Research Article

A Bibliometric Analysis for Global Trends and Full View of the Autophagy in Ischemic Stroke from 2006 to 2022

Lijuan Song,[1,2,3] Yige Wu,[1] Shuwen Yuan,[1] Kexin Liu,[1] Qing Wang,[1] Dong Ma,[3] and Cungen Ma [iD] [1,2]

[1]*The Key Research Laboratory of Benefiting Qi for Acting Blood Circulation Method to Treat Multiple Sclerosis of State Administration of Traditional Chinese Medicine/Research Center of Neurobiology, Shanxi University of Chinese Medicine, Jinzhong 030619, China*
[2]*Department of Physiology, Shanxi Medical University, Taiyuan 030001, China*
[3]*Department of Neurosurgery, Sinopharm Tongmei General Hospital, Datong 037003, China*

Correspondence should be addressed to Cungen Ma; macungen@sxtcm.edu.cn

Lijuan Song and Yige Wu contributed equally to this work.

Autophagy plays a key role in ischemic stroke, but its mechanism remains to be elucidated. In order to explore the effect of autophagy on ischemic stroke, bibliometric analysis and view tools are used to identify the directions of the global research trends and construct full view of the autophagy in ischemic stroke from 2006 to 2022. The research hotspots of autophagy related to ischemic stroke are visually analyzed and generated various visual maps to display publications, authors, sources, countries, organizations, and keywords. By bibliometric analysis, it can be seen that the investigations of autophagy in ischemic stroke is focused on both brain injury and neuroprotection. The impact of a variety of inflammatory factors and signaling pathways on autophagy following an ischemic stroke is also studied. Autophagy plays an important role in all phases of ischemic stroke. It is of great significance to guide the development of treatment plans for ischemic stroke.

1. Introduction

Ischemic stroke is a common disease in older adults, and it mostly occurs due to embolization of an artery that supplies blood to a particular area of the brain [1, 2]. Due to the high incidence of common chronic diseases, such as hypertension and diabetes [3, 4], more attention should be paid to the rapid development of the aging population. Ischemic stroke is the third leading cause of death and disability in the world [5], and it causes a significant economic burden to society due to the gradual increase in global expenditure on related medical and health care services and drug expenses [6]. As a regulatory mechanism of cellular component degradation and circulation, autophagy can quickly respond to energy supply and malnutrition [7–9] and promote clearance of aggregated proteins and damaged organelles under stress [10, 11]. Autophagy plays a key role in ischemic stroke because it is involved in the regulation of oxidative metabolic function and cell death after ischemic stroke, and a variety of autophagy-related signal pathways and cytokines are closely related to the damage and repair after ischemic stroke [12–14]. There is no consensus on the role of autophagy in ischemic stroke, and research on whether autophagy is beneficial or harmful to ischemic stroke is also deepening, which has attracted widespread interest in clarifying the dual role of autophagy after ischemic stroke [15].

The effects of autophagy in ischemic stroke have attracted the extensive attention of researchers, which is reflected by the increase in the number of relevant publications. In terms of the current research hot spots, work on the role of autophagy in ischemic stroke focuses on specific signal receptors,

signal pathways, and cytokines. Therefore, assessing the role of autophagy in ischemic stroke through bibliometric analysis is an effective means to guide the trend and direction of related fields.

As a tool widely used for qualitative and quantitative analysis of global scientific literature, bibliometric analysis can effectively show the knowledge structure and possible development trend of specific fields through information visualization [16–18]. Bibliometric analysis has been performed in the research field of nervous system diseases [19, 20]. However, the specific mechanism of autophagy in ischemic stroke is still unknown [21], and the role of autophagy in ischemic stroke cannot be ignored. Previous studies have not reported the overall research status of autophagy and ischemic stroke around the world. As a result, emerging researchers interested in this field have a long research cycle, uneven quality of relevant scientific research articles, and confusion about research direction and current research hot spots. These researchers need to spend a substantial amount of time reading and understanding the relevant research. Therefore, bibliometric analysis is helpful to sort out important, effective, and meaningful information from a core database to guide scientific research [22]. In the first bibliometric study of autophagy in the process of ischemic stroke, we analyzed the relationship between authors and publications in terms of ischemic stroke type, year of citation, and other aspects. This is helpful to form a correct understanding of the specific mechanism and role of autophagy in ischemic stroke. Our bibliometric analysis can provide researchers with a better understanding of autophagy in ischemic stroke by exploring past and present work, and it may assist in pointing out effective hot spots and directions for future research.

At present, the mechanism of autophagy in ischemic stroke has been initially expressed and described, but the effect of autophagy itself has not been well recognized, and the evaluation of autophagy is often two-sided. The dynamic changes brought by autophagy in ischemic stroke are a complex process, which still needs a substantial amount of scientific research and exploration. How to correctly apply autophagy, target the autophagy process, and influence the development and outcome of ischemic stroke is still a great challenge for researchers. In view of the complexity of the effect of autophagy on ischemic stroke and a large number of problems to be solved, we hope to provide a reference for possible hot spots and current and future trends for current researchers in related fields through this literature econometric analysis, and at the same time, we hope to inspire useful thinking for new members of this field.

The rest of this paper is organized as follows: Section 2 discusses related work, followed by the materials and methods designed in Section 3. Section 4 shows the analysis results, and Section 5 concludes the paper with summary and future research directions.

2. Related Work

Since 2006, when a small number of researchers focused on exploring the effect of autophagy on ischemic stroke [23, 24], the number of related studies has been increasing, and more and more researchers have been involved in work in this field. The number of published papers has also increased rapidly during the past decade and will likely continue to increase in the future. To visualize the knowledge structure, we use bibliometric analysis and view tools in order to study the effect of autophagy in ischemic stroke. The approach allows us to identify the directions of the global research trends, which is an effective means of knowledge management for researchers in the era of information explosion [25]. In the first study of the effect of autophagy on ischemic stroke by econometric analysis of the literature, we identify the current research focus and possible future research directions by revealing the number and distribution of the literature in this field, as well as the changes in contributions of authors, countries, and institutions.

Through the analysis of the publications, we show that there has been an increasing research interest in ischemic stroke and autophagy since 2006; especially after 2016, the popularity of the topic has dramatically increased, even becoming an indispensable part of research in the treatment of ischemic stroke [26]. A growing number of scientists are working in this area. This reflects the relationship between productivity and development of the discipline over the years.

Through the analysis of article types, we find that most of the hot publication types focused on articles and there are few relevant critical articles, which is an important limitation of the current literature in this field. The lack of guidance by critical articles creates difficulties for the selection of research priorities and future research directions.

Based on the cited number analysis of single articles, we find that articles from the top journals in the related fields (e.g., nature and immunity) received higher average citation numbers than those from other journals (e.g., cellular physiology and biochemistry and neural regeneration research). This may indicate that the influence of the journal itself also determines the dissemination level of an article and there are still unreasonable phenomena in the use of information.

We analyze the number of national and institutional publications using a visual map co-created by VOSviewer. Based on the generated data visualization, China and the United States represent the countries that have contributed the most to the study of the effects of autophagy in ischemic stroke. As the earliest, most invested, and most important country in this field, it is understandable that China is ahead of other countries in this field. Many influential teams come from various organizations in China and the United States, such as Shanghai Jiao Tong University, Fudan University, Zhejiang University, Harvard University, and Massachusetts General Hospital. Many scientists from China and the United States have been involved in elucidating the specific mechanisms by which autophagy affects the various stages of ischemic stroke. Many institutions from China and the United States have received preferential adjustment of resources from relevant national policies due to the increased attention to ischemic stroke research in recent years. However, the visualization also shows that although China and the United States are currently the leaders in this field and there is a close interaction between the two

countries; there is little cooperation between other countries. Thus, strengthening communication and cooperation among other countries may further promote this field of research in the future.

The knowledge mapping of keyword co-occurrence network through VOSviewer can be combined with deeper literature reading to obtain richer information [27]. The number of citations of an article can reflect the influence and dissemination of the article and indirectly also show the level of quality of the article [28]. We find that the first two articles to study the effect and role of autophagy in ischemic stroke [23, 24] are also the most frequently cited ones. Linking autophagy to oxidative stress and pathological features after ischemic stroke, or demonstrating mitochondrial fission during autophagy as a key component of early ischemic stroke, they have paved a number of possible paths for subsequent researchers. Related research has inspired thinking about the specific role of autophagy in ischemic stroke [29], extended the mechanism of mitochondria in the process of autophagy [30–32], and deepened thinking about the role of oxidative stress in ischemic stroke [33, 34]. The use of bibliometric analysis enables us to investigate the pathogenesis of diseases in a more accurate way, and the model of big data also makes it more feasible to explore future research directions and focus on specific concerns [35]. In the field of ischemic stroke and autophagy, through the econometric analysis of the literature published in the past decade, we found that both BNIP3 and LC3 are research hot spots and their interactions play a key role in non-selective autophagy after ischemic stroke. Mitochondrial BNIP3 binds to autophagosome LC3 to regulate cell death in ischemic stroke [36–38]. Mitochondrial dysfunction during ischemic stroke affects the level of autophagy, involving metabolic imbalance, oxidative stress, apoptosis, endoplasmic reticulum stress, and many other aspects, which may provide inspiration for the development of new targeted therapies for ischemic stroke [39–45]. Cellular responses to ischemic stroke are represented by autophagy, which is an adaptive mechanism [46]. Removal of damaged organelles, protein aggregates, and excess cell debris caused by ischemic stroke through autophagosome-lysosomal degradation helps to reduce cell stress [47, 48]. In this context, autophagy is an important cellular process that maintains cell homeostasis and organism survival. However, over-induced autophagy is considered harmful and plays a key role in neuronal cell death. Further studies are necessary to elucidate these issues of autophagy in cerebral ischemia.

3. Materials and Methods

3.1. Data Policy and Selection Criteria. We systematically analyzed the role of autophagy in ischemic stroke by visual analysis. The literature data of the present bibliometric study came from WOSCC (Web of Science Core Collection). In order to obtain as much literature data as possible for extensive research, we used the following search terms: "Autophagy" AND "Ischemic Stroke" OR "Ischemic Strokes" OR "Ischaemic Stroke" OR "Ischaemic Strokes" OR "Cryptogenic Stroke" OR "Cryptogenic Strokes." There were no
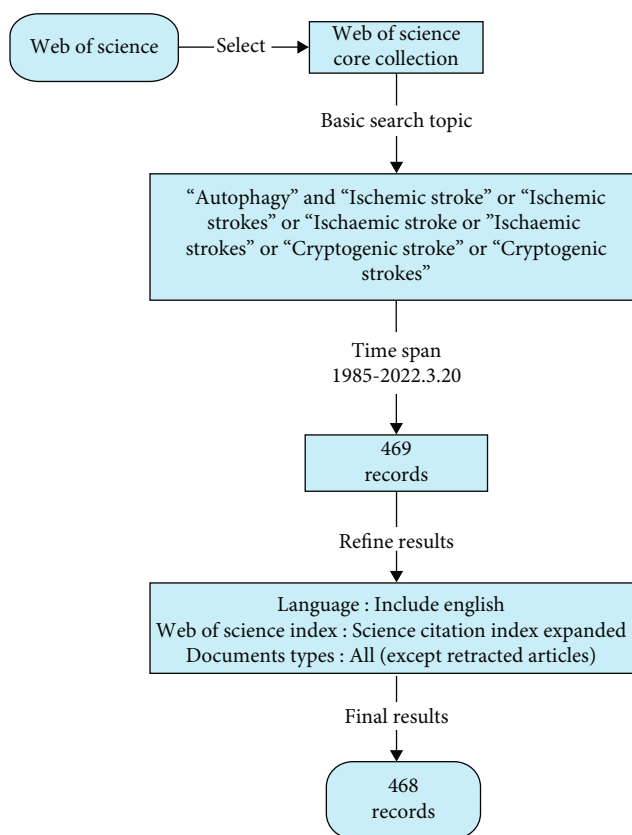

Figure 1: Search flowchart detailed steps in the identification and screening of papers.

restrictions in terms of data categories, and the literature covered the period from 2006 to March 20, 2022. According to the above criteria, we retrieved 469 articles that were limited to English in terms of language and Science Citation Index Expanded in terms of source. After excluding one retracted article, a total of 468 results were obtained. The search flowchart detailed steps in the identification and screening of papers is shown in Figure 1.

3.2. Data Analysis. Data are collated and analyzed using Microsoft Excel. GraphPad Prism 8 software is used for data plotting and statistical analysis. The results of the author, country, organization, and keyword cluster analysis are presented using VOSviewer software. In addition, we conduct data processing and visual analysis through the bibliometric analysis website (https://bibliometric.com), CiteSpace 5.8.R3, and Bibliometrix.

4. Analysis of Experimental Data

4.1. Analysis of the Number of Publications and Citations. From 2006 to March 20, 2022, a total of 468 relevant articles have been published. The time distribution of the published literature is shown in Figure 2, in which the histogram represents the number of publications per year for all retrieved articles. The line graph represents the trend of the number of publications. In addition, due to the statistical time problem in this study, the published data from 2022 are
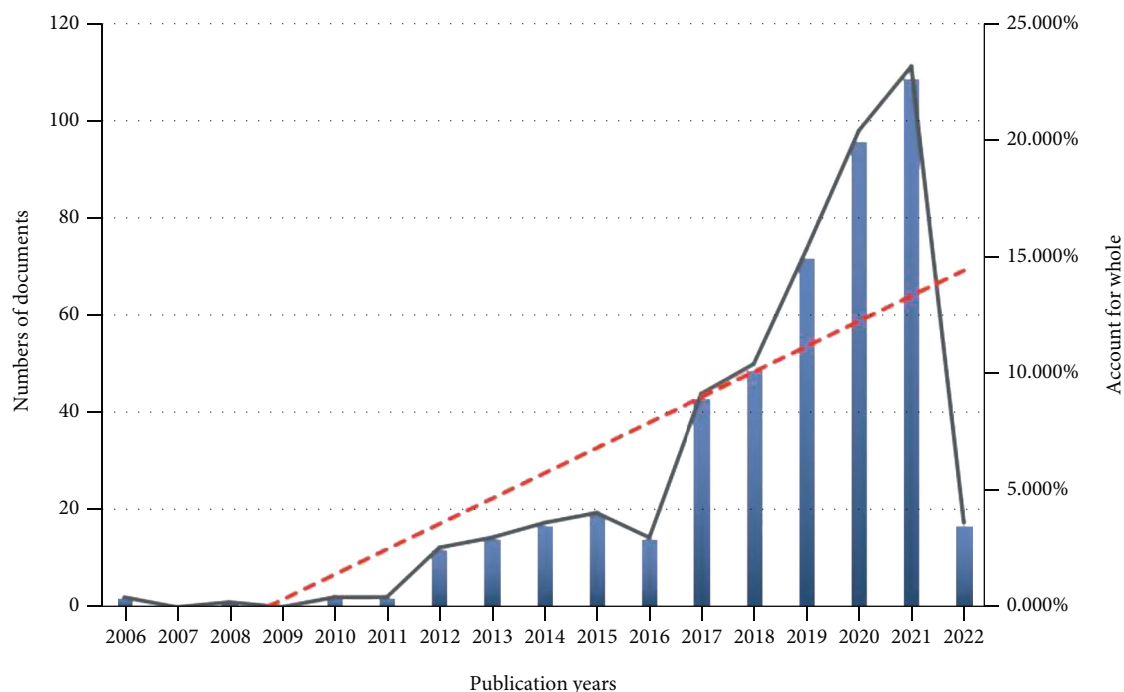
FIGURE 2: Number of articles published per year.

FIGURE 3: Number of publications in the top ten related journals.

not comprehensive; nevertheless, according to the trend in recent years, it is expected that the number of relevant articles in 2022 will keep rising as compared with previous years. The trend line shows exponential growth in the number of articles. As shown in the line chart, the number of published articles increase rapidly from 2006 ($n = 14$, 2.990%) to 2020 ($n = 109$, 23.241%), indicating that the role of autophagy in ischemic stroke has rapidly become a hot topic in the past five years, and a similar trend is expected in the future.

4.2. Analysis of the Highest Cited Articles. We conduct a citation analysis of the relevant articles, and the top 10 cited publications with high citation frequency. The number of

citations ranges from 142 to 526. In particular, the first ranking article, "Nitric oxide-induced mitochondrial fission is regulated by dynamin-related GTPases," was published in 2006 by Barsoum et al., representing the growing interest of scientists around the world in the field of neurons since earlier forerunner focused on the role of autophagy in ischemic stroke. "Oxidative stress and pathophysiology of ischemic stroke: Novel therapeutic opportunities," published by Rodrigo et al., ranked second and was cited 344 times in total. The third highest cited article, with 286 citations, is "Cerebral ischemia-hypoxia induces intravascular coagulation and autophagy" and was published by Adhami et al. in 2006. Most of the top 10 cited publications focused on oxidative stress, cytokines, and signaling pathways, reflecting
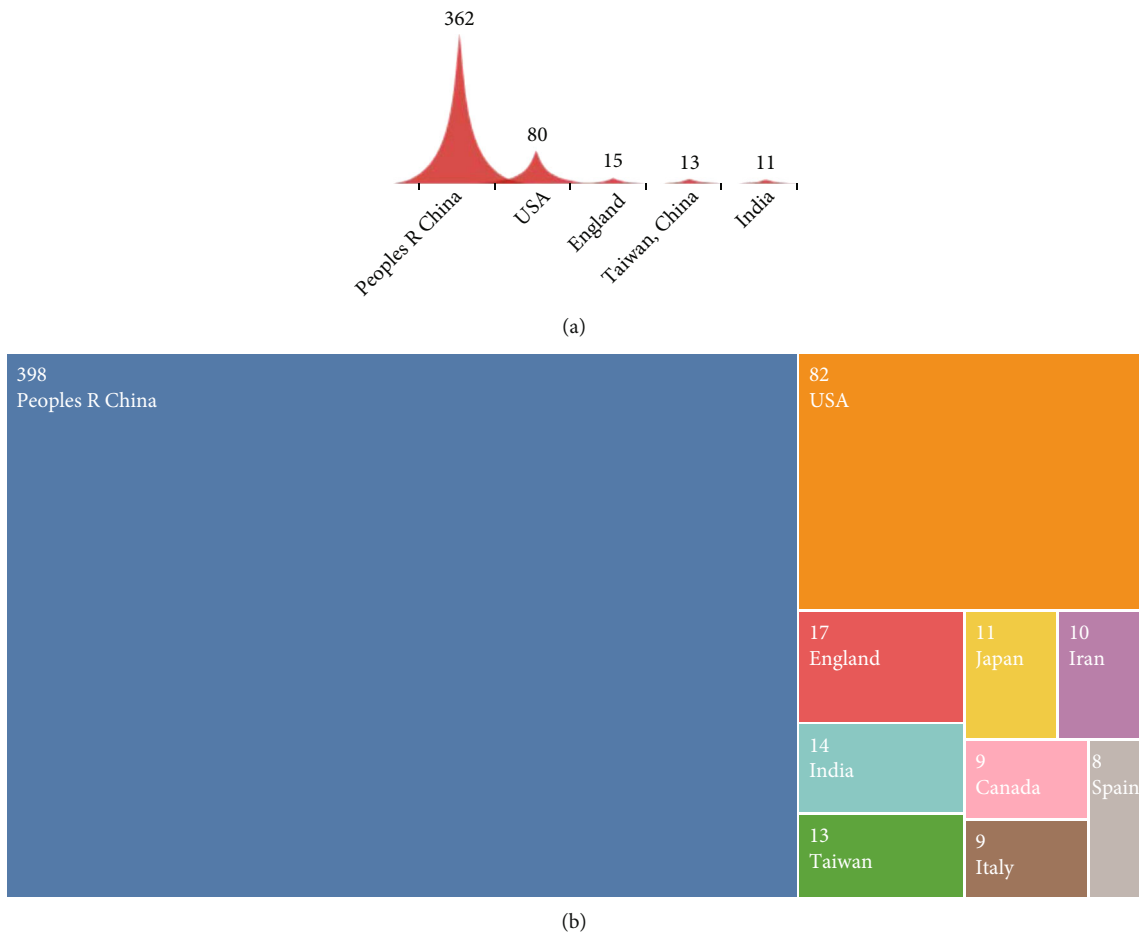
(a)

(b)

FIGURE 4: Analysis of countries. (a) Top 5 countries by number of publications. (b) The distribution of Top 10 countries in the world studying ischemic stroke and autophagy.

Top 5 keywords with the strongest citation bursts

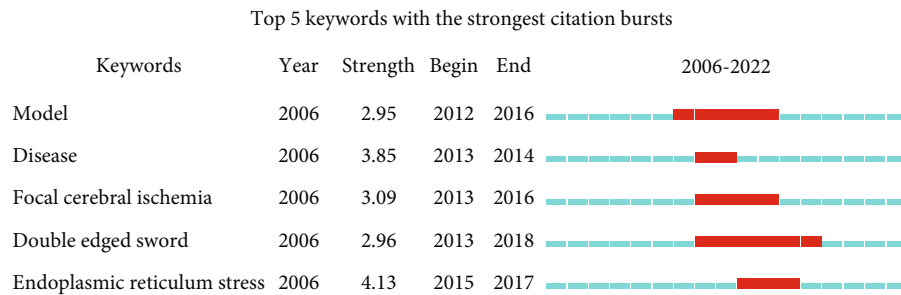| Keywords	Year	Strength	Begin	End	2006-2022
Model	2006	2.95	2012	2016	
Disease	2006	3.85	2013	2014	
Focal cerebral ischemia	2006	3.09	2013	2016	
Double edged sword	2006	2.96	2013	2018	
Endoplasmic reticulum stress	2006	4.13	2015	2017	

FIGURE 5: Top 5 keywords with the strongest citation bursts.

the importance of these aspects for the effects of autophagy on ischemic stroke. These articles provide a good guide for subsequent research, which is supported by the high number of citing articles influenced by their content.

4.3. Analysis of the Journals. Data analysis of the journals from 2006 to present shows that the articles on autophagy in ischemic stroke are published in different journals and an analysis of the source of the publications helps us to identify the core journals in this field. As shown in Figure 3, the most prolific journals are molecular neurobiology and neu-roscience, with 13 articles each. However, the most influen-tial journal in the field of autophagy in ischemic stroke is autophagy, which published only five related articles and ranked first with an impact factor of 16.016. The number of articles on microglia autophagy published in each journal can be used as a measure of the journal's interest in this area. Considering the number of publications and impact factors, autophagy is probably the most influential journal. Journals with the largest number of publications in the related fields play a pillar role as key nodes and have extensive communi-cation with other journals.

4.4. Analysis of Authors and Co-Authorship. With the increasing interest in autophagy and ischemic stroke, more and more authors have been paying attention to this direction.

This is beneficial for probing the distribution of documents by analyzing core authors. The evaluation criteria of core authors included the number of published documents, total cited number, and H-index. Similarly, we also analyzed the number of co-cited authors and citations. Miao and Wang from Japan wrote the largest number of articles on microglia autophagy, and their citation numbers were surprisingly similar to the number of articles, which is related to their frequent cooperation in related studies. The findings of the analysis of co-cited authors also supported this. Moreover, these authors have the largest number of articles in the related fields, which prove their extensive influence and leadership in the research field of the correlation between ischemic stroke and autophagy, guiding many researchers to devote themselves to this direction.

4.5. Analysis of Countries and International Cooperation. We found that a number of countries have contributed to the publications on the role of autophagy in ischemic stroke. The top five countries are as follows: China (362), the United States (80), the United Kingdom (15), Taiwan (13), and India (11). Through data analysis, VOSviewer, we plotted the extent of the number of documents issued between different countries, as shown in Figures 4(a) and 4 (b). According to the picture and VOSviewer analysis, as a pillar of the research on autophagy in ischemic stroke, China has a close research relationship with the United States, the United Kingdom, and other countries, but there is little scientific cooperation in related fields between the other countries.

According to VOSviewer and WOS analysis, we found that the most prolific organizations are Capital Medical University, Soochow University China, and Zhejiang University, with 23, 15, and 15 articles, respectively, followed by 14 references from Jilin University. It is worth noting that Shanghai Jiao Tong University ranked the top in the list of published articles, but its articles were of high quality and have had a significant impact on related research of other organizations. Institutions from the United States cooperate closely and frequently. Among the top 10 issues, all of them are from China, which proves that China has strong research strength and fruitful results on autophagy in ischemic stroke. It is important to note that the number of articles published by other organizations in China has increased dramatically in recent years. It is not difficult to see the rapid development of emerging organizations, such as Guizhou University, Chongqing Med University, and Chinese Med SCI, in the study of autophagy and ischemic stroke, which may become the backbone of this field in the future.

4.6. Analysis of Keyword Co-Occurrence Cluster. Keywords show the theme concepts and core ideas of a paper, and they can briefly describe the specific research hot spots. We used VOSviewer, Citespace, and other software to draw charts. Through keyword clustering analysis, we find that most of the studies focused on apoptosis and cell death, which may be related to autophagy playing a key role in these processes.

Based on the keyword hot spot trend chart in Figure 5, it is obvious that explosive studies mainly focused on the study of autophagy-related effects through the modeling of ischemic stroke and an exploration of the "double-edged sword" role of autophagy in ischemic stroke. Likewise, cytokines and signaling pathways related to autophagy in ischemic stroke have also received extensive attention in recent years, and autophagy of neurons, astrocytes, and microglia has also become a current hot research subject. The number of autophagy in ischemic stroke-related keywords also shows an exponential explosion of growth indicating that more researchers have shifted their attention to autophagy and ischemic stroke.

5. Conclusion and Future Work

As the first bibliometric analysis of the effect of autophagy in ischemic stroke, this study is of great significance, but there are still some limitations. The data sources of the full text were journals included in the WOSCC, and some articles were omitted because they had not been included in WOSCC. The quality of the included papers is uneven, and some small differences affect the drawing expression using CiteSpace and VOSviewer software. The selection of keywords may have led to omission of some relevant articles. The differences in the selection of keywords in these articles are the main reason why some of them were not included in our literature analysis.

Despite the limitations mentioned above, we believe that this study can demonstrate the overall progress and trend of related research on the effect of autophagy on ischemic stroke. It provides meaningful insights for researchers and a valuable reference for them to obtain objective data in this field.

Data Availability

The simulation experiment data used to support the findings of this study are available from the corresponding author upon request.

Conflicts of Interest

The authors declare no conflict of interest. The funders had no role in the design of the study; in the collection, analyses, or interpretation of data; in the writing of the manuscript; or in the decision to publish the results.

Authors' Contributions

LS, YW, SY, and KL contributed to the search and assessment of the available literature. LS and YW mainly wrote the manuscript. QW, DM, and CM interpreted the results of previous studies and revised the manuscript. All authors approved the final version of the manuscript before submission. Lijuan Song and Yige Wu share first authorship.

Acknowledgments

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