



Articles on hemorrhagic shock published between 2000 and 2021: A CiteSpace-Based bibliometric analysis

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ABSTRACT

Objective: To conduct a bibliometric analysis of literature on hemorrhagic shock published between 2000 and 2021 with the help of Citespace to explore the current status, hotspots and research trends in this regard, with the results presented in a visualized manner.

Methods: The data over the past 22 years were retrieved from the Web of Science (WOS) Core Collection database and downloaded as the “Full Record and Cited References”. Cooperative analysis, cluster analysis, co-citation analysis, and burst analysis were performed based on the data on countries/regions, institutions, journals, authors, and keywords through Citespace.

Results: A total of 2027 articles were retrieved. The number of annual publications fluctuated but was generally on an upward trend. The United States stands out as the most productive country (989 articles), the University of Pittsburgh the most productive publishing institution (109 articles), SHOCK the most cited journal (1486 articles), TAO LI the most productive author (40 articles), DEITCH EA the most cited author (261 times of citation), hemorrhagic shock the most frequent keyword (725 times of occurrence), and “traumatic brain injury” the most covered article in keyword clustering (29 articles). The burst analysis revealed Harvard University as the institution with the highest strength value and the Journal of Trauma and Acute Care Surgery the most important journal. It was also concluded that HASAN B ALAM, AARON M WILLIAMS, and LIMIN ZHANG may continue to publish high-quality articles in the future. In the meanwhile, both “protect” and “transfusion” were considered the hotspots and trends in current research.

Conclusions: The United States has been a major contributor to the publication of the articles over the past 22 years, with the most productive publishing institution, the most cited journal, and the most cited author all coming from the US. Hemorrhagic shock, injury, resuscitation, trauma, models, activation, expression, fluid resuscitation, rats, and nitric oxide are hot topics in relevant research. According to the keyword burst analysis, the areas related to “protect” and “transfusion” may rise as the research directions in the future. However, since the hotspots in the research of hemorrhagic shock are short-lived and fast-changing, the researchers should pay more attention to the development trend in this field.

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1. Introduction

Hemorrhagic shock is a pathological process induced by traumatic hemorrhage, surgical bleeding, gastrointestinal bleeding, insufficient systemic effective circulating blood volume, and inadequate perfusion of tissues and organs, accompanied by tissue hypoxia, cellular metabolic disorders, and impaired organ function as the major physical changes and the activation of certain mechanisms for organ perfusion protection [1]. The term “shock” was used for the first time in the French physician Le Dran’s description of the clinical manifestations of a soldier wounded in a war. In retrospect of its original meaning, however, “shock” referred to hemorrhagic shock caused by trauma in the true sense [2].

Though cardiac disease remains the leading cause of death in the United States [3], trauma stands out as the leading cause of death in people aged 46 years old and below when stratified by age [4]. Hypothermia, acidemia, and coagulation disorders, which are common after resuscitation from hemorrhagic shock, are collectively referred to as the “lethal triad”, of which the problems associated with coagulation are the deadliest [5,6]. Capable of preventing coagulation disorders, the damage control resuscitation (DCR) method allows the patients to be treated surgically [7]. Currently, DCR has been adopted by the US Department of Defense and is widely used in numerous medical treatment centers [8].

At present, massive investigations have been performed on hemorrhagic shock around the world. Despite a large amount of literature collected in the Pubmed and Web of Science (WOS) databases, it is still not easy for the readers and researchers to search through numerous literature to identify research hotspots and trends. Facilitating analysis of articles, as well as abstracts, keywords and citations [9], published on journals, bibliometrics can help us to quickly understand the contributions of and collaborations among different countries, institutions, journals, and researchers in relevant fields. In the meanwhile, the keyword co-occurrence and burst analyses also respond to research hotspots and trends [10].

In previous studies, bibliometric analyses have been conducted on a variety of diseases such as depression, cardiovascular disease, and diabetic nephropathy [11–14]. However, no bibliometric analysis of hemorrhagic shock has ever been reported. Be aware of this gap in research, we adopted Citespace to map the information of the literature and analyze both the past and current statuses, hotspots, and development trends in the research of hemorrhagic shock. We will conduct an analysis focusing on the following research questions: What have been the main research directions and hot topics in the field of hemorrhagic shock over the past 22 years? Which countries, institutions, or authors have published the highest quantity or most influential literature in this field? What are the emerging research hotspots or frontiers in the future trends and development of hemorrhagic shock research?

Evaluative bibliometrics is a quantitative scientific field that has emerged as a powerful tool for assessing research performance and identifying influential articles that impact medical practice and foster new research ideas [15]. In this study, we employed the CiteSpace software as the tool of choice. CiteSpace, a Java-based application for bibliometric analysis, integrates bibliometrics, data mining algorithms, and information visualization methods [16] to present the results through nodes and linkages. This software was developed by Professor Chaomei Chen of the School of Computing and Information at Drexel University and released to the public in 2004 [17].

2. Materials and methods

2.1. Data source and search strategy

All data were obtained from the WOS Core Collection database on November 29, 2022, with the editions for selection determined as “ALL”.

The data retrieval strategy is listed as follows: (I) Title = “hemorrhagic shock”; (II) Document type = article or review article; (III) Language = English; and (IV) Time span = 2000–2021. The specific search formula is depicted as follows: (((TI=(“hemorrhagic shock”)) AND LA=(English))) AND DT=(Article OR Review)) AND DOP=(2000-01-01/2021-12-31). A total of 2027 relevant articles were acquired, and the contents of the literature records were determined as “Full Record and Cited References”, with the documents exported in the “plain text file” format. The exported data included titles, keywords, references, etc., all of which were further analyzed.

2.2. Analysis tools

CiteSpace V5.8. R3 was used in this study to analyze hemorrhagic shock-related studies between 2000 and 2021, so as to sort out the research hotspots and trends. The variations in node color in the plot reflects the changes over time; node size is positively correlated with the frequency; and the connecting lines indicate the cooperation, co-occurrence, and citation among nodes; node type is determined according to the type of the analysis; and the nodes with a centrality greater than 0.1 are marked by a purple circle in the outside.

2.3. Setting of parameters and data analysis

Four separate folders, namely “input”, “output”, “data” and “project”, were created for the project. The data were checked in the first place, revealing no duplicate files according to the results. The time span was set from January 2000 to December 2021. CiteSpace V5.8. R3 was used to input the downloaded documents as per the following procedures: (I) The time slice was set to be 1 year; (II) The

association strength algorithm was determined as the “Cosine”; (III) Pruning pathfinder was selected as the network cropping method; (IV) The node threshold was set to be g-index $k = 10$; (V) The network type included country/region, institution, journal, author, citation, keyword, and burst analysis; (VI) The algorithm log-likelihood rate (LLR) was adopted to name different clusters in cluster analysis; and (VII) The confidence of the clustering results was assessed using the modularity Q value (Q-value) and weighted through the mean silhouette value (S-value). A Q-value greater than 0.3 meant a significant clustering structure; a reasonable clustering was represented by a S-value >0.5 ; and a S-value >0.7 indicated a convincing clustering [18]. Microsoft Office Excel 2019 was used to draw statistical charts.

3. Results

3.1. Number and research trends of articles published

A total of 2027 articles and reviews were retrieved according to the methodology under the search strategy. The variations in the number of annual publications indicated the pace and progress of the research on this topic, as well as the level of interest in this field [19]. According to the search results, the articles published in the theme of “hemorrhagic shock” were divided into two phases in a broad sense, namely a rapid growth phase between 2000 and 2011 and a steady progression phase between 2012 and 2021 (Fig. 1).

The rapid growth phase witnessed the initial exploration of the disease, as well as the increase in the number of related publications year by year. Despite a decrease in individual years during this period, the number of publications rose in fluctuations as a whole. The last decade is considered a steady progression phase, as evidenced by an overall stable annual publication of the hemorrhagic shock literature. No significant downward trend has occurred during this period, indicating that researchers still have a greater interest in hemorrhagic shock, and the research tends to be deepened. Nevertheless, another minor upward trend occurred between 2018 and 2021. By fitting a trend line to the cumulative number of the publications, a quadratic curve fit with $R^2 = 0.9994$ was revealed, which was favorable in fit and reliable in trend line. This indicated that the total number of the publications will increase more rapidly in the future.

3.2. Analysis of cooperation among countries/regions

The country module in Citespace was used to analyze the countries/regions related to the articles, generating a total of 61 nodes and 57 connections (Fig. 2). As shown in Table 1, the top 5 countries/regions contributing to the greatest number of the articles were the USA, China, Germany, Japan, and France. Sweden, England, the Netherlands, Italy, and Denmark were the top 5 countries/regions with the highest centrality, indicating the superior quality of the articles published in these countries/regions. The linkages between the nodes of different countries/regions also indicated closer collaboration among countries in the research of hemorrhagic shock. The United States ranked first for 989 articles and a centrality greater than 0.1, outperforming other countries and regions not only for the number of the articles published but also the superior quality of the articles.

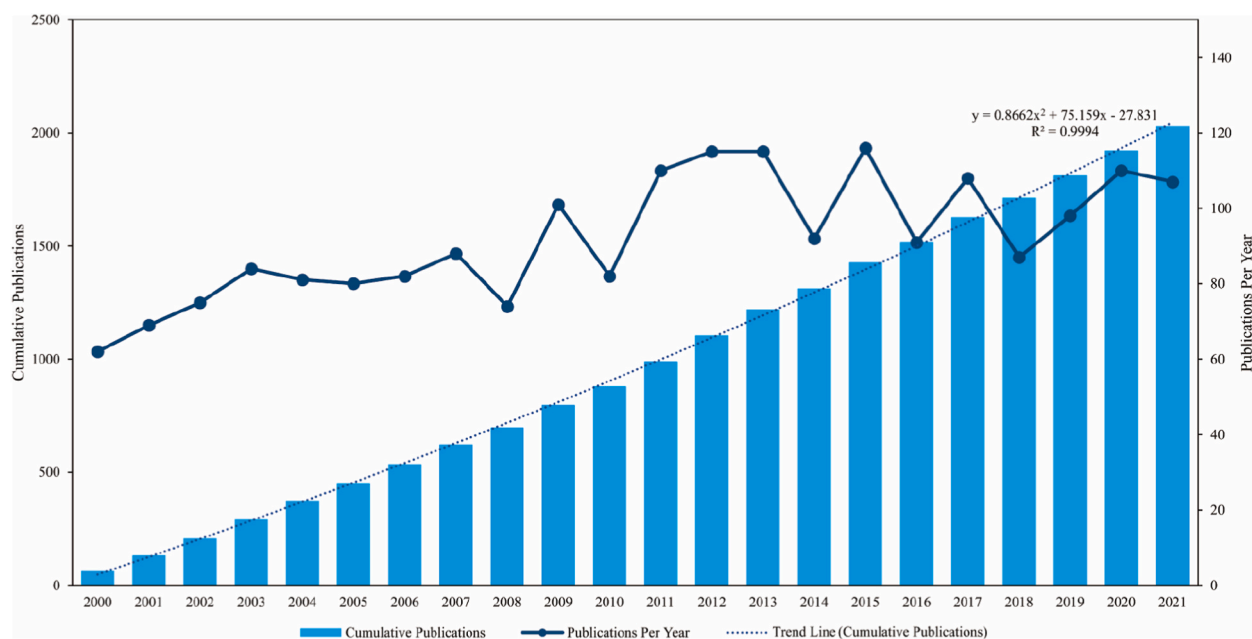


Fig. 1. Annual trends of publications on hemorrhagic shock.

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 DOI: 10.1016/j.shock.2023.02.011
 Keywords: Shock; Trauma; Hemorrhagic shock; Resuscitation; Hemorrhage; Hemostasis
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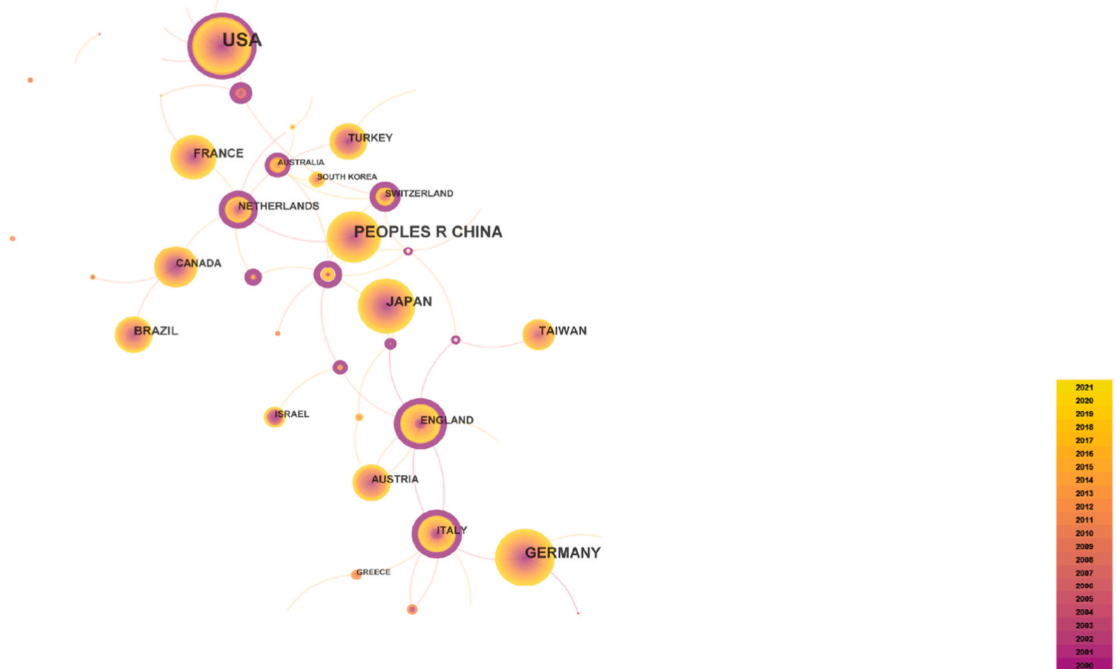


Fig. 2. Network of cooperation among countries/regions. The figure shows the names of the countries/regions with more than 20 publications. The node size is proportional to the number of the publications, and the variations in color within the node correlates with the year of activity, with the color of purple representing an earlier time of activity while the color of yellow denoting an active time close to the present. Countries/regions with a centrality greater than 0.1 are marked by a purple circle outside the node.

Table 1
 Top 5 Countries/regions with the publications and centrality.

Rank	Counts	Country/Region	Centrality	Country/Region
1	989	USA	0.54	SWEDEN
2	370	PEOPLES R CHINA	0.4	ENGLAND
3	155	GERMANY	0.33	NETHERLANDS
4	142	JAPAN	0.3	ITALY
5	65	FRANCE	0.27	DENMARK

3.3. Analysis of institutional cooperation

The analysis of the institutions, carried out via the institution module in Citespace, generated 293 nodes and 246 connections (Fig. 3). According to Table 2 that illustrates the top 5 institutions in the number of the publications, University of Pittsburgh took the lead for 109 publications, followed by University of Medicine and Dentistry of New Jersey, University of California San Diego, Uniformed Services University of the Health Sciences, and Third Military Medical University in order. The top 5 institutions with the highest centrality included Harvard University, Uniformed Services University of the Health Sciences, University of California San Diego, University of Washington, and The University of Texas Health Science Center at Houston. Two of the institutions, namely Uniformed Services University of the Health Sciences and University of California San Diego, performed excellently in both quality and quantity. Two clusters of institutional collaboration are presented in Fig. 3, with one of the clusters containing Harvard University, University of Michigan, and Uniformed Services University of the Health Sciences, while the other covering University of Medicine and Dentistry of New Jersey, University of California San Diego, and Rutgers State University Medical Center.

3.4. Co-citation analysis of journals

Co-citation analysis of journals helped identify popular journals and track the latest research. A total of 363 nodes and 426 links were obtained (Fig. 4) after analysis through Citespace. According to Table 3 and in terms of the number of citations, the top 5 journals included SHOCK, THE JOURNAL OF TRAUMA, CRITICAL CARE MEDICINE, JOURNAL OF SURGICAL RESEARCH, and ANNALS OF SURGERY, all of which are important reference journals in the research of hemorrhagic shock. As for centrality, the top 5 journals were FEBS LETTERS, MOLECULAR AND CELLULAR BIOCHEMISTRY, PROCEEDINGS OF THE NATIONAL ACADEMY OF SCIENCES OF THE

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 Pruning: Pathfinder

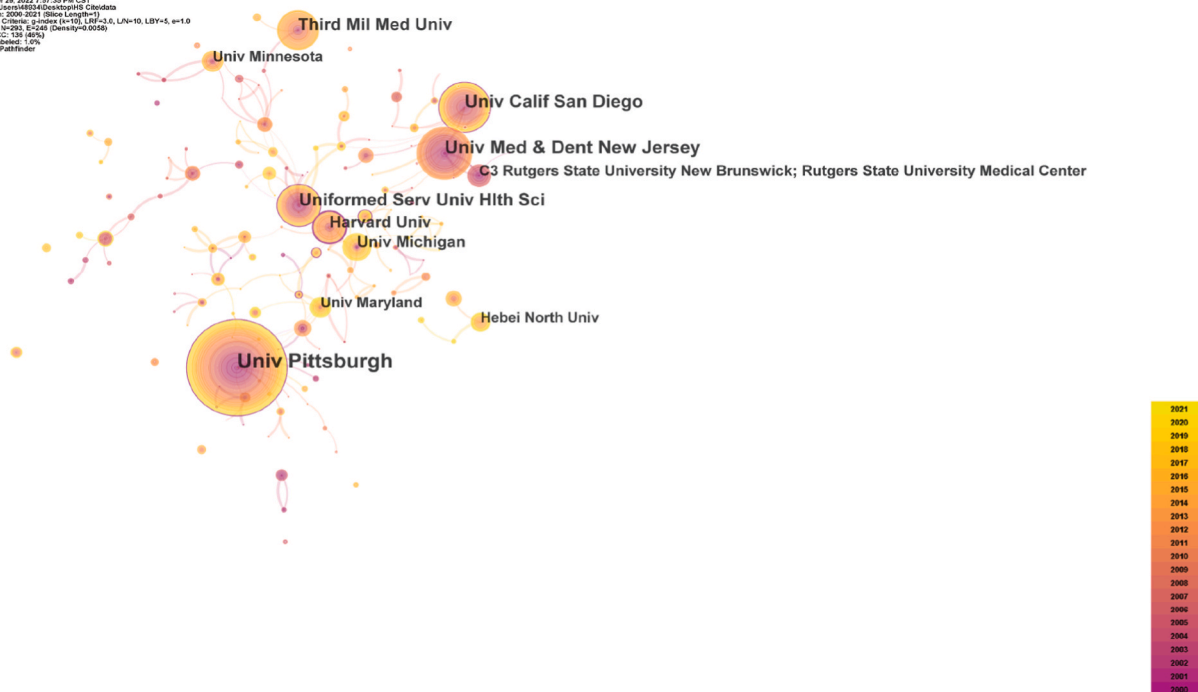


Fig. 3. Institutional cooperation co-occurrence. The figure shows the names of the institutions with more than 20 publications. The node size is proportional to the number of the publications, and the variations in color within the node correlates with the year of activity, with the color of purple representing an earlier time of activity while the color of yellow denoting an active time close to the present. Institutions with a centrality greater than 0.1 are marked by a purple circle outside the node.

Table 2

Top 5 institutions with the largest number of publications and the highest centrality.

Rank	Counts	Institutions	Country/Region	Centrality	Institutions	Country/Region
1	109	University of Pittsburgh	USA	0.2	Harvard University	USA
2	61	University of Medicine and Dentistry of New Jersey	USA	0.19	Uniformed Services University of the Health Sciences	USA
3	56	University of California San Diego	USA	0.12	University of California San Diego	USA
4	47	Uniformed Services University of the Health Sciences	USA	0.12	University of Washington	USA
5	46	Third Military Medical University	CHINA	0.12	The University of Texas Health Science Center at Houston	USA

UNITED STATES OF AMERICA, ANNALS OF INTERNAL MEDICINE, and JOURNAL OF BIOCHEMISTRY, which are significantly influential in the field of hemorrhagic shock.

Fig. 5 presents the journal overlay map of references in the research of hemorrhagic shock, which reflects the scientific field categorization. The citing journals are listed on the left while the cited journals on the right. The citing and cited journals are connected by citation links in the direction from the citing journal to the cited journal, by which the citation paths are reflected by different colored lines that represent different citation paths. As shown in the Dual map, the citing journals mainly focused on the fields of Molecular/Biology/Immunology and Medicine/Medical/Clinical, both of which point to the cited journals of Molecular/Biology/Genetics and Health/Nursing/Medicine, with four of them forming four major citation links that have not yet given rise to a sizeable multidisciplinary cross-sectional study. By analyzing the other fields of the citing journals, it was revealed that Physics/Material/Chemistry, Veterinary/Animal/Science, Neurology/Sports/Ophthalmology, and Psychology/Education/Health may be the research directions in the future.

3.5. Analysis of author collaboration

Analysis of author collaboration revealed the core authors and the collaboration among authors. A total of 431 authors were researched, with their relationships plotted by 639 connecting lines (Fig. 6). Most of the nodes had multiple connections with several

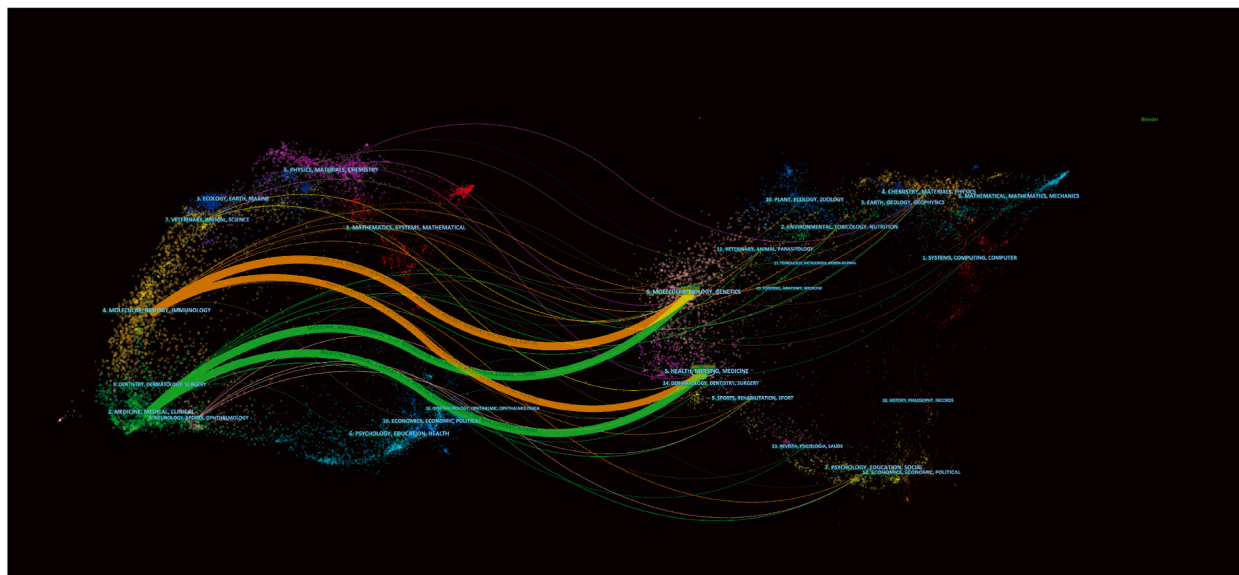


Fig. 5. Journal overlay map. The citing journals are listed on the left while the cited journals on the right, with the two sides connected by citation links.

November 26, 2023 8:42:11 PM CEST
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 Nodes Labeled: 1.1%
 Pruning: Pathfinder

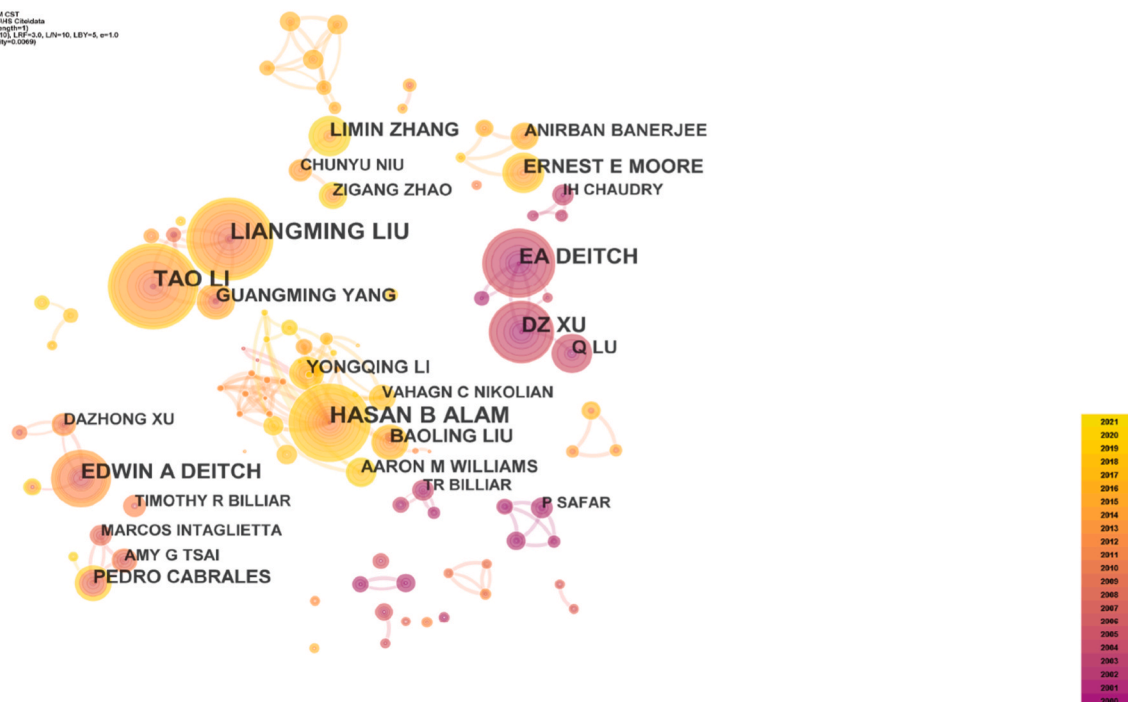


Fig. 6. Author collaboration co-occurrence. The figure shows the abbreviated names of the authors with more than 10 publications. The node size is proportional to the number of the publications, and the variations in color within the node correlates with the year of activity, with the color of purple representing an earlier active time while the color of yellow denoting an active time close to the present.

Table 4
Top 5 authors with the largest number of publications.

Rank	Counts	Author	Centrality	Country/Region
1	40	TAO LI	0	China
2	39	LIANGMING LIU	0	China
3	37	HASAN B ALAM	0.01	USA
4	32	EA DEITCH	0	USA
5	29	DZ XU	0	USA

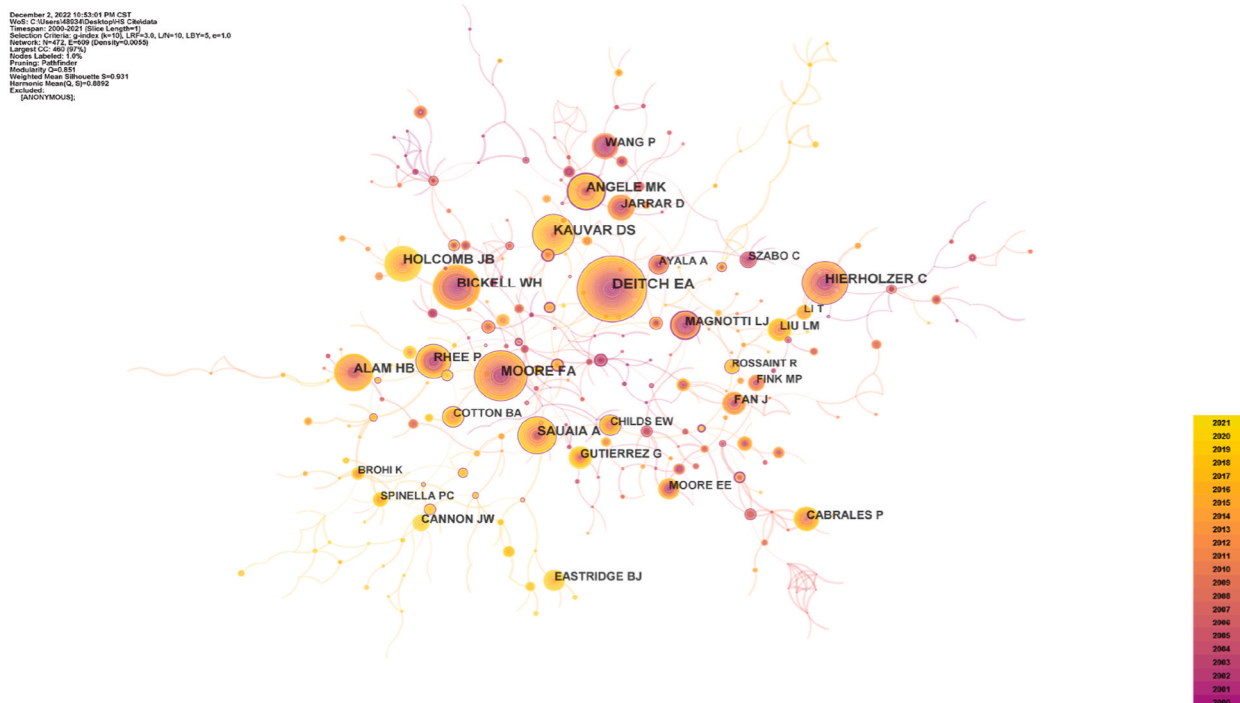


Fig. 7. Author co-citations. The graph shows the abbreviated names of the authors with more than 30 citations. The node size is proportional to the number of the citations, and the variations in color within the node correlates with the year of activity, with the color of purple representing an earlier time of activity while the color of yellow denoting an active time closer to the present. Authors with a centrality greater than 0.1 are marked by a purple circle outside the node.

authors (Table 5) included DEITCH EA, MOORE FA, KAUVAR DS, HIERHOLZER C, and BICKELL WH. The top 5 authors after centrality calculation were ANGELE MK, MAGNOTTI LJ, BOUGLE A, CHIU CJ, and LEE CC.

3.7. Keyword co-occurrence analysis

A total of 293 keywords with 394 concatenations were found based on keyword co-occurrence (Fig. 8). Table 6 shows the top 10 keywords with the highest frequency of occurrence. According to the results about frequency, “hemorrhagic shock” as a disease name undoubtedly ranked the first, with the remaining 9 keywords (“injury”, “resuscitation”, “trauma”, “model”, “activation”, “expression”, “fluid resuscitation”, “rat”, and “nitric oxide”) reflecting the major contents in the research of hemorrhagic shock over the past 22 years, of which “trauma” and “expression” had a centrality greater than 0.1.

Table 5
Top 5 authors with the largest number of cited articles and the highest centrality.

Rank	Frequency	Cited Author	Centrality	Cited Author
1	261	DEITCH EA	0.32	ANGELE MK
2	172	MOORE FA	0.25	MAGNOTTI LJ
3	152	KAUVAR DS	0.24	BOUGLE A
4	137	HIERHOLZER C	0.23	CHIU CJ
5	134	BICKELL WH	0.22	LEE CC

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 Largest CC: 293 (100%)
 Nodes Labeled: 1.0%
 Pruning: Pathfinder

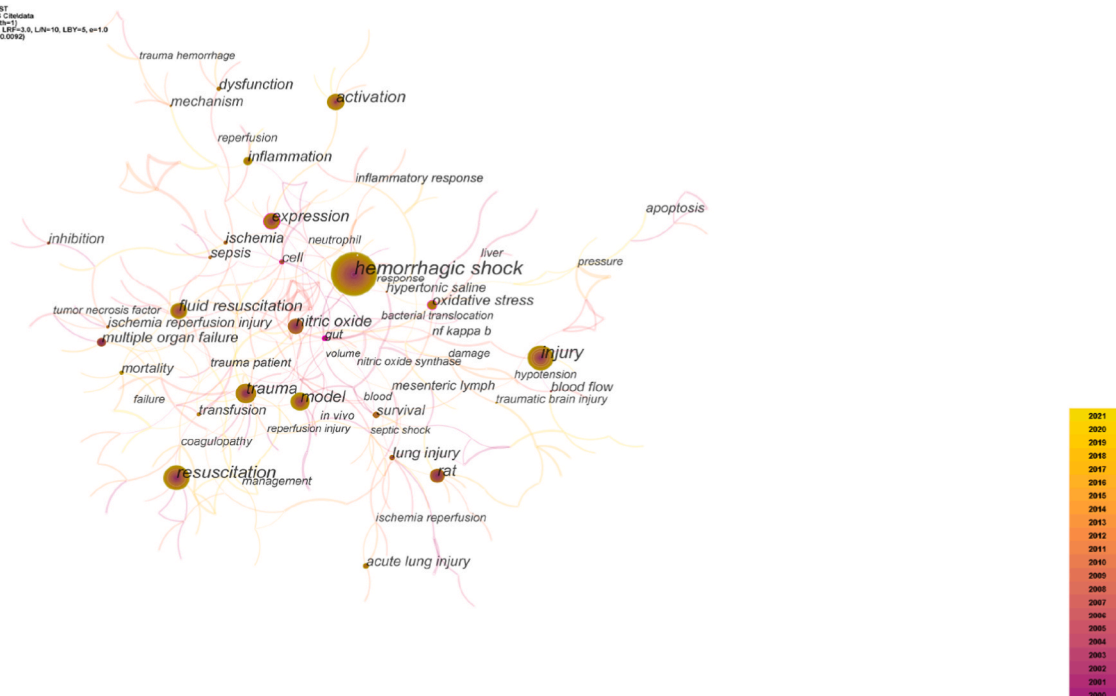


Fig. 8. Keyword co-occurrence. The figure shows the names of the keywords with a frequency greater than 30 times. The node size is proportional to the frequency of occurrence, and the variations in color within the node correlates with the year of activity, with the color of purple representing an earlier time of activity while the color of yellow denoting an active time close to the present. Keywords with a centrality greater than 0.1 are marked by a purple circle outside the node.

Table 6
 Top 10 keywords with the highest frequency of occurrence.

Rank	Frequency	Centrality	Keyword
1	725	0.06	hemorrhagic shock
2	322	0.03	injury
3	311	0.05	resuscitation
4	243	0.2	trauma
5	214	0.06	model
6	204	0.07	activation
7	190	0.29	expression
8	187	0.02	fluid resuscitation
9	174	0.09	rat
10	171	0.04	nitric oxide

3.8. Keyword time zone map

The keyword time zone map depicts the changes in keywords in different periods, so it facilitated our understanding of the research hotspots and their evolutions from the perspective of time. The top 3 keywords were selected based on the count value for each individual year to draw the keyword time zone map. As shown in Fig. 9, no obvious dividing points nor changes were spotted in the research direction of hemorrhagic shock; basically, the research hotspots in each year all centered on the 3 aspects of etiology, pathology and treatment, indicating that the current research on hemorrhagic shock is still comprehensive, multidimensional and in-depth, which contributes to a comprehensive understanding of this disease. In the meanwhile, it should be noted that the emergence of the expression “fresh frozen plasma” in 2009 implies the rise of component blood resuscitation, and the emergence of the expression “damage control resuscitation” in 2015 has come as a more recognized principle for resuscitation at present.

3.9. Keyword clustering analysis

Keyword clustering referred to an interconnected network of clusters formed by keywords involving similar research topics, and the connotations behind each cluster were identified by the titles used at a high frequency in respective containing articles. The clustering results on the keywords of hemorrhagic shock are shown in Fig. 10. A total of 16 clusters (Table 7) were obtained, mainly covering

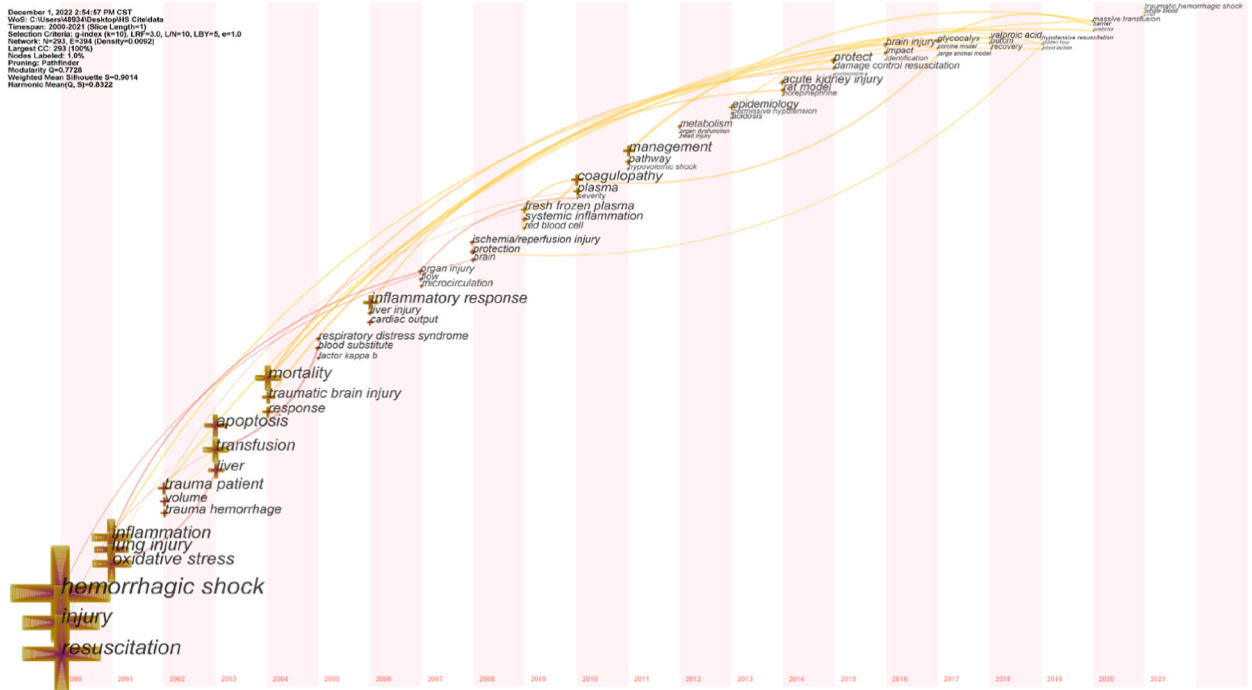


Fig. 9. Keyword time zone map. The top 3 keywords in ranking per year are selected according to the count value. The node size is proportional to the count value.

“traumatic brain injury”, “fresh frozen plasma”, “bacterial translocation”, “hemorrhagic shock”, “uncontrolled hemorrhage, etc. In combination with the timeline graph (Fig. 11), it was found that #0 traumatic brain injury, #5 activation, #7 mortality, and #12 trauma have already emerged as a research topic over the past 22 years, while the research on #13 arginine vasopressin started in a later period than the other clusters.

3.10. Burst analysis

Burst analysis was a useful method for discovery of hot terms receiving special attention from relevant scientific communities over a certain period of time. The burst analysis in this study involves such elements as the study subject, the strength value, the first appearance year, the burst start year, the burst end year, and the timeline. The timeline is presented in gray, green, and red; the color of gray indicates that no relevant research has appeared in the current period, the color of green represents the duration of relevant research, and the color of red denotes the period for the outbreak of relevant research.

The burst analysis of institutions, cited journals, authors, and keywords is presented in the end of this paper (Fig. 12). Harvard University had the largest strength value among all the institutions, while University of New Jersey had the longest burst duration (Fig. 12a). Journal of Trauma and Acute Care Surgery exhibited the highest strength value among all the cited journals (Fig. 12b). In terms of the authors, DZ XU, who has published excellent articles, had the largest strength value (11.75), while HASAN B ALAM had the longest burst duration (Fig. 12c). According to the burst analysis of keywords, through “gut” was rated with the largest strength value, its burst duration ended in 2005 (Fig. 12d). In addition, “transfusion” has appeared as a new popular keyword since 2017 (Fig. 12d).

4. Discussion

Bibliometric research can help us quickly grasp research hotspots and trends, but the selection of time span is a delicate issue. A shorter time span can provide a more precise reflection of current research dynamics, but it may result in information gaps, leading to incomplete research findings. A longer time span can incorporate earlier literature, but it can increase the complexity of the data and blur the current research focus and trends. Considering the existing literature review articles, we believe that a time span of approximately 20 years is an appropriate research interval [15,20]. Within this time frame, the quantity of research literature is sufficiently abundant to provide a comprehensive understanding of the field of hemorrhagic shock without altering the overall trends.

Citespace was used to perform the bibliometric analysis of the studies on hemorrhagic shock that had been included in the WOS core set between 2000 and 2021. This is an attempt to fill a research gap in this area. The results of the bibliometric analysis were categorized as the general information, the research hotspots, and the research trends, respectively.

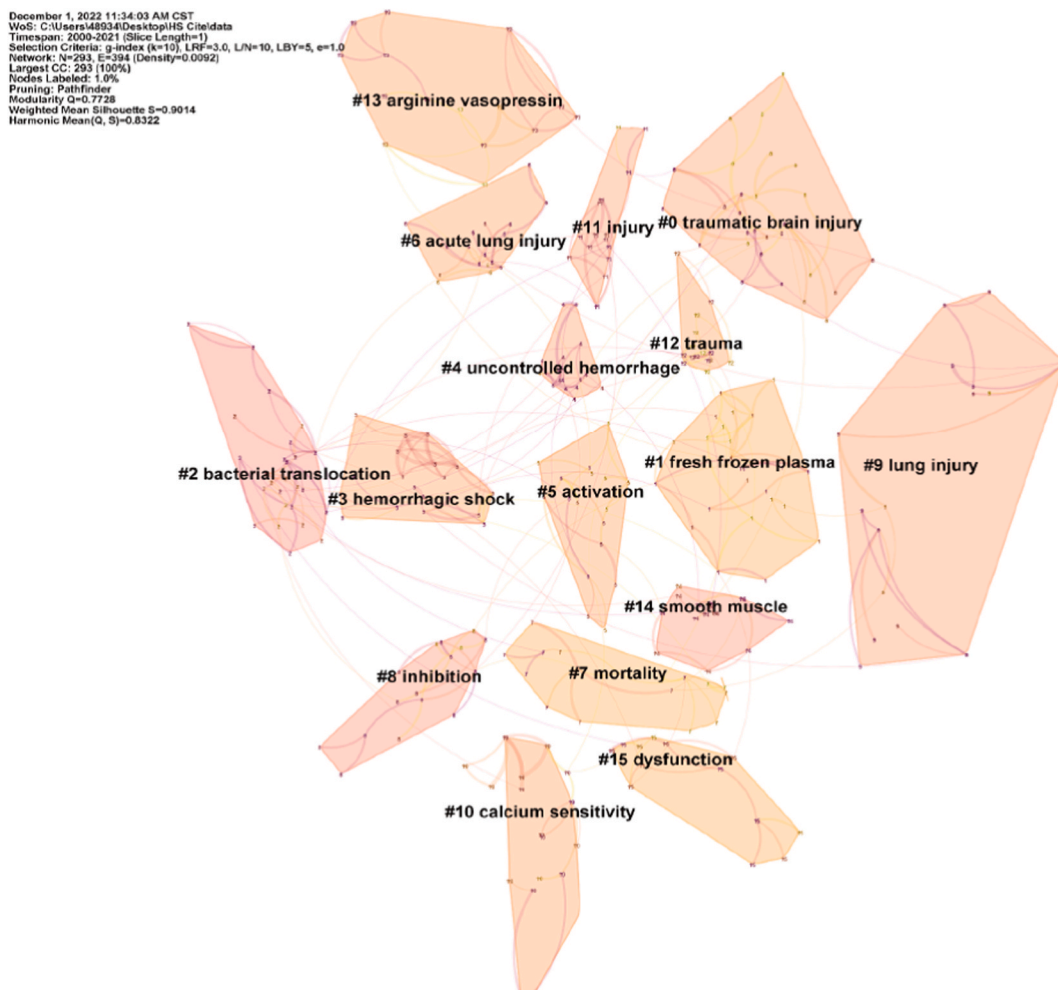


Fig. 10. Keyword clustering. The cluster names are marked in black, and the cluster numbers are marked in increasing order from 0. A smaller number of clusters indicates the inclusion of more articles.

4.1. General information

A large number of articles on hemorrhagic shock have been published worldwide. Although the past decade has witnessed no significant rise in the number of the publications in this regard, a quadratic function fitted curve to the cumulative number of the publications indicated that research in this area will grow faster in the future. In the United States, while cardiovascular disease remains the leading cause of death [3]. However, when age is taken into account, it is observed that trauma-induced hemorrhagic shock becomes the primary cause of mortality among individuals aged 46 and below [4]. Consequently, there has been a growing focus on hemorrhagic shock. Increasingly, people recognize the significance of understanding and addressing hemorrhagic shock, leading to a substantial body of research and publications in this field.

In terms of individual countries, the United States takes the lead absolutely in the research of hemorrhagic shock for a great number of publications and a high score in centrality. Despite its second place in the number of publications, China was rated with a low centrality, and the quality and influence of Chinese articles need to be further improved. China is the only developing country among the top 5 countries/regions with the highest publications and centrality, while the rest are all developed countries/regions. This indicated that the developed countries/regions are more advanced in the research in this regard, which may be attributed to the fact that the developed countries/regions have access to more research funds and richer medical resources, so they can carry out more cutting-edge clinical and basic research.

From the perspective of institutions, the top 4 of the 5 institutions with the highest number of posts all come from the United States. More impressively, even all the top 5 institutions with the highest centrality come from the United States, too. University of Pittsburgh leads the way in terms of the number of publications, with its most influential article in the research of hemorrhagic shock—*Prehospital Plasma during Air Medical Transport in Trauma Patients at Risk for Hemorrhagic Shock*, a clinical cohort study that demonstrates a significant improvement in mortality reduction when plasma is given prehospitally to patients in hemorrhagic shock (23.2% vs. 33.0%;



Fig. 11. Keyword clustering timeline.

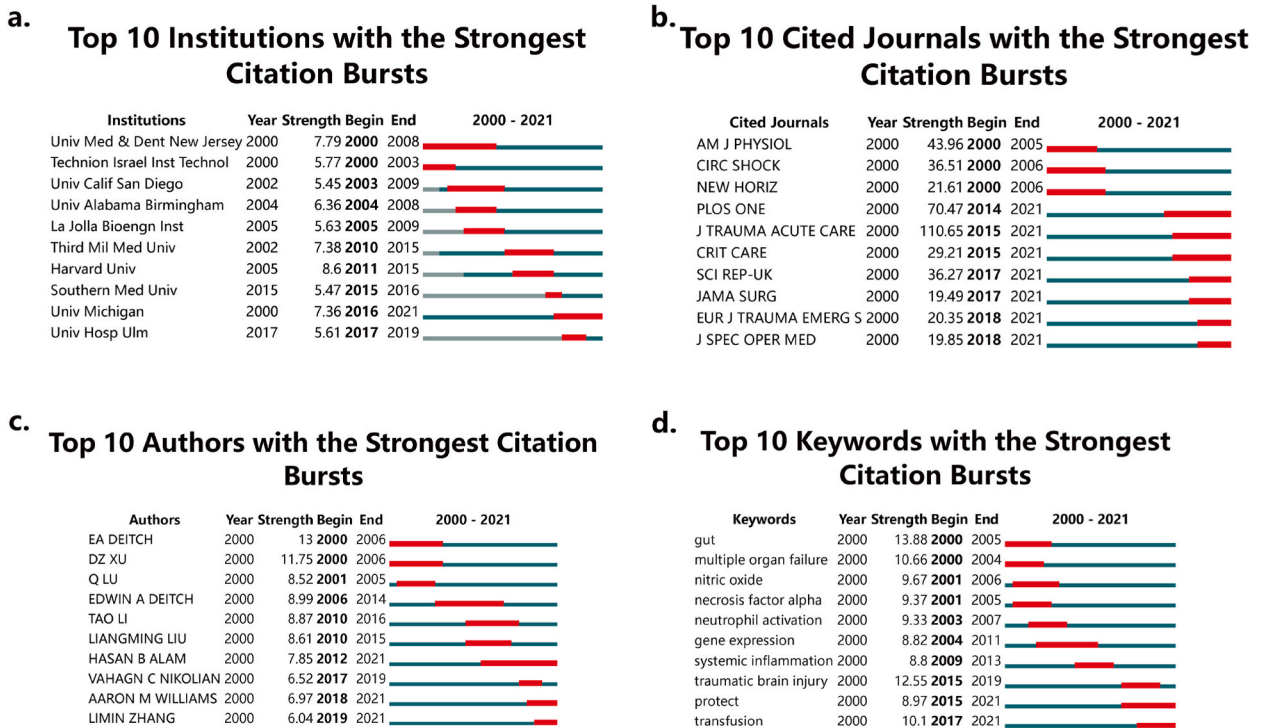


Fig. 12. Burst analysis. (a) Burst analysis of institutions; (b) Burst analysis of cited journals; (c) Burst analysis of authors; and (d) Burst analysis of keywords. The timeline of the burst-time in gray indicates that no relevant studies have appeared in the current period, the timeline in green represents the duration of relevant studies, and the timeline in red denotes the study period of the burst of relevant studies.

difference, -9.8% ; 95% confidence interval, -18.6 to -1.0% ; $p = 0.03$) [21]—published in *New England Journal*. However, University of Pittsburgh has fewer partnerships with other institutions. University of Medicine and Dentistry of New Jersey, enjoying the second place among institutional publications, focuses on the research of intestinal barrier dysfunction, lung injury, and inflammatory pathway activation induced by hemorrhagic shock [22–26]. University of California San Diego, the third-ranked institution in this regard, has participated in a study focusing more on the effects of different resuscitation treatments on hemorrhagic shock, in addition to its participation in the evaluation of such resuscitation solutions as polyethylene glycol-modified human hemoglobin (MalPEG-Hb) and Hypertonic saline in animals. As revealed in the articles published in its name, MalPEG-Hb improves microvascular blood flow as well as oxygen transport [27], and Hypertonic saline reduces inflammatory responses and apoptosis despite its failure in decreasing mortality in shocked mice [28,29]. In terms of clinical trials, University of California San Diego is participating in a multicenter randomized double-blind trial for evaluation of the efficacy of human polymerized hemoglobin (PolyHeme). This trial is the first of its kind to assess the survival of the patients initiated on resuscitation with a hemoglobin-based oxygen carrier at the scene of injury, exhibiting more adverse effects of PolyHeme [30].

An analysis of the authors revealed that Chinese and American authors still enjoy a predominant position, as evidenced by the constitution of the core group of authors centering on them. TAO LI and LIANGMING LIU, who collaborate with each other more frequently, made the first assertion on optimal resuscitation of blood pressure after uncontrolled hemorrhagic shock in rats, discovered the beneficial effects from appropriate lowering of body temperature during shock, and revealed the role of Rho kinase in improving vascular responsiveness by modulating vascular calcium sensitivity after hemorrhagic shock [31–33]. One of HASAN B ALAM's classic studies is dedicated to the use of the Yorkshire pig model for traumatic brain injury and hemorrhagic shock to explore the protective effects of mesenchymal stem cell-derived exosomes on the nervous system [34]; it is due to this model that the use of fresh frozen plasma in reducing brain injury and brain edema has identified [35]. Based on a comprehensive analysis of the publications by HASAN B ALAM, this author mainly focuses on the following three areas as his research hotspots [34–37]: resuscitation of hemorrhagic shock in large animals, combination of hemorrhagic shock and traumatic brain injury, and exosome treatment of hemorrhagic shock.

Observing the research activity of countries, institutions, and authors, it is evident that institutions and researchers from developed countries possess a notable research advantage. This can be attributed to the substantial research funding invested by these developed countries in the field of scientific research. The allocation of funding tends to favor institutions and individuals with higher productivity, stimulating them to produce more and higher-quality articles. This phenomenon, known as the Matthew effect, perpetuates their leading position in the field. Additionally, frequent and close collaborations among universities in the United States, possibly based on regional and language affiliations, have formed collaborative networks between institutions. Scientists may benefit from these collaborations, resulting in increased quantity and quality of scientific output. While China has experienced a significant increase in scientific output with increased investments, the quality of articles may be compromised due to potential issues arising from improper allocation strategies [38–41].

4.2. Research hotspots

The research hotspots associated with hemorrhagic shock were mainly derived from the analysis of keywords. Firstly, the keyword co-occurrence analysis was interpreted from the following three perspectives: etiology, pathophysiology, and treatment.

In terms of etiology, many causes can induce hemorrhagic shock, among which “injury” and “trauma” are considered the same type of causes. Since 30% of patients die of massive bleeding after injury [1], “injury” and “trauma” are regarded as the hotspots of concern.

The keywords including “model”, “activation”, “expression”, “rat” and “nitric oxide” were given priority to in the pathophysiological analysis. Firstly, since hemorrhagic shock is an acute and critical condition, it is more difficult for randomized controlled studies with a high level of evidence to achieve the research goals. As a result, basic studies in animals have become indispensable in the process of research, during which it is crucial to replicate animal models of hemorrhagic shock that are close to clinical conditions. Rats are commonly used as the animal model of hemorrhagic shock due to their moderate size and rich blood volume as well as easy operation of vascular cannulation and convenient monitoring of blood pressure [42]. Due to the systemic circulation of blood, which is essential for maintaining organ function, hemorrhagic shock can result in multi-organ damage involving the activation of various pathways and alterations in protein expression. Following hemorrhagic shock, pattern recognition receptors (PRRs) mediate the rapid response of the “first line of defense” innate immunity to damage-associated molecular patterns (DAMPs) and pathogen-associated molecular patterns (PAMPs), leading to inflammation activation. Extracellular cold-inducible RNA-binding protein (eCIRP), as a DAMPs, is released into the extracellular space during hemorrhagic shock, activating STING (Stimulator of IFN genes) via the TLR4/MyD88/TRIF pathway to intensify inflammation [43]. Moreover, eCIRP induces the participation of macrophages, neutrophils, and other immune cells in the inflammatory response [44]. Subsequent activation of the complement system leads to widespread release of cytokines, further exacerbating the inflammatory response. While complement activation is generally beneficial as it aids in pathogen clearance and response to danger signals, uncontrolled complement activation can lead to the occurrence of sepsis [45–47]. On the other hand, following hemorrhagic shock, activation of the complement fragment C4d can deposit on the surface of red blood cells, which may interfere with their deformability, preventing them from passing through capillaries and exacerbating tissue hypoxia. Although a corresponding increase in the release of nitric oxide, which has vasodilatory effects, occurs from red blood cells, this is still insufficient to alleviate the hypoxic condition [48,49]. The potential of nitric oxide to promote microcirculation and protect cardiac function has garnered significant attention. If exogenous nitric oxide supplementation is administered during hemorrhagic shock, it can prevent arteriolar constriction, increase functional capillary density, enhance venous return, stabilize post-shock heart rate, maintain improved hemodynamic conditions, and alleviate tissue ischemia [50,51]. Nitric oxide can also exert its effects on the lymphatic circulation system through ATP-sensitive potassium channels. This is manifested as an enhancement of early lymphatic

contractions and a reduction in late lymphatic contractions [52]. Microscopic investigations have gradually unveiled the essence of hemorrhagic shock.

Major treatments for hemorrhagic shock, which are the same as those for shock induced by other causes, rely on resuscitation or fluid resuscitation. Because of massive loss of circulating blood, resuscitation is necessary for the maintenance of vital signs. Therefore, the research of resuscitation mainly focuses on the types of resuscitation fluids, the timing of resuscitation, and the optimal blood pressure for resuscitation.

In terms of the types of resuscitation fluids, the most classic controversy lies on the choice of colloid and crystalloid fluids. In the early 1940s, the medical community recognized the key to resuscitating shock lies in restoring circulating blood volume. However, the choice of fluid for resuscitation became a controversial focal point. In military conflicts during the 20th century, the occurrence of acute renal failure (ARF) resulting from inadequate renal perfusion due to a rapid decrease in circulating blood volume caused by trauma was frequently observed. As experience with fluid resuscitation accumulated, the mortality rate of patients with acute renal failure decreased significantly. However, the emergence of adult respiratory distress syndrome (ARDS) was observed [53]. Subsequently, prospective randomized controlled trials comparing crystalloid and colloid fluid resuscitation were conducted. It was found that compared to crystalloid fluid, the use of colloid fluid resuscitation increased the mortality rate of hemorrhagic shock by 4%, with no significant difference in the occurrence of pulmonary dysfunction [54,55]. And due to the potential risk of hydroxyethyl starch causing renal failure, it has currently receded to the periphery [56]. There are also opinions suggesting that the administration of large volumes of crystalloid fluids may be harmful. Crystalloid fluids could dilute the blood, affect coagulation function, and even lead to higher mortality rates. As a result, the transfusion of blood components gradually gained popularity since the World War II [57,58]. The search for optimal blood components to achieve goals such as correcting coagulation disorders and reducing mortality rates [53, 59]. In terms of mortality rates, early observational analyses have found that prehospital administration of packed red blood cells (PRBC) and plasma is associated with lower mortality rates compared to crystalloid fluids [58]. However, correcting coagulopathy is challenging. Fresh frozen plasma has been found to be more effective than lyophilized plasma in treating coagulation dysfunction [21, 60]. Lyophilized plasma does not improve coagulation function or reduce the occurrence of complications [60,61]. Research has also shown that blood dilution has minimal effects on coagulation following trauma and hemorrhagic shock in the absence of hypothermia and acidosis [62]. In order to correct coagulation disorders, guided resuscitation based on thromboelastography (TEG) can improve coagulation and reduce the need for plasma and platelet transfusions [63]. When the restoration of coagulation function is not satisfactory with fresh frozen plasma alone, further consideration can be given to the use of combined fibrinogen supplementation [64]. Currently, researchers are actively exploring better therapeutic strategies, and we anticipate the emergence of such advancements.

In the late twentieth century, thanks to the development of uncontrolled hemorrhage models, Bickell et al. [65] successfully evaluated the effect of conventional rapid volume expansion in a large animal model of uncontrolled hemorrhagic shock for the first time, revealing that aggressive fluid resuscitation may exacerbate bleeding and increase mortality when blood loss is not effectively controlled. This conclusion is supported by several other results in animal experiments [66,67], suggesting that bleeding may be worsened if aggressive fluid resuscitation is tried prior to hemostasis. According to a prospective study by Bickell et al. [68], fluid resuscitation should be performed after hemostasis is achieved through damage control surgery (DCS) for patients with trauma-induced massive blood loss, thus revealing the sequence of hemostasis and resuscitation in treatment. Moreover, achieving faster hemostasis can significantly reduce the 30-day mortality rate, as well as the incidence of acute kidney injury (AKI), ARDS, multiple organ failure (MOF), and sepsis [69].

Optimal resuscitation blood pressure has also been a major concern in hemorrhagic shock over the past half century. The initial preference for massive fluid resuscitation to reverse massive blood loss was considered a golden standard for some time in the past, but this treatment protocol has limitations from the perspective of time. In addition, the most serious adverse consequences of excessive resuscitation, namely the “lethal triad” composed of hypothermia, acidosis and hypothermia, have been gradually recognized [5,6].

Table 7
Keyword clustering.

Cluster ID	Size	Silhouette	Terms
#0	29	0.939	traumatic brain injury
#1	27	0.765	fresh frozen plasma
#2	26	0.799	bacterial translocation
#3	19	0.941	hemorrhagic shock
#4	18	0.923	uncontrolled hemorrhage
#5	18	0.925	activation
#6	18	0.97	acute lung injury
#7	17	0.807	mortality
#8	16	0.974	inhibition
#9	16	1	lung injury
#10	16	0.965	calcium sensitivity
#11	15	0.889	injury
#12	15	0.831	trauma
#13	15	0.966	arginine vasopressin
#14	15	0.921	smooth muscle
#15	13	0.921	dysfunction

TAO LI et al. [32] were the first to investigate optimal resuscitation blood pressure in animals, and Morrison et al. [70] conducted the first prospective randomized study to reveal that controlling mean arterial pressure to 50 mmHg reduces the risk of coagulopathy and death. Alexander Tran et al. [71] performed a meta-analysis for the treatment of permissive hypotension and evaluated the primary outcomes in a total of 1158 patients, thus disclosing that permissive hypotension may have a survival benefit over conventional resuscitation and may also reduce blood loss as well as blood product utilization.

Summarizations were drawn for the keyword clustering analysis from the following three perspectives: 1) etiology and hemorrhagic shock, 2) pathophysiology and complication, and 3) treatment and outcome.

Etiology and hemorrhagic shock: #0traumatic brain injury, #3hemorrhagic shock, #4uncontrolled hemorrhage, #11injury, and #12trauma (Fig. 11, Table 7). The aforesaid keyword clusters were used to study hemorrhagic shock from an etiological perspective. Based on previous studies, it was revealed that trauma is one of the main etiologies for hemorrhagic shock, which was consistent with the results of #11 and #12. In combination with the analysis of #0, it was found that cranial trauma combined with hemorrhagic shock appears to be the focus of attention, because hemorrhagic shock can further exacerbate neuronal death if it occurs after cranial trauma [72]. #4 is mainly involved for the type of hemorrhagic shock animal modeling. The current animal models are divided into the controlled hemorrhagic shock model and the uncontrolled hemorrhagic shock model. With the controlled hemorrhagic shock model, shock blood pressure and blood loss can be controlled, respectively, and the degree of shock can be controlled artificially; on top of that, the model is highly reproducible. The uncontrolled hemorrhagic shock model, which is mainly caused by uncontrolled massive blood loss to the shock state through blunt force injury [73], is closer to clinical conditions despite poor reproducibility of the model.

Pathophysiological and complication studies: #2bacterial translocation, #5activation, #6acute lung injury, #8inhibition, #9lung injury, #10calcium sensitivity, #14smooth muscle, and #15dysfunction (Fig. 11, Table 7). These keyword clusters are involved mainly in pathophysiological changes and complications associated with hemorrhagic shock. Bacterial translocation is defined as the process by which intestinal bacteria and/or their products spread from the intestinal lumen to extraintestinal sites through the intestinal barrier. This includes mesenteric lymph nodes (MLN), systemic circulation, and distant organs [74]. Due to ischemia of intestinal mucosa in hemorrhagic shock, the dysfunction of the intestinal barrier causes the bacteria to translocate to the peripheral lymph nodes or into the blood, leading to inflammatory responses as a result [75,76]. Current research indicates that C-peptide can protect the intestinal barrier and prevent bacterial translocation [77]. Activation of Toll-like receptor 4 (TLR4) in intestinal epithelial cells following hemorrhagic shock leads to acute lung injury [26]. Activation of TLR4 in the intestinal epithelium following hemorrhagic shock leads to increased endoplasmic reticulum (ER) stress, intestinal cell apoptosis, and release of high mobility group box 1 (HMGB1). This, in turn, results in pulmonary cell apoptosis, elevated levels of myeloperoxidase (MPO), monocyte chemoattractant protein 1 (MCP1), and interleukin 6 (IL-6) in the lungs, ultimately leading to acute lung injury. The internalization of the tight junction protein ZO-1 in the pulmonary epithelium may be associated with HMGB1 signaling in the intestinal epithelium [78]. Despite resuscitative treatments, intestinal barrier dysfunction persists, accompanied by significant elevation of HMGB1 levels, increased lung MPO activity, and pulmonary protein leakage. These findings suggest that the occurrence of acute lung injury cannot be prevented [77]. The combination of the two clusters of #5 and #8 also led to the finding of such keywords as activation pathway, inflammation response, inhibition of activated protein kinase, and HO-1 on the timeline (Fig. 11), indicating that the mainstream studies focus on the changes in proteins at the molecular level, such as the inflammation and pathways in hemorrhagic shock. Studies have shown that trauma can induce a “genomic storm,” leading to alterations in at least 80% of cellular functions and pathways [79]. Changes in signaling pathways and inflammatory responses ultimately lead to organ dysfunction. Therefore, the primary objective of pathway research is to prevent organ dysfunction. For example, inhibiting the activation of I κ B kinase, Bruton’s tyrosine kinase, and the JAK/STAT pathway can alleviate organ damage and functional impairment associated with hemorrhagic shock [80–82]. Hemorrhagic shock is characterized by a typical imbalance between oxygen supply and demand [81]. The use of antioxidants can alleviate oxidative stress damage during the resuscitation phase of hemorrhagic shock [83]. Heme oxygenase-1 (HO-1), as an antioxidant, can mitigate the damage caused by hemorrhagic shock [84]. Specifically, upregulation of HO-1 can prevent apoptosis of intestinal mucosal epithelial cells following hemorrhagic shock [85]. Early induction of HO-1 can reduce post-hemorrhagic shock inflammation, decrease the amount of resuscitation fluid required, and alleviate pulmonary edema [86]. Conversely, inhibiting HO-1 expression exacerbates tissue inflammation and cell apoptosis [87]. #10calcium sensitivity is a major manifestation in the contractile function of the vascular smooth muscle, which is desensitized to calcium in hemorrhagic shock; in addition, it is considered a major cause of intractable hypotension [88]. If hemorrhagic shock is accompanied by hypocalcemia, it indicates a lower survival rate, as well as significant blood transfusion requirements and coagulation disorders [89,90]. The cause of calcium desensitization may be related to mesenteric lymphatic reflux [91]. Mesenteric lymphatic drainage can restore calcium sensitivity [92]. #15dysfunction mainly refers to various dysfunctions caused by hemorrhagic shock, such as mitochondrial dysfunction [93], liver and kidney dysfunction [94], and multi-organ failure in severe cases [95]. This is associated with bacterial translocation, activation of inflammatory responses, and ischemia-reperfusion injury during the process of hemorrhagic shock [1,78]. How to mitigate organ dysfunction is currently a focus in the treatment of hemorrhagic shock. As mentioned earlier, ensuring intestinal barrier function, reducing inflammatory responses, and implementing antioxidant therapy are viable approaches.

Treatment and outcome studies: #1fresh frozen plasma, #7mortality, and #13arginine vasopressin (Fig. 11, Table 7). #1fresh frozen plasma is one of the resuscitation fluids for patients in shock and a hotspot in relevant research. As shown in Fig. 11, coagulopathy and acidosis were spotted on the timeline of #1, both of which are manifestations of lethal triad. As a blood product as well as a colloid fluid, fresh frozen plasma can improve coagulation and reduce acidosis in patients [96,97]. #13 The administration of vasopressin as an adjunctive therapy aims primarily to maintain blood pressure and correct the state of shock. However, it is regrettable that elevated blood pressure in patients with hemorrhagic shock may be associated with increased mortality [98,99]. Although some studies have indicated that vasopressin has the advantage of reducing the use of blood products during resuscitation

[100], such conclusions have also been questioned by peers. The key point lies in the variability of patient severity among different studies [101]. In terms of reducing mortality, vasopressin is not considered an ideal drug. #7mortality, which serves as the major outcome variable in various clinical studies, is like a measurement of the effectiveness of treatments for hemorrhagic shock. As a life-threatening disease, the greatest harm of hemorrhagic shock is its potential to cause patient mortality. Therefore, our primary goal in treatment is to reduce the mortality rate. The main outcome of numerous clinical studies focuses on the changes in mortality rate [8, 102].

In summary, resuscitation for hemorrhagic shock should be conducted with the following three aspects taken into consideration: timing, resuscitation fluid, and optimal blood pressure, in order to reduce the occurrence of the lethal triad. Previously, DCS was a commonly used resuscitation strategy, which involved three steps: abbreviated surgical control of bleeding and contamination, intensive care unit (ICU) resuscitation, and planned definitive surgery. This approach aimed to correct acidosis, prevent hypothermia, but did not address the issue of coagulopathy [103]. DCR has become the consensus for treatment at present, and the major principles of DCR include minimization of crystalloid, permissive hypotension, transfusion of a balanced ratio of blood products, and goal-directed correction of coagulopathy [104]. DCR is a comprehensive management approach aimed at reducing the occurrence of the lethal triad, with a primary focus on correcting coagulopathy [105]. DCR involves interventions targeting coagulation throughout the disease process. It not only investigates the efficacy of resuscitation with different ratios of blood components [8] but also utilizes agents such as tranexamic acid [106] and coagulation factor concentrates [107] to improve coagulation. The implementation of DCR provides patients with a more comprehensive treatment approach, undoubtedly enhancing survival rates [108].

4.3. Research trends

1) Institutions: As revealed by burst analysis, Harvard University enjoys a key position among all the institutions for a strength value of 8.6, which was consistent with the ranking of centrality in the institutional cooperation analysis. In terms of the research trends in the future, University of Michigan witnessed the advent of its burst-time in 2016 and its continuation until 2021. Moreover, with a strength value of 7.36, University of Michigan is significantly influential; therefore, it is reasonable to assume that it will continue to make outstanding contributions in the field of hemorrhagic shock in the future. 2) Cited Journals: Journal of Trauma and Acute Care Surgery was rated with a strength value of 110.65, verifying its ultimate importance among the cited journals. Since the burst-time duration of this journal began in 2015 and ended in 2021, its publication of high-quality articles on hemorrhagic shock will continue at high odds for some time in the future. 3) Authors: There is no denying that DZ XU, whose strength value was rated as 11.75, has published superb articles in the field of hemorrhagic shock; however, his burst-time duration only lasted between 2000 and 2003. In spite of the blue color in the timeline after 2003 for this author, the attention to him is not as much as in early years. HASAN B ALAM, AARON M WILLIAMS, and LIMIN ZHANG show a stronger research potential according to the timeline, especially HASAN B ALAM who is the most prominent for the longest burst-time duration. In addition, the three authors also exhibit a potential to publish high-quality articles in the future, so they deserve high attention from the academics. 4) Keywords: “Transfusion” has risen as a new popular keyword since 2017. “Protect” and “transfusion” are the keywords still in the red time period, so the two areas are worth exploring in future research. However, the burst-time duration of all keywords have lasted for a short period of only 4–7 years in general, indicating the rapid changes in research hotspots in the research of hemorrhagic shock.

5. Significance and limitations

Bibliometric analysis plays a significant role in understanding the development of research fields and identifying relationships within the research domain. Through Citespace bibliometric analysis, we can gain insights into the research dynamics and trends in the field of hemorrhagic shock. This helps uncover major research directions, hot topics, and knowledge gaps, providing guidance for further investigations. Citespace visualizes the academic network within the research field, showcasing collaboration relationships among researchers, key authors, and seminal publications. This facilitates the establishment of research collaboration networks, promotes knowledge exchange and cooperation, and provides valuable information for scholars and decision-makers in the field. For junior researchers, reading articles from highly cited authors and journals (Tables 3 and 5) can aid in rapidly grasping the major achievements in the field of hemorrhagic shock. Senior researchers can choose to collaborate with authoritative institutions and authors (Tables 2, 4 and 5) to foster disciplinary advancements. Targeting high-impact journals (Table 3) may be a primary goal for manuscript submissions. Encouragingly, Citespace also facilitates the process of evidence-based medicine (EBM), enabling the more efficient identification of best evidence, benefiting EBM practitioners and clinical physicians [109].

Our study also has limitations. Firstly, there are limitations regarding the databases used. Since Citespace relies on the constraints of scientific measurement, it is unable to perform integrated analysis across multiple databases [110]. Citespace software is highly compatible with the WOS database [111]. WOS has been widely accepted by researchers and is considered a common tool for retrieval and bibliometric analysis due to its high-quality and comprehensive data. Therefore, like many previous studies in the field of bibliometrics, we selected the WOS database as our data source [20]. Secondly, there are limitations in the analysis results. We conducted a macroscopic evaluation of the included literature, which does not allow for an assessment of the individual value of each article. Therefore, bibliometric analysis cannot replace systematic retrieval [112]. Furthermore, the current state of bibliometric analysis is only temporary, as more research is published, further statistical analysis of bibliometrics related to hemorrhagic shock will be required.

6. Conclusion

In summary, the publication volume on hemorrhagic shock is expected to continue increasing in the future. The United States remains a core country in this field, exerting significant influence. China is also actively involved in researching and expanding the impact of hemorrhagic shock studies. Pittsburgh University holds a prominent position among institutions, and the University of Michigan is gradually leading the development of the field. The journal *SHOCK* has published a substantial number of influential articles in this area, while *Journal of Trauma and Acute Care Surgery* may publish higher-quality articles in the future. The published research has revealed the pathophysiological processes of various pathway activations during hemorrhagic shock and identified the advantages of blood component resuscitation. The future focus of research is likely to remain on treatment strategies centered around DCR.

Author contribution statement

Haoran Ye: Conceived and designed the experiments; Performed the experiments; Analyzed and interpreted the data; Contributed reagents, materials, analysis tools or data; Wrote the paper. Yuan Du, Yueting Jin: Performed the experiments; Analyzed and interpreted the data. Fangyu Liu: Analyzed and interpreted the data. Yuhong Guo, Shasha He: Conceived and designed the experiments; Wrote the paper.

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Data availability statement

Data included in article/supplementary material/referenced in article.

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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