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Treatment of Vascular Cognitive Impairment: A Bibliometric Analysis over a 12-Year Period

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Abstract: Purpose: The treatment of vascular cognitive impairment is a key point in the field of neuromedicine. Although a lot of research has been carried out, there are few bibliometric studies in this field. This article analyzes the main characteristics of the treatment of vascular cognitive impairment in the past 12 years, and can better contribute to the understanding of the emerging research trends and hotspots related to the treatment of vascular cognitive impairment. Methods: The authors searched for "vascular cognitive impairment" and "treatment" in articles in Web of Science Core Collection database from 2010 to 2022. We analyzed countries, institutions, journals, authors, references, and key words. Through CiteSpace version 6.1.R3 and VOSviewer version 1.6.18, the authors carried on the retrospective bibliometric analysis and draw the atlas. Results: A total of 1923 articles were published from 2010 to 2022. Neurology is the journal with the largest number of citations, while the United States, Capital Med Univ and WANGY are the countries, institutions and authors with the largest number of publications. The research hotspots are cerebral amyloid angiopathy, C-reactive protein, cerebral microvascular disease, blood-brain barrier, white matter lesions, amyloid β-peptide, cholinesterase inhibitors and so on. ConclusionEvery year, more and more articles are published in the treatment of vascular cognitive impairment and great progress has been made. The United States has made the most outstanding contribution in this important area. Cerebral amyloid angiopathy, C-reactive protein, cerebral microvascular disease, blood-brain barrier, white matter lesions, amyloid β-peptide, cholinesterase inhibitors are research hotspots. Neurovascular units, apoptosis, blood-brain barrier, Nf-kb, neuroinflammation may be the frontier of research. The focus of the treatment of vascular cognitive impairment is lifestyle changes, early intervention of vascular risk factors, and improvement of memory function.

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1. Introduction

Vascular cognitive impairment (VCI) is the whole range of cognitive function changes caused by vascular factors, covering the pathogenesis of vascular mild cognitive impairment to dementia. The most serious form of VCI is vascular dementia (VaD)1.With the aging of population structure, the incidence of VCI and cerebrovascular diseases is increasing year by year, and the number of potential cases related to dementia is huge. As the pathogenesis of VCI is not clear, there is no targeted intervention drugs used in clinic, and the drug treatment of VCI is mostly focused on VaD. Some clinical studies have found that cholinesterase inhibitor (Donepezil) and N-methyl-D-aspartic acid antagonist (Meigang) have some effects on the cognitive function of VCI2. However, the existing treatment methods still have shortcomings. The curative effect of Donepezil is limited, and most of the patients are accompanied by diarrhea, dizziness, fatigue and other adverse reactions3. It is not recommended to be widely used in clinical4.The existing drugs are not enough to meet the needs of people with vascular cognitive impairment, indicating that it is urgent to find safe and effective drugs. Although a large number of studies have been done on the treatment of VCI, there is a lack of comprehensive bibliometric analysis and evaluation, so it is necessary to quantitatively describe the published non-uniform manuscripts.

CiteSpace software is a visualization software developed by Professor Chen Chaomei of Drexel University in 20045, which helps to quickly discover basic knowledge structures in the research field and detect potential research frontiers and trends6.The VOSviewer software developed by the Science and Technology Research Center of the University of Leiden in the Netherlands can be used to construct bibliometric maps to evaluate research directions and hotspots in the literature7.Therefore, in this study, CiteSpace and VOSviewer were used to bibliometrically analyze the publications about the treatment of VCI. The purpose of this study is to report the scientific achievements in VCI treatment research from the Science Network (2010-2022), analyze the main characteristics of related articles, and identify emerging research trends and hotspots, so as to provide reference for follow-up research.

2. Methods

2.1. Data Collection and Search Strategy

Articles on the treatment of vascular cognitive impairment were searched from the Scientific Web Core Collection (WoSCC) from 2010 to 2022. The search strategies were as follows: topic = (vascular cognitive impairment) and (treatment); a total of 2012 articles were retrieved. A total of 1923 articles are included in language (English) and literature types (articles or review articles). After extraction, the data retrieved from WoSCC are downloaded and transferred to CiteSpace and VOSviewer for bibliometric analysis. The retrieval strategy used in this study is shown in figure 1.

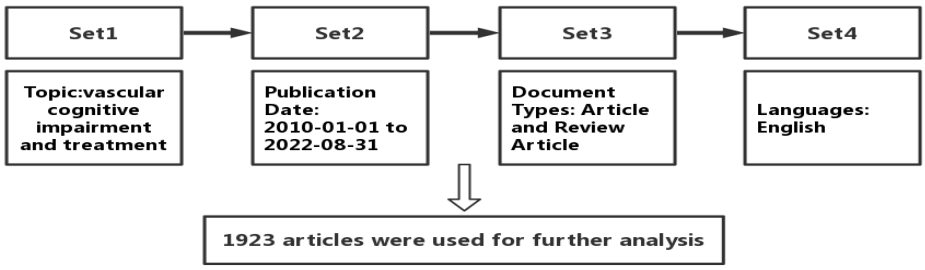

Figure 1. Search strategy

2.2. Data Analysis Method

CiteSpace and VOSviewer software are used for co-occurrence analysis and visualization map drawing, and the obtained data are imported into MicrosoftExcel2019 to generate charts. In general, the larger the node is, the higher the frequency is, and the number and thickness of connections between nodes represent the closeness; centrality is the index to measure the importance of nodes in the network, and the nodes whose centrality is more than 0.1 are key nodes.

3. Result

3.1. Basic Information

At first, 1923 related articles were searched for this study. There are 1922 articles after deleting duplicates. The number of annual articles on the treatment of VCI increased from 82 in 2010 to 153 in 2022, with a steady increase in annual production, peaking in 2021 with a total of 231 articles. Overall, the enthusiasm of researchers for the treatment of VCI continues unabated.

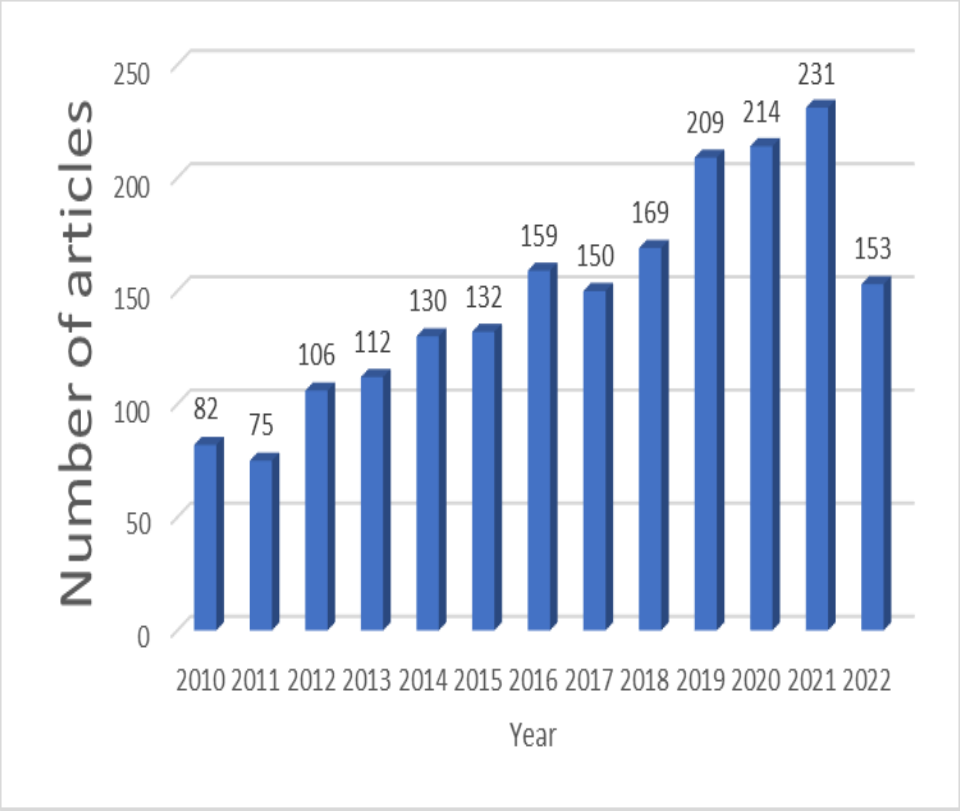

Figure 2. The number of original articles on the treatment of VCI each year from 2010 to 2022

A total of 81 countries and regions have contributed to the articles analyzed in this study. Figure 3 shows the top 10 most productive countries based on the affiliation of the newsletter authors. The United States has the largest number of publications (n=603), followed by China (n=466) and the UK (n=179) ranked second and third respectively.

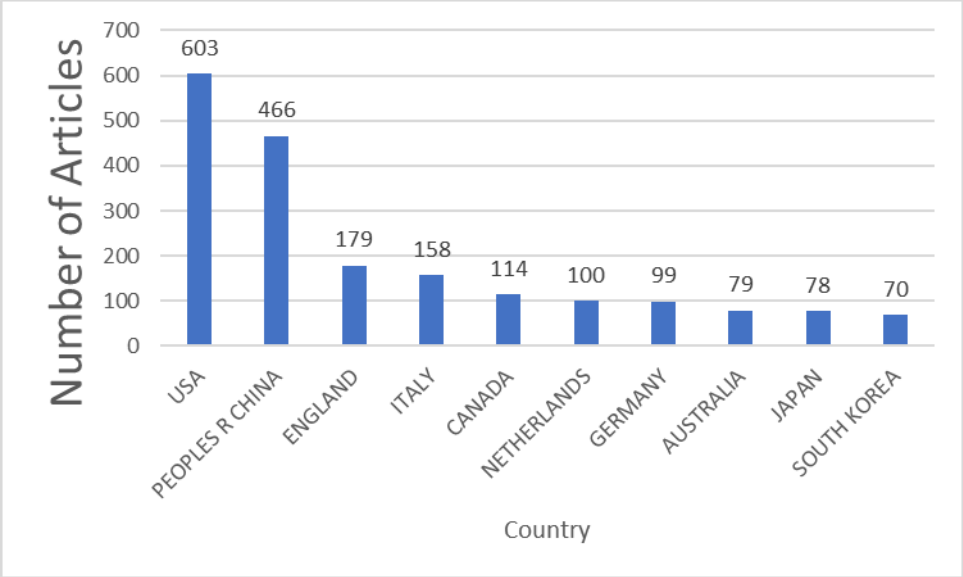

Figure 3. Top 10 countries with the largest number of publications

3.2. Distribution of Countries and Institutions

Statistical analysis shows that 435 institutions from 81 countries have published articles about the treatment of VCI. The United States has the largest number of publications, accounting for about 3/10 of the total, indicating that American research is influential. Moreover, the United States has a high international recognition rate for the treatment of VCI and has a great influence. GREECE has the largest centrality (1.17), which has some influence in this field, although the number of articles published in the country is small.

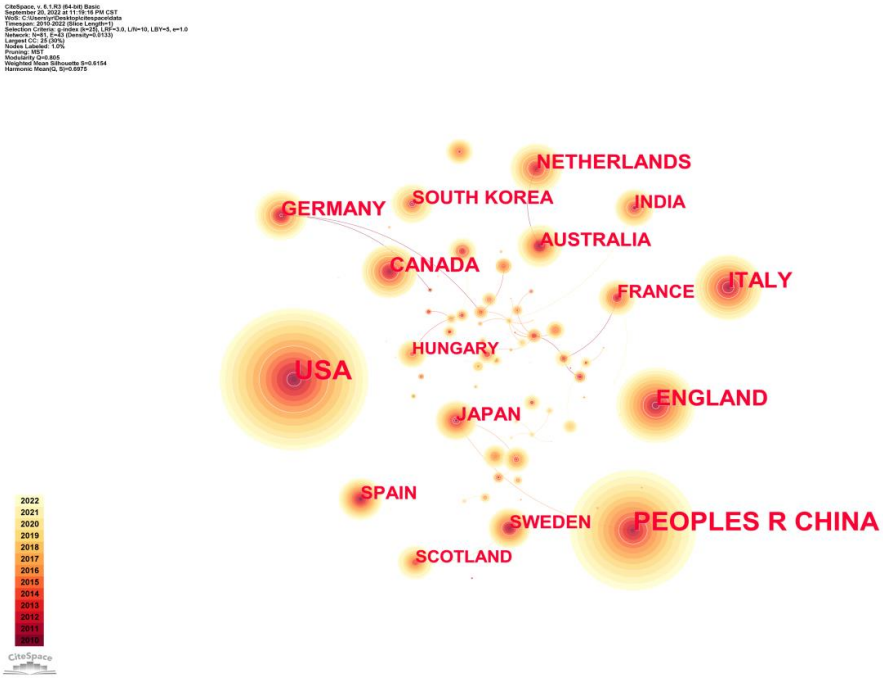

Figure 4. Country/region analysis

Table 1. Top ten countries with the strongest centrality

Ranking	Institution	Centrality	Frequency
1	GREECE	1.17	17
2	POLAND	0.87	26
3	FINLAND	0.77	14
4	NORWAY	0.7	11
5	SAUDI ARABIA	0.66	8
6	MALAYSIA	0.66	17
7	CZECH REPUBLIC	0.66	11
8	TURKEY	0.66	18
9	PHILIPPINES	0.61	5
10	VIETNAM	0.58	4

Using CiteSpace, a co-occurrence map of institutions focused on treating VCI was generated (figure 5). A total of 435 nodes were identified. Each node represents an institution whose size corresponds to the number of publications. Links between nodes represent collaboration, while wider links represent closer collaboration.

Figure 5. Institutional analysis

The top 10 research institutions in the field of treatment of VCI are listed in Table 2. The organization that published the most articles was Capital Med Univ, with 41 articles, followed by Univ Oklahoma and Newcastle Univ. According to centrality, the top organization is Western Univ, followed by Univ Cambridge and Prevent Alzheimer Dis PAD2020.

Table 2. Top Ten Institutions with the Largest Number of Publications.

Ranking	Frequency	Institution	Ranking	Centrality	Institution
1	41	Capital Med Univ	1	0.57	Western Univ
2	40	Univ Oklahoma	2	0.55	Univ Cambridge
3	32	Newcastle Univ	3	0.41	Prevent Alzheimer Dis PAD2020
4	31	Univ Toronto	4	0.39	Karolinska Inst
5	29	Harvard Med Sch	5	0.36	Lund Univ
6	27	Kings Coll London	6	0.31	Queens Univ Belfast
7	26	Univ Szeged	7	0.3	UCL
8	26	Univ Edinburgh	8	0.3	Rush Univ
9	26	Univ Calif San Francisco	9	0.3	Karolinska Univ Hosp
10	26	Univ Cambridge	10	0.22	Cardiff Univ

3.4. Analysis of Cited Periodicals

Table 3. Top ten periodicals with the most citations

Ranking	Periodical	Frequency	Total link strength
1	Neurology	5789	217391
2	Stroke	5327	167618
3	J Alzheimers Dis	2786	96938
4	Lancet Neurol	2171	87360
5	Neurobiol Aging	2048	82051
6	Alzheimers Dement	1827	78418
7	Arch Neurol-Chicago	1768	76042
8	Lancet	1695	62479
9	PLOS ONE	1693	48201
10	J NEUROSCI	1626	47132

The articles were published in 796 periodicals, and the top 10 periodicals with the most citations are listed in Table 3. The periodicals listed in the decreasing order of co-cited periodicals are "Neurology", followed by "Stroke" and "J Alzheimers Dis".

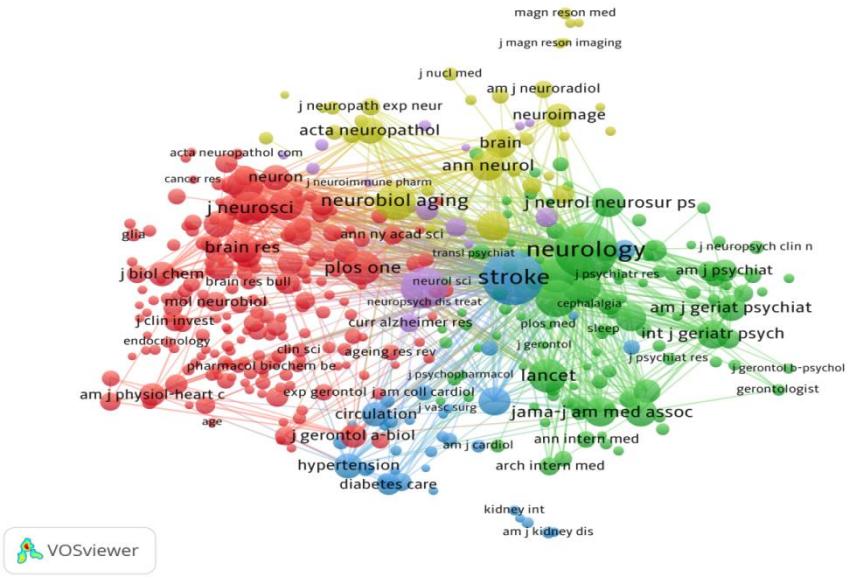

Figure 6. Co-cited periodicals

A co-referenced periodical map is generated using VOSviewer (figure 6). Each node represents a co-citation periodical, and the links between the nodes indicate the common citation frequency of these periodicals. The larger the node, the higher the frequency of common citations of periodicals. Therefore, Neurology is considered to be the most influential journal in the field of treatment of VCI.

3.5. Author Analysis

The co-occurrence diagram of the co-cited author is generated using CiteSpace (figure 7). There are 783 nodes and 404 links. Each node represents an author whose size is proportional to the number of publications, and larger nodes represent more publications. The links between the nodes represent cooperation, which shows that most of the the authors' studies are not carried out in isolation, but forms multiple research teams. The most frequently cited authors are IADECOLAC (317 times), followed by GORELICKPB (309 times) and KALARIARN (252 times).

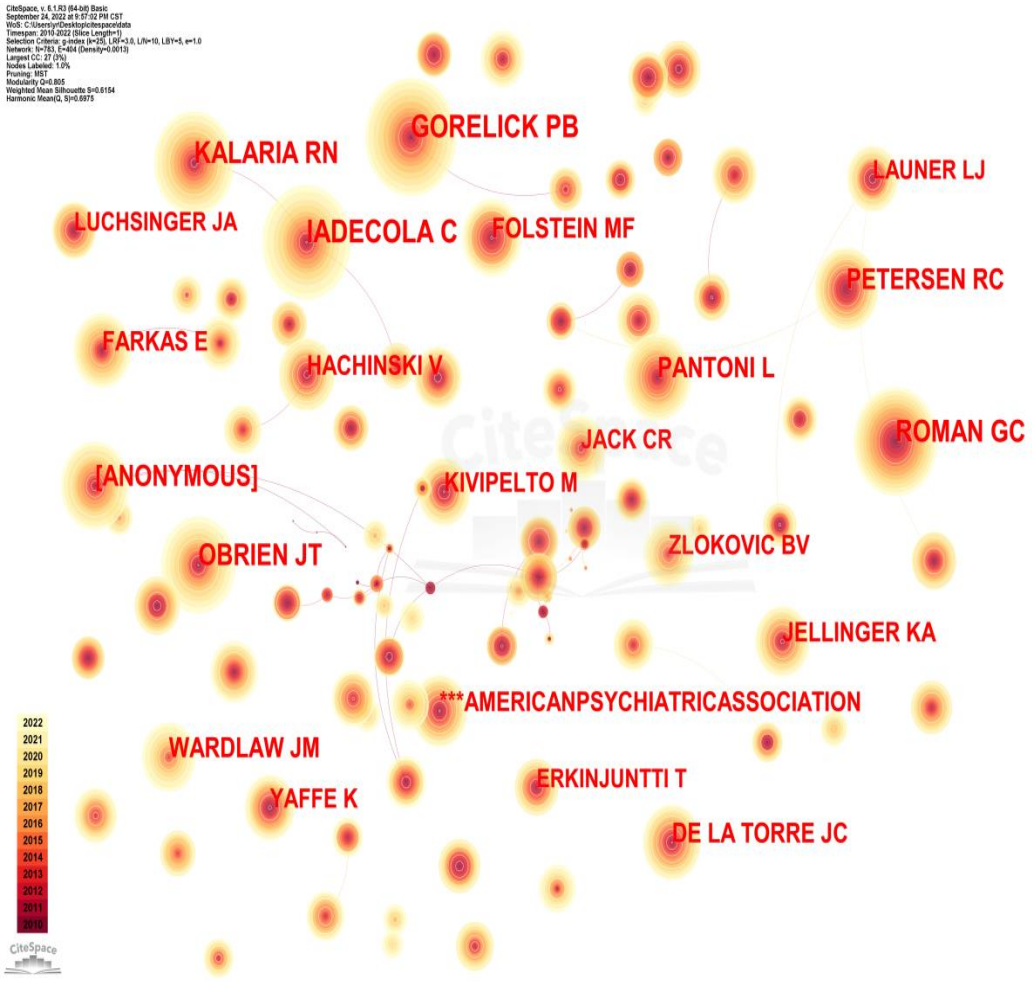

Figure 7. Co-cited author

The top 10 authors of the volume of articles are listed in Table 4. The authors who published the most papers were WANG Y (46 articles), followed by ZHANG J (35 papers), UNGVARI Z (35 articles), CSISZAR A (34 articles) and TARANTINI S (31 articles). The highest centrality of KIM S is 0.51.

Table 4. The top 10 authors with the largest number of published papers and the highest centrality

Ranking	Frequency	Author	Ranking	Centrality	Author
1	46	WANG Y	1	0.51	KIM S
2	35	ZHANG J	2	0.41	CHEN C
3	35	UNGVARI Z	3	0.28	YANG W
4	34	CSISZAR A	4	0.27	DUERING M
5	31	TARANTINI S	5	0.26	BIESSELS G
6	29	WANG X	6	0.24	WANG H
7	27	CHEN C	7	0.24	ZLOKOVIC B
8	26	WANG L	8	0.23	HACHINSKI V
9	26	LI Y	9	0.2	ZHANG J
10	25	ZHANG X	10	0.19	LI C

3.6. Analysis of Co-Citation References

The first five cited references and centrality are listed in table 5. Gorelick PB (2011), The most commonly cited articles are published in Stroke magazine.

Table 5. The top 5 references cited most frequently

Ranking	Cited reference	Representative author	Journal	Frequency	Publication year
1	Vascular Contributions to Cognitive Impairment and Dementia A Statement for Healthcare Professionals From the American Heart Association/American Stroke Association	Gorelick PB	Stroke	94	2011
2	Vascular dementia	Obrien JT	Lancet	62	2015
3	The pathobiology of vascular dementia	Iadecola C	Neuron	51	2013
4	Vascular cognitive impairment	Van DERFLIERWM	Nat Rev	46	2018
5	The diagnosis of dementia due to Alzheimer's disease: Recommendations from the National Institute on Aging-Alzheimer's Association workgroups on diagnostic guidelines for Alzheimer's disease	Mckhann GM	Alzheimers Dement	45	2011

3.7. Keyword Analysis

The keywords for treating VCI are shown in figure 8. This analysis reflects the research hotspots in different periods and can predict the trend in the future. After removing the subject words related to retrieval strategies, it can be found that oxidative stress, risk factors, quality of life and chronic hypoperfusion occur repeatedly. The highest centrality was cerebral amyloid angiopathy, followed by amyloid β-peptide. Using CiteSpace to analyze the explosive key words from 2010 to 2022, neurovascular unit, apoptosis, blood-brain barrier, Nf κ b and neuroinflammation are the focus of research in recent years.

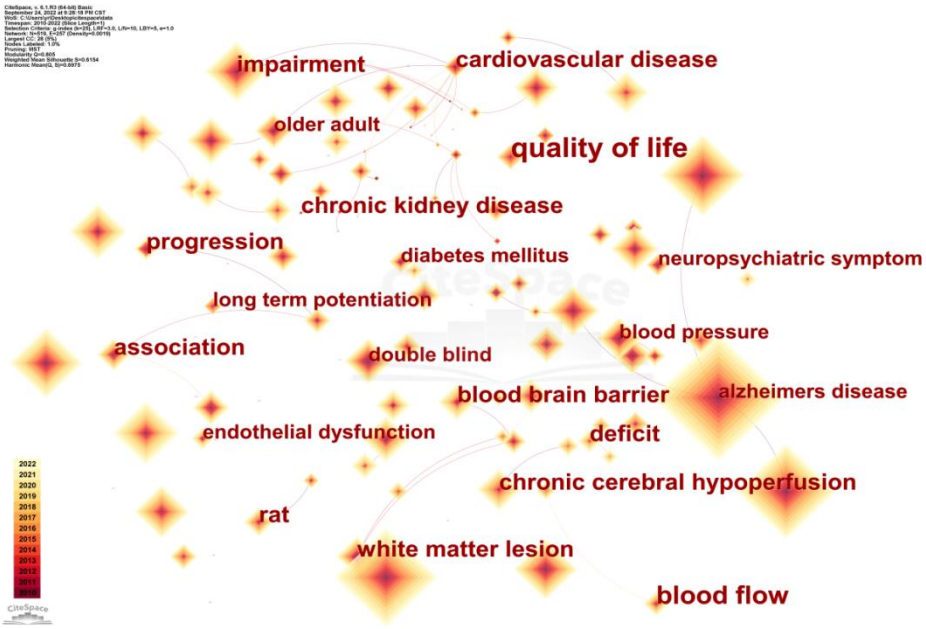

Figure 8. Keyword analysis

Table 6. Keyword centrality analysis

Ranking	Centrality	Words	Frequency
1	1.16	cerebral amyloid angiopathy	51
2	1.14	a beta	58
3	1.12	c reactive protein	19
4	1.01	cerebral small vessel disease	36
5	1.01	blood brain barrier	102
6	1	white matter lesion	96
7	0.99	white matter hyperintensity	91
8	0.97	amyloid beta peptide	13
9	0.91	cholinesterase inhibitor	28
10	0.9	neuropsychiatric symptom	40

Top 25 Keywords with the Strongest Citation Bursts

Keywords	Year	Strength	Begin	End	2010 - 2022
double blind	2010	7.35	2010	2012	
decline	2010	6.79	2010	2012	
incident dementia	2010	6.24	2010	2015	
criteria	2010	5.92	2010	2013	
metabolic syndrome	2010	5.8	2010	2016	
blood pressure	2010	5.1	2010	2012	
placebo controlled trial	2010	4.87	2010	2011	
amyloid precursor protein	2010	4.74	2011	2013	
alzheimer disease	2010	4.49	2011	2012	
white matter lesion	2010	4.39	2011	2012	
atherosclerosis	2010	5.26	2012	2015	
executive dysfunction	2010	4.62	2012	2014	
national institute	2010	5.72	2013	2015	
mitochondrial dysfunction	2010	4.34	2016	2018	
mice	2010	7.68	2017	2018	
in vivo	2010	6.12	2017	2018	
signaling pathway	2010	4.78	2017	2020	
neurotrophic factor	2010	4.37	2017	2018	
inhibition	2010	6.94	2019	2022	
protein	2010	5.68	2019	2022	
neurovascular unit	2010	5.42	2019	2022	
apoptosis	2010	4.84	2019	2022	
blood-brain barrier	2010	4.27	2019	2022	
nf kappa b	2010	7.01	2020	2022	
inflammation	2010	6.29	2020	2022	

Figure 9. Highly explosive keywords

4. Discuss

This study analyzed the data of papers related to treatment of VCI collected by WOS core database. The authors searched the literature from 2010 to 2022 and used econometric analysis software to summarize the general information, research hotspots and trends in the treatment of VCI.

In the past 12 years, the number of annual publications on the treatment of VCI has generally increased, indicating that more and more attention has been paid to the research on the treatment of VCI. The United States showed the strongest research strength in the treatment of VCI, accounting for 31.3% of all publications, followed by China and the United Kingdom. The United States has strong scientific research strength, and China and Britain have also played an important role in promoting this field. In addition, the institution with the largest number of publications is Capital Med Univ, and the top centrality institution is Western Univ, which reflects its impact on the treatment of VCI.

Among the top 10 cited journals, “Neurology” has the highest citation frequency and the highest link strength, reflecting the international influence of the periodical in the field of VCI. From the view of the number of articles published, the research on the treatment of VCI has gradually become a hot spot and has been widely concerned by the international community. However, at

present, there is no obvious cooperation group between institutions and authors, and most of them are in a more independent research state. The cooperation between institutions can promote the development of therapeutic VCI research. Therefore, it is particularly important to strengthen the cooperation between institutions and authors.

In keyword analysis, hot keywords included cerebral amyloid angiopathy, C-reactive protein, cerebral microvascular disease, blood-brain barrier, white matter lesions, amyloid β-peptide, cholinesterase inhibitors, and neuropsychiatric symptoms. In addition, neurovascular units, apoptosis, blood-brain barrier, Nf κ b and neuroinflammation have become the focus of research.

Cerebrovascular disease and other neurodegenerative diseases as the most common VCI co-disease, there are overlapping pathological mechanisms between them, which have been two major problems that people strive to overcome. Among them, amyloid beta peptide8and cholinergic system9are the key contents in the study of the molecular mechanism of diseases in this direction, and oxidative stress and neuroinflammation are the key therapeutic targets10.The mechanism of neurovascular units and cerebral blood flow is an important part of the potential pathophysiological process of VCI11.Hypertension12,diabetes13and hyperlipidemia14problems not only increase the risk of vascular dementia, but also adversely affect the quality of life and social burden of patients, all of which are closely related to aging15.In addition, white matter lesion is significantly associated with episodic memory and working memory, and white matter damage is a strong predictor of cognitive function16.Increasing the research on neuropathology and neuroimaging may provide new ideas for disease diagnosis, drug development and clinical treatment in this direction.

Risk factors associated with VCI include age, education, exercise, smoking and drinking. Studies have shown that the prevalence of cognitive impairment increases with age and decreases with the increase of education17.Physical activity can improve cognition and brain function through different molecular and cellular mechanisms18.Exercise is directly associated with cognitive changes by regulating brain-derived neurofactors (BDNF) and insulin-like growth factor-1 (IGF-1), as well as promoting neurogenesis and angiogenesis19. It has been reported that smoking and drinking are common risk factors, which are significantly correlated with cognitive function20,and other health conditions, especially cardiovascular and cerebrovascular diseases. Therefore, lifestyle change is a key link in the treatment of VCI.

Philip B Gorelick's article, as the most frequently cited paper, this scientific statement provides a comprehensive review of VCI, summarizes potential opportunities for prevention and treatment, and suggests that reducing vascular risk factors is an important research approach21.So far, the United States FDA and the European Drug Administration have not approved drugs for symptomatic treatment of VCI. Cholinesterase inhibitors and Meigang are recognized drugs for the treatment of Alzheimer's disease. Although they are not very effective, they are beneficial in mixed cases of vascular dementia and Alzheimer's disease22.Cholinesterase inhibitors are more effective in patients with cortical injury and hippocampal atrophy, while Meigang is more effective in patients with subcortical vascular dementia23.Some studies have reported that Donepezil can improve cognitive function, but not as a whole24.The risk of VCI can also be reduced by treating vascular disease or maintaining vascular health, such as controlling blood pressure, fasting blood glucose and total cholesterol to avoid cognitive decline25.

4.1. Advantages and Limitations

As far as we know, this is the first bibliometric analysis of the treatment of VCI. In our study, we downloaded articles about the treatment of VCI for nearly 12 years from the WOS core collection and reported more objective and comprehensive results. However, our research has some limitations. The data analyzed are only retrieved from WOS, not other databases. Therefore, there may be a

certain gap between the analysis results and the actual situation. Another limitation is to limit articles to English-only publications, which may result in incomplete information. In addition, only 12 years of data from the WoSCC database were retrieved, and articles prior to 2011 were not included in the analysis.

5. Conclusion

Through the visual analysis of CiteSpace and Vosviewer software, the in-depth research in the field of treatment of VCI and the future research direction has a certain reference significance. After years of practice in many countries, the understanding of the disease is getting deeper and deeper. Although there is no symptomatic treatment for VCI, it can reduce the risk of VCI by promoting and maintaining vascular health, as well as lifestyle intervention to restore normal cognition in patients with vascular mild cognitive impairment. The bibliometric analysis of the literature on the treatment of VCI is of great significance for researchers to identify the research hotspots and the preface of the research.

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Data Availability

Data sharing is not applicable to this article as no new data were created or analysed in this study.

Conflict of Interest

The author states that this article has no conflict of interest.

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