Science Foundation of China, the National Institute of Diabetes and Digestive and Kidney Diseases and the National Heart, Lung, and Blood Institute, and the other funding agencies belong to Germany, Australia, and Japan respectively, reflecting the high priority given to SA-AKI research by national-level research programs. Among the top ten funding agencies, five are from the United States, indicating substantial support for research in this area from American funding bodies. The outstanding publication and citation frequency of the US in this field is attributed to the robust backing from these funding agencies.

4. Discussion

In the past 10 years, the research on SA-AKI has gradually deepened and enriched. In order to further accurately predict the hotspots and provide suggestions for future prospects, this study used bibliometric techniques to analyze the latest literature in this field from January 2013 to August 2023, providing a reference for scientists to discover the hotspots and frontiers.

4.1. Co–occurrence keyword cluster analysis

We retrieved 6509 relevant studies based on the Web of Science database, and according to the annual analysis, we found that the number of research papers increased year by year, indicating that SA-AKI research has received widespread attention from scholars around the world. The United States ranked first in terms of publication volume, followed by China, while scholars from France, Australia, Canada and other countries published a large number of highly cited papers. In terms of country/region cooperation, the United Kingdom, Canada and others played a pivotal role, while researchers from Asian countries/regions such as China need to further strengthen cross-national and cross-regional exchanges and cooperation. Many institutions have carried out a large number of studies and have outstanding advantages in publishing papers. This is not only due to the high attention paid by scholars from both countries to SA-AKI, but also inseparable from the strong support of the US Department of Health and Human Services, the National Natural Science Foundation of China and others. Among the top 10 research institutions in terms of publication volume, five are located in the United States, two are located in China, and the rest are located in Australia, Canada and the United Kingdom respectively, indicating the attention and importance of medical institutions in the United States, China and others to this field. The intermediary centrality values of medical institutions in the United States and Australia are high, and they carried out extensive and

Table 4. Top 10 highly cited studies on SA-AKI.

Rank	Title	First Author	Journal	Journal Impact Factor (2022)	Year	Citation frequency
1	The third international consensus definitions for sepsis and septic shock (sepsis-3)[15]	Sean M. Bagshaw	Journal of the American Medical Association	120.7	2016	651
2	Surviving sepsis campaign: International guidelines for management of sepsis and septic shock: 2016[16]	Andrew Rhodes	Intensive Care Medicine	38.9	2017	293
3	Acute kidney injury from sepsis: Current concepts, epidemiology, pathophysiology, prevention and treatment[12]	Sadudee Peerapornratana	Kidney International	19.6	2019	262
4	Surviving sepsis campaign: International guidelines for management of severe sepsis and septic shock, 2012[2]	R. P. Dellinger	Intensive Care Medicine	38.9	2013	239
5	Acute kidney injury in sepsis[17]	Rinaldo Bellomo	Intensive Care Medicine	38.9	2017	232
6	Sepsis associated acute kidney injury[9]	Jason T Poston	British Medical Journal	105.7	2019	197
7	Epidemiology of acute kidney injury in critically ill patients: the multinational AKI-EPI study[14]	Eric Hoste	Intensive Care Medicine	38.9	2015	181
8	A unified theory of sepsis-induced acute kidney injury: Inflammation, microcirculatory dysfunction, bioenergetics, and the tubular cell adaptation to injury[18]	Hernando Gomez	Shock	3.1	2014	149
9	Hydroxyethyl starch 130/0.42 versus ringer's acetate in severe sepsis[19]	Anders Perner	New England Journal of Medicine	158.5	2012	138
10	Global, regional, and national sepsis incidence and mortality, 1990–2017: Analysis for the global burden of disease study[20]	Kristina E. Rudd	Lancet	168.9	2020	127

in-depth exchanges and cooperation. The cooperation, interaction, complementarity and construction between different countries or institutions have far-reaching significance. China and other countries should promote the establishment of cross-national and cross-regional research centers in the next step, ensure stable multi-center exchange and cooperation research, strive to publish higher quality and highly cited articles, and improve academic influence. In terms of author contribution, Professors John A. Kellum, Rinaldo Bellomo and Claudio Ronco are undoubtedly authoritative authors in SA-AKI, leading the world in terms of publication volume, citation frequency and collaboration.

4.2. Hotspots and Research Trends

The highly cited papers on SA-AKI mainly focus on the mechanism, prognosis, management, severity, scoring and treatment of SA-AKI. Scholars are eager to find new breakthroughs in research directions and achieve the integration of prevention and treatment of SA-AKI. "Machine learning", "kinase", "hemodynamics", "renal microcirculation" and "mitochondria" dominate the recent research. The cluster analysis of high-frequency keywords and references can identify the hotspots and frontiers of SA-AKI research, among which "infection", "guideline", "score" and "definition" are the research hotspots based on the time-overlay map. Delving deeper into the research, it is crucial to explore the underlying mechanisms of SA-AKI, as this understanding is pivotal for the development of effective treatment strategies.The current research on SA-AKI mainly includes two aspects: one is to explore the mechanism of SA-AKI, including oxidative stress, mitochondrial activation, inflammatory response at the molecular and cellular level, and renal perfusion, immunity, repair at the organism level[21]; the other is to improve the early warning mechanism of SA-AKI, using scoring mechanism, machine learning, hemodynamic monitoring, biomarker detection and other methods for accurate monitoring and management.

4.2.1. Related mechanisms

Sepsis-associated acute kidney injury (SA-AKI) involves multiple pathophysiological mechanisms, such as microcirculatory dysfunction, inflammation, microRNA, extracellular vesicles, autophagy, inflammatory reflex pathway, vitamin D and metabolic reprogramming[21]. Moreover, recent studies have revealed the roles of innate immune system, renal mitochondrial dysfunction, ferroptosis, circRNA and histone methylation modification in SA-AKI[22-27]. Li *et al*.[28] demonstrated that the pathogenesis of SA-AKI was dependent on the circulating inflammatory mediators by comparing it with ischemia-reperfusion induced acute kidney injury. Targeting these inflammatory mediators could be a promising therapeutic strategy to mitigate kidney damage in sepsis. Furthermore, at the cellular level, several interventions that modulated the pathogenic process of SA-AKI were recently validated, indicating that molecules such as Lyn, miR-23a-3p, USF2, BAM15 and inhibition of aerobic glycolysis could ameliorate sepsis-induced AKI[29-33]. The identification of these specific molecules offers hope for more targeted and effective treatments for SA-AKI. In animal models, the therapeutic effects of calcium hydroxybenzenesulfonate, selective casein kinase 2 alpha inhibitor, forsythiaside A, ginsenoside Rg1 and choline on SA-AKI were also confirmed[34-38]. These preclinical studies are crucial in advancing our understanding of SA-AKI and laying the groundwork for potential future clinical trials. However, it is important to note that further research is needed to fully understand the mechanisms of action and safety profiles of these interventions before they can be widely adopted in clinical practice.

4.2.2. Prospects

Based on the above analysis, we have some suggestions for the future development of SA-AKI research: a. SA-AKI has a more complex pathophysiological mechanism than AKI caused by other reasons, and persisting in basic research at the molecular, cellular and animal levels is a prerequisite for SA-AKI early warning and treatment; b. Based on the predictive role of novel biomarkers for subclinical AKI, it is urgent to further realize their clinical application; c. The efficacy study of SA-AKI drugs has not yet yielded positive results, but recovery from SA-AKI is possible and is associated with a reduction in mortality. Therefore, when developing SA-AKI treatment strategies, priority should be given to revealing the mechanisms that promote renal recovery and restore function[5,39,40].

4.3. Limitations

This study also has some limitations. First, since bibliometric analysis software is difficult to analyze data from multiple databases, our study only includes the Web of Science core collection database, and more comprehensive integrated analysis requires data from Scopus, PubMed and CNKI. Second, this study only included English literature, and did not analyze literature reports in other languages, so we may have missed some research hotspots, especially as Chinese literature reports have shown an upward trend in recent years.

In summary, based on bibliometric analysis, this study explored the current status of SA-AKI research publication volume in the past 10 years. At present, the publication volume in this field is increasing year by year, with the United States and China contributing the most; in addition, national/regional institutions have given great support to this type of research. Keyword cluster analysis shows the current stage of research hotspots, and the analysis of highly cited and co-cited literature provides the best reference for researchers in this field. However, it is worth

Data availability statement

The data supporting the findings of this study are available from the corresponding author upon request.

Authors' contributions

Study concept and design: SPZ. Acquisition of data: MHY, QLH, CLZ; Analysis and interpretation of data: SPZ, MHY, QLH; Drafting of the manuscript: SPZ, MHY, QLH; Critical revision of the manuscript for important intellectual content: SPZ, CLZ; Statistical analysis: MHY, QLH; Study supervision: SPZ.

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Edited by Liu JJ

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