Cerebral small vessel disease: a bibliometric analysis

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Abstract

Background
Cerebral small vessel disease is a common neurological disease, and its incidence is increasing year by year worldwide. In recent years, research on cerebral small vessel disease has gained more and more attention. Our research aims to visualize publications to identify the hotspots and frontiers of cerebral small vessel disease research, and to provide reference and guidance for further research.

Methods
Publications related to cerebral small vessel disease were searched from the Web of Science Core Collection and screened according to inclusion criteria. Citespace 5.8.R3 was used to evaluate and visualize results, including generating web maps and analyzing annual publications, countries, institutions, bibliographic and co-cited references, and keywords, in this article, we use Citespace and VOSviewer for the 2012 Cerebral small vessel disease and bibliometric analysis from January 1, 2022 to April 30, 2022.

Results
A total of 3037 papers related to cerebral small vessel disease were retrieved, and the number of published papers showed a steady upward trend. Among them, Neuroimaging standards for research into small vessel disease and its contribution to ageing and neurodegeneration, the most symbolic references in the eld of cerebral small vessel disease has been cited a total of 438 times. Stroke is the most active journal (227 articles) and Usa publishes up to 800 articles. Harvard Med SchUniv Edinburgh (133 papers) and Charidimou (85 papers), who are the institutions and authors who have made the most contributions in this field, respectively. Among the keywords, most of them are related to the pathogenesis of cerebral small vessel disease. After 2018, gut-brain axi and cortex are the keywords with the strongest number of cited outbreaks. There is increasing evidence that cerebral small vessel disease is a research frontier and may remain a research hotspot in the future.

1. Introduction
Cerebral small vessel disease (CSVD) is a common neurological disease, a group of diseases with small perforating arteries and arterioles (diameter 40-200 μm), capillaries and venules of the brain as the main lesions. It is the most common cause of vascular dementia, accounting for 25 percent of ischemic strokes and most hemorrhagic strokes(Agirman et al., 2021). It is commonly associated with Alzheimer's disease and exacerbates the resulting cognitive impairments, which are responsible for approximately 50% of dementias worldwide. In China, lacunar infarction caused by cerebral microvascular disease accounts for 25% to 50% of ischemic stroke, which is higher than that in Western countries. It is foreseeable that CSVD will be a major disease affecting the quality of life of the elderly in the future(Thrippleton et al., 2019). Therefore, CSVD will be a great challenge in the field of encephalopathy, and its underlying pathogenesis needs to be further studied.

In recent years, cerebral small vessel disease has gained more attention in various research fields, and numerous academic journals have published articles related to CVSD research. However, few studies have systematically investigated the scientific achievements and current state of the field from a worldwide perspective. Therefore, it is extremely important to use visual analysis to reveal the global status, future research trends and hotspots of CSVD research. Bibliometrics, first defined by Pritchard in 1969, is a visualization method that quantitatively evaluates the contributions of research fields using methods such as mathematics and statistics (Ma et al., 2021). Bibliometrics can not only accurately reveal research trends in a certain field, but also an important method to predict research hotspots and frontiers(Sabe et al., 2022). Therefore, we used Citespace and VOSviewer to conduct a bibliometric analysis of cerebral small vessel disease research from 2012 to 2022, to investigate the research progress and hotspots in the field of cerebral small vessel disease, and to help researchers quickly understand the research of cerebral small vessel disease The status quo and the development of research strategies to provide some literature data support for researchers’ research on cerebral small vessel disease(Shen et al., 2022).
2. Methods

2.1 Source of bibliometric data and search strategies

The Web of Science Core Collection (WOSCC) was chosen as the primary data source for data retrieval, a canonical online database considered the most authoritative database of scientific publications in various fields of study. The data retrieval time is from 2012-01-01 to 2022-04-30, and the set retrieval formula is [subject=(cerebral small vessel disease)] and [language=(English)] and [year range=(2012-2022)], deduplicate the search results, and delete non-representative entries such as conference call for papers, news, errata, etc. As of 2022-04-30, 3037 publications were finally screened in the Web of Science database. Since the set time span does not include the literature for the 8 months after 2022, the data for 2022 is not complete, and the research analysis does not represent the whole year. Considering that the database is updated regularly, all data are obtained within one day to avoid potential discrepancies. The flow chart of the research data analysis is shown in Figure 1. The data used in this study were downloaded directly from public databases, and no further animal experiments were performed, so the approval of the ethics committee or informed consent was not required.

2.2 Data export and extraction

The WoSCC database is considered one of the most comprehensive, systematic and authoritative databases in the world and is widely used for biometric analysis and visualization of scientific literature. The search parameters are set as follows: time slice (Years Per Slice) is 2012-01-01 to 2022-04-30, years per slice (1), links (strength=cosine;scope=within slices); selection criteria (g-index ,k=25), pruning (pathfinder + pruning sliced network); Node Types select "Author", "Keyword", "Institution", "Country", "Reference", "Cited Author", "Cited Journal"; selection criteria (g-index k=25). Citespace 5.8.R3 is used for visual data analysis to analyze keywords, co-cited references and trends. A visual map created using the VOS viewer (Leiden University Science and Technology Research Centre, Leiden, The Netherlands) has nodes representing countries, institutions, authors or keywords, which can be connected by co-authors, citations, co-citations and co-occurrence analysis. We use the VOS viewer to perform a similar analysis of countries or regions, map their evolution, classify keywords with high co-occurrence frequencies into clusters, and create density visualizations (Zhan et al., 2022).

3. Results

3.1 Publication outputs and trends

A total of 3037 articles related to cerebral small vessel disease were retrieved. In order to investigate the research trend of cerebral small vessel disease, as shown in Figure 2, the number of papers published each year was displayed in the form of a histogram. From 2012 to 2021, the number of related publications has increased year by year, which indicates that the research on cerebral small vessel disease is paying more and more attention. As of April 30, 2022, 143 papers have been published in 2022. The sum of the citation frequency is 53506, and the average citation frequency of each article is 17.6.

3.2 Fund source

The top ten major funding sources are shown in Table 1. The National Institutes Of Health Nih Usa and the United States Department Of Health Human Services are the most funded institutions (both 524 times), followed by the European Commission (368 times), the National Natural Science Foundation Of China Nsfc (305 times), Nih National Institute Of Neurological Disorders Stroke Ninds (256 times), funding agencies from USA, European Union and China have provided more sponsorship in this field.
| Rank | Fund Source                                      | Country/territory | Frequency |
|------|-------------------------------------------------|-------------------|-----------|
| 1    | National Institutes Of Health Nih Usa           | USA               | 524       |
| 2    | United States Department Of Health Human Services| USA               | 524       |
| 3    | European Commission                             | European Union    | 368       |
| 4    | National Natural Science Foundation Of China Nsfc| China             | 305       |
| 5    | Nih National Institute Of Neurological Disorders Stroke Ninds | USA | 256       |
| 6    | Nih National Institute On Aging Nia              | USA               | 256       |
| 7    | Uk Research Innovation Ukri                     | England           | 241       |
| 8    | Medical Research Council Uk Mrc                 | England           | 235       |
| 9    | Ministry Of Education Culture Sports Science And Technology Japan Mext | Japan | 130       |
| 10   | National Institute For Health Research Nihr     | USA               | 117       |

Table 1 Top 10 funding sources in the field of cerebral small vessel disease

3.3 Countries and institutions

A map of the geographic distribution of global publications shows that articles on cerebral small vessel disease are mainly published in Europe, North America, and Asia (Figure 3). All publications were published in 78 countries, (Table 2) lists the top 10 countries and institutions for cerebral small vessel disease publications, USA is the country with the largest number of publications (800), followed by China (662 articles) and the Netherlands (424 articles), Usa was cited the most (23,608 times) and reached the highest H-index (71). Figure 4 shows that USA attaches great importance to cooperation and has close cooperation with China, France, South Korea, and Italy. The top 10 institutions include 4 Dutch institutions, 3 UK institutions, 2 US institutions and 1 Chinese institution. Among them, Harvard Med Sch is the scientific research institution with the largest number of published papers (137 articles), followed by Univ Edinburgh (133 articles), Univ Cambridge (104 articles), Univ Med Ctr Utrecht (101 articles). The VOS viewer generates a network visualization map for institutional collaboration, and Figure 5 shows that Harvard Med Sch and Univ Med Ctr Utrecht, Univ Edinburgh and Univ Cambridge, and Capital Med Univ, Fudan Univ, and Shandong Univ have a close relationship.
| Rank | Country/territory | Frequency | Citations | Average citation | H-index | Rank | Institution | Frequency | Country |
|------|-------------------|-----------|-----------|------------------|---------|------|-------------|-----------|---------|
| 1    | USA               | 800       | 23,608    | 25.14            | 71      | 1    | Harvard Med Sch | 137       | Usa     |
| 2    | China             | 662       | 8,158     | 10.78            | 39      | 2    | Univ Edinburgh  | 133       | England |
| 3    | Netherlands       | 424       | 12,754    | 27.67            | 56      | 3    | Univ Cambridge  | 104       | England |
| 4    | England           | 399       | 11,462    | 26.47            | 56      | 4    | Univ Med Ctr Utrecht | 101 | Netherlands |
| 5    | Germany           | 290       | 7,961     | 24.35            | 48      | 5    | Leiden Univ     | 92        | Netherlands |
| 6    | Japan             | 234       | 4,029     | 14.49            | 33      | 6    | Massachusetts Gen Hosp | 92 | Usa |
| 7    | France            | 231       | 6,202     | 24.42            | 42      | 7    | Capital Med Univ | 79       | China |
| 8    | South Korea       | 195       | 3,272     | 15.29            | 30      | 8    | Radboud Univ Nijmegen | 73 | Netherlands |
| 9    | Italy             | 168       | 3,689     | 20.05            | 32      | 9    | UCL           | 66        | England |
| 10   | Canada            | 167       | 5,050     | 26.58            | 38      | 10   | Maastricht Univ | 62       | Netherlands |

Table 2 The distribution of the top 10 countries/regions and institutions by the number of cerebral small vessel disease publications

3.4 Journal Analysis

A total of 3037 articles related to cerebral small vessel disease were published in 74 journals. (Table 3) lists the top 10 journals with the most articles published in cerebral small vessel disease. Stroke is the journal with the most articles (227 articles) (7.47%). (IF2022=7.19), followed by Neurology (4.70%) (IF2022=8.77) and Journal Of Stroke Cerebrovascular Diseases (4.01%) (IF2022=1.787), with 143 and 122 publications, respectively, Neurology reached the highest H-index (48), with the most total citations (6301) and average citations (43.46). Among them, in the JCR partition, there are 4 in District 2, 4 in District 3, 2 in District 4, and 1 in District 1.
Table 3 Top 10 journals publishing research articles on cerebral small vessel disease

3.5 Among the 3037 papers related to cerebral small vessel disease research, (Table 4) lists the top 10 authors with the most published papers. Andreas and Charidimou published the most papers (85 papers), followed by Joanna M Wardlaw and Hugh S Markus, There are 78 and 76 papers respectively, all of them are authors who have a certain influence in the field of cerebral small vessel disease. Figure 6 shows the co-occurrence map of authors in the study of cerebral small vessel disease.

Table 4 Top 10 authors of cerebral small vessel disease publications

3.6 Reference

From 2012 to 2022, a total of 3037 publications were visually analyzed using Citespace 5.8.R3, and a co-citation analysis of references was performed. After setting parameters, a visual co-citation map of the identified documents was generated. Table 5 lists the 10 most cited references during the study period, which not only laid the foundation for further research on the mechanism of cerebral small vessel disease, but also provided a theoretical basis for the study of cerebral small vessel disease. The most cited
paper is Neuroimaging standards for research into small vessel disease and its contribution to ageing and neurodegeneration published by Wardlaw, JM in 2013, with 438 citations. Figure 7 shows the co-occurrence map of the first author of the literature.

| Rank | First author | Journal                        | Year | Citations |
|------|--------------|--------------------------------|------|-----------|
| 1    | Wardlaw, JM  | Lancet Neurology               | 2013 | 438       |
| 2    | Wardlaw, JM  | Lancet Neurology               | 2013 | 193       |
| 3    | Pantoni, L   | Lancet Neurology               | 2010 | 172       |
| 4    | Wardlaw, JM  | Lancet Neurology               | 2019 | 129       |
| 5    | Staals, J    | Neurology                      | 2014 | 120       |
| 6    | Prins, ND    | Nature ReviewsNeurology        | 2015 | 72        |
| 7    | Gorelick, PB | Stroke                        | 2011 | 68        |
| 8    | Staals, J    | Neurobiology Of Aging          | 2015 | 67        |
| 9    | Lau, KK      | Neurology                      | 2017 | 64        |
| 10   | Shi, YL      | Stroke And Vascular Neurology  | 2016 | 62        |

Table 5 Top 10 most cited articles in cerebral small vessel disease research

3.7 Research hotspot analysis

3.7.1 Keyword co-occurrence analysis Keywords are extracted from 3037 publications and are a very important part of the research. Keyword co-occurrence analysis provides a reasonable description of research hotspots, and emergent keywords can represent research fronts within a period of time (Xu et al., 2022). Through the network visualization analysis of keywords through VOS viewer, a keyword co-occurrence map of cerebral small vessel disease is generated, as shown in Figure 8, and it is determined that synonyms and similar keywords will be merged in the research on cerebral small vessel disease from 2012 to 2022. After combining synonyms and similar keywords, the top 20 ranked keywords in terms of frequency can be seen (Table 6).

| Rank | Keywords                              | Frequency | Rank | Keywords                       | Frequency |
|------|---------------------------------------|-----------|------|--------------------------------|-----------|
| 1    | confidence interval                   | 390       | 11   | trial                          | 182       |
| 2    | odds ratio                            | 293       | 12   | disorder                       | 182       |
| 3    | dysfunction                           | 291       | 13   | intracerebral hemorrhage       | 180       |
| 4    | ischemic stroke                       | 273       | 14   | mutation                       | 179       |
| 5    | pressure                              | 260       | 15   | Cerebral autosomal dominant arteriolopathy | 171    |
| 6    | cerebral amyloid angiopathy           | 244       | 16   | cerebral blood flow            | 165       |
| 7    | leukoencephalopathy                   | 214       | 17   | artery                         | 164       |
| 8    | infarction                            | 212       | 18   | protein                        | 162       |
| 9    | subcortical infarct                   | 209       | 19   | memory                         | 160       |
| 10   | cadasil                               | 199       | 20   | vascular dementia              | 147       |

Table 6 High-frequency keywords for cerebral small vessel disease research

3.7.2 Keyword Cluster Analysis

Based on the keyword co-occurrence analysis, cluster analysis is performed, and tag clustering is performed by the Likelihood Ratio (LLR) algorithm (Du Y et al., 2022). As shown in Figure 9, the clustered modularity Q value is 0.3949, while the mean contour value S
value is 0.697. Generally speaking, a Q value > 0.3 represents a significant clustering structure; if the average cluster contour value S > 0.5, the clustering is generally considered to be reasonable. If the S value > 0.7, the clustering result is considered convincing. A total of 10 clusters were formed by keywords in this study, which demonstrated the knowledge structure and dynamic change process in the field of cerebral small vessel disease to a certain extent.

Cluster analysis was conducted according to the similarity of keywords. The results showed that the current research on cerebral small vessel disease mainly focuses on three aspects: #0 and #7 are disease research fields, mainly related to the sequelae caused by cerebral small vessel disease, including keywords such as stroke, dementia, cognitive impairment, etc. #1, #3, #4 are pathological changes of cerebral small vessel disease, mainly including small arteriosclerosis, sporadic and hereditary cerebral amyloid angiopathy and other hereditary small vessel disease. #2, #5, #6, #8, #9 are the influence changes caused by cerebral small vessel disease, including Lacunar cerebral infarction, White matter lesions, Cerebral microbleeds, Enlarged perivascular space, and Brain atrophy and Recent small subcortical infarct, see Table 7.

| Cluster ID | Size | Silhouette | Mean(Year) | Top Terms (LSI) |
|------------|------|------------|------------|-----------------|
| #0         | 70   | 0.583      | 2015       | major depressive disorder; cognitive decline |
| #1         | 68   | 0.637      | 2015       | arterial stiffness; amyloid-beta protein precursor; blood-brain barrier |
| #2         | 63   | 0.713      | 2015       | white matter hyperintensities; diffusion tensor imaging; deep gray matter; brain atrophy |
| #3         | 62   | 0.684      | 2014       | cerebral amyloid angiopathy; arterial stiffness; |
| #4         | 62   | 0.702      | 2015       | pulse wave velocity; pulsatility; population-based study; small vessel disease score; risk factors; pressure |
| #5         | 61   | 0.648      | 2015       | white matter; perivascular space; atherosclerosis |
| #6         | 60   | 0.823      | 2013       | normal-appearing white matter; white matter hyperintensities; enlarged perivascular spaces |
| #7         | 59   | 0.642      | 2014       | ischemic stroke; cognitive screening; transient ischemic attack; acute ischemic stroke |
| #8         | 48   | 0.75       | 2016       | subcortical infarct; leukencephalopathy |
| #9         | 32   | 0.826      | 2016       | perivascular space; glymphatic system; global cerebral atrophy |

Table 7 Clustering table

3.7.3 Keyword co-occurrence analysis

According to the detection of emerging words with high frequency and fast growth rate within a period of time, keywords with high burst intensity are an important indicator reflecting research hotspots, frontiers and latest trends (Figure 10). A total of 25 emergent words were detected, and the rotterdam scan had the highest burst intensity (intensity = 15.42), followed by white matter lesion (intensity = 7.94) and outcm (intensity = 7.33). It is worth noting that “national institute” (2018-2022, 5.04), “outcm” (2019-2022, 7.33), “gut-brain axi” (2019-2022, 5.95), “connectivity” (2019-2022, 5.81), “cortex” (The citation burst of keywords such as 2020-2022, 5.26) continued until 2022, indicating that these research directions are likely to become new research hotspots in the future.

### 4. Discussion

#### 4.1 General Information

We performed a bibliometric analysis of 3037 articles related to cerebral small vessel disease. As shown in Figure 2, the number of global publications on cerebral small vessel disease has shown a steady upward trend. Currently, 143 articles have been published in 2022, although The data for 2022 is incomplete, and it is expected that the production of articles in 2022 will increase, which indicates that research related to cerebral small vessel disease is increasingly attracting the attention of scholars.
Bibliometric analysis takes the global literature pattern and literature characteristics as research objects, including countries, institutions, authors, and journals over a period of time (Liu et al., 2019). In terms of country/regional analysis, research centres in this field are concentrated in Europe, North America and Asia. The USA is the most productive country, with a much higher number of publications than other countries/regions, which is closely linked to funding sponsorship by funding agencies. In terms of research institutions, strengthening the cooperation between different institutions or teams is extremely important for future basic or clinical trials of cerebral small vessel disease. Among the published journals, Stroke, Neurology and Journal Of Stroke Cerebrovascular Diseases are the top 3 journals with the most publications. Andreas, Charidimou, Joanna M Wardlaw, and Hugh S Markus are among the top 3 authors in the field of cerebral small vessel disease by volume.

4.2 Bibliography Analysis

Co-citation analysis is generally used as a method to evaluate the academic influence of journals or scholars, who are all authors with certain academic influence (Dong et al., 2022). Wardlaw JM et al. published the most influential papers with the most citations (438 times). Through further research, it was found that Wardlaw JM et al. (Dong et al., 2022) People published several articles mainly on the mechanism, clinical significance and aging and neurodegeneration of cerebral small vessel disease. Lau, KK et al. (Lau et al., 2017) (2017) found that a higher total CSVD score was associated with an increased risk of recurrent ischemic stroke. In therapy, Wardlaw, JM et al. (Lau et al., 2017) (2019) found emerging targets for new therapies including brain barrier integrity, vascular reactivity, vascular compliance, perivascular inflammation or myelin repair. Shi, YL et al. (Shi and Wardlaw, 2016) (2016) believed that new research should consider drugs targeting the endothelium and blood-brain barrier to prevent and treat CSVD. At the same time, changing traditional risk factors and healthy lifestyles are also an important prevention and treatment method.

4.3 Hotspots and Frontiers

Keyword is the most representative term for a concise overview of the topic of the article. Keyword co-occurrence analysis, as a commonly used bibliometric method, can reveal the development trend of research hotspots (Zhou et al., 2021; Sabe et al., 2022). Meanwhile, the keywords with the strongest citation burst can provide a reasonable prediction of the hotspots and frontiers of research on cerebral small vessel disease. Using VOSviewer and Citesease, keywords identified from WoSCC can be grouped into 10 clusters representing the main research directions and frontiers in cerebral small vessel disease (Sabe et al., 2022). According to cluster analysis, the researchers found that the pathogenesis of CSVD has cross effects with chronic cerebral ischemia, endothelial dysfunction, blood brain barrier (BBB) damage, inflammatory response, genetic factors, and neurobiochemical factors. Mechanism related to (Thrippleton et al., 2019; Bordes et al., 2022; Bai et al., 2022). Recent subcortical infarct, white matter hyperintensities (WMH), Cerebral microbleed (CMB), enlarged perivascular spaces (PVS), and brain atrophy are six imaging hallmarks of cerebral small vessel disease, and these imaging markers have been shown to be associated with dysfunction (Di Donato et al., 2017; Markus, 2021; Zanon et al., 2021).

The main symptoms of patients with CSVD include lower extremity motor dysfunction characterized by gait disturbance and cognitive dysfunction characterized by impaired executive function (Chen et al., 2019). White matter lesions (WMLs) are more common in the elderly. The symptoms of WMLs are subtle, such as cognitive impairment, dementia and depression. They are usually symmetrically distributed in the white matter including the pons and brain stem on imaging, and also in the deep gray matter (Wu et al., 2022; Hu et al., 2022). White matter hyperintensities (WMH) are the most important predictors of gait dysfunction, and more severe WMH-related defects are located in the internal capsule, Centrum semiovale), periventricular frontal lobe, etc (Rudilosso et al., 2022; Cheng et al., 2022). The number of lacunar infarcts is a predictor of executive dysfunction, presumably due to damage to the frontal-subcortical circuit, decreased connectivity and metabolism within the prefrontal cortex, and ultimately executive dysfunction (Huang et al., 2022; Tian et al., 2022). Cerebral microhemorrhages are an important imaging marker for amyloid cerebrovascular disease (CAA). Hashimoto T found that the number of CMBs is positively correlated with the extent and degree of white matter lesions, and CMBs-related cognitive impairment is mainly reflected in visuospatial perception, executive function, and orientation ability (Best et al., 2022; Nannoni et al., 2022). Another common manifestation of CAA is cognitive impairment, which may be secondary to ischemic injury caused by CAA, which manifests as a spectrum of symptoms ranging from subjective concerns to severe dementia (Mcaleese et al., 2021; Nannoni et al., 2022).

Arterial stiffness is a common pathological change in cerebral small vessel disease, and arterial stiffness may be one of the causes of cerebral small vessel disease and cognitive impairment (Elyas et al., 2021; Hase et al., 2020). Researchers have found
that severe stroke can lead to right paralysis and aphasia, and even can cause dementia. A large area of necrosis can be seen in the left hemisphere, including the presence of neurofibrillary tangles and amyloid plaques in the hippocampus and frequent amyloid plaques in the cerebral cortex, thickening of arterial walls, perivascular spaces are also found. Enlargement, arteriosclerosis, microbleeds, and white matter thinning are consistent with features of CSVD and underscore the importance of the gut-vagus-brain axis in late-onset post-stroke dementia (Jiaerken et al., 2021). Furthermore, age- and hypertension-related cerebral small vessel disease are also major determinants of cognitive decline and disability in the elderly (Dobrynina et al., 2022; Goldstein et al., 2022). At present, treatment measures are mainly based on the characteristics of risk factors, the type and severity of biomarkers, and the severity of clinical sequelae. In clinical practice, blood pressure lowering, thrombolysis, and antiplatelet therapy are mostly used (Arba et al., 2019; Pan et al., 2022; Du H et al., 2022). Unlike large vessels, small vessels are difficult to image directly. Therefore, when CT fails to make a definite diagnosis of disease, MRI can display the corresponding parenchymal lesions, which is more helpful for the identification and monitoring of cerebral small vessel disease (van den Brink et al., 2022; Cai et al., 2021).

The burst map shows that Cortex and gut-brain axi are the latest burst terms in recent years, indicating that these are the latest research hotspots in the field. Gut-brain axi is a two-way pathway between the gastrointestinal system and the central nervous system, involving nerve, endocrine, immune and other aspects. The gut microbiota has a symbiotic relationship with intestinal cells, and plays an important role in basic physiology such as digestion, growth and immune defense. The intestinal microbiota has a symbiotic relationship with enterocytes and plays a role in fundamental physiological processes such as digestion, growth and immune defense. The gut microbiota maintains bidirectional interactions with major parts of the central nervous system through direct and indirect pathways (Tonomura and Gyanwali, 2021). Components of the microbiome may enhance systemic inflammation and amyloid fibril formation, ultimately leading to amyloid deposition, and brain microvasculature inflammation caused by gut microbiome or microbiome metabolites may affect brain parenchyma. Studies have shown that the gut microbiome is associated with characteristics that suggest the presence of CSVD, and that the gut microbiome or its metabolites may influence the presence of CSVD through the microbiome-gut-brain axis (Nelson et al., 2021).

Cerebral small vessel disease is considered a whole-brain disease, and white matter hyperintensity (WMH), a hallmark imaging feature of cerebral small vessel disease, is associated with distant cortical atrophy and cortical thickness (Arba et al., 2019). Cortical thickness has a significant effect on gait performance, with cortical thickness dominated by orbitofrontal and ventrolateral prefrontal cortex, inferior parietal lobe, cingulate area and visual association cortex, positively correlated with stride length (Wang et al., 2022). Thickness of primary and supplementary motor cortex and cingulate cortex was positively correlated with stride frequency, whereas thickness of orbitofrontal and ventrolateral prefrontal cortex, anterior cingulate cortex, especially inferior parietal and superior temporal gyrus were negatively correlated with stride width. Cortical atrophy was associated with cognitive impairment in patients with moderate to severe WML or lacunar infarction, and reducing the severity and progression of white matter hyperintensity may help prevent secondary brain atrophy and cognitive impairment (Lin et al., 2022).

Combined with the results of keyword co-occurrence analysis and burst map, some risk factors and etiologies of cerebral small vessel disease have been identified, but there are still many questions about the exact pathogenesis and the relationship between these risk factors and pathogenesis, and the disease Biomarkers are also evolving. In recent years, the related research on the brain-gut axis has been widely used in the diagnosis and prognostic treatment of various diseases, and the research on the brain-gut axis in encephalopathy has become a new research direction for scientific researchers. The research of cerebral small vessel disease may still be the frontier and hotspot in the future (Nelson et al., 2021).

5. Conclusion

We analyzed the research progress, hotspots and frontiers in this field, studied cerebral small vessel disease through bibliometric analysis, and revealed the future research prospects. Currently, research on cerebral small vessel disease is in a rapid development stage, and since 2012, publications related to cerebral small vessel disease have steadily increased. At the same time, we identified leading countries, institutions, and leading scholars in the field, and analyzed journals and representative literature. Cortex and gut-brain axi are the latest research hotspots through keyword co-occurrence analysis and burst graph emergence detection. It is worth noting that the mechanism of cerebral small vessel disease is still unclear and needs further study. In conclusion, bibliometric analysis provides objective insights into the research of cerebral small vessel disease, full of opportunities and challenges.
Declarations

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Conflicts of Interest

The authors declare no conflicts of interest, financial, or otherwise.

Authors'Ethical Approval

This paper has been approved by the ethical review board of the Guangxi University of Chinese Medicine.

Contributions

W. M., Y.Y., and T.X. contributed equally to this work. X.M. conceived of the study and revised the manuscript for important intellectual content. Y.Y., N.L., T.X., and Y.X. performed the literature search and contributed all the figures. W.M. edited the manuscript.

Informed consent

All authors have read and approved the content of the manuscript.

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**Figures**

**Figure 1**

Flow chart of research and analysis of cerebral small vessel disease
Figure 2

Number of annual publications on cerebral small vessel disease research from 2012 to 2022

Figure 3

Map showing distribution of cerebral small vessel disease research across different regions.
Geographical distribution map of global publications related to cerebral small vessel disease.

**Figure 4**
The cross-country collaborations visualization map.

**Figure 5**
Institutional Cooperation Map
Figure 6

Author co-occurrence map
Figure 7
reference co-occurrence map

Figure 8
Co-occurrence map of keywords for cerebral small vessel disease research
Figure 9

Cluster view of cerebral small vessel disease research
### Top 25 Keywords with the Strongest Citation Bursts

| Keywords                  | Year | Strength | Begin | End  | 2012 - 2022 |
|---------------------------|------|----------|-------|------|--------------|
| rotterdam scan            | 2012 | 15.42    | 2012  | 2016 |---------------|
| white matter lesion       | 2012 | 7.94     | 2012  | 2013 |---------------|
| population                | 2012 | 7.03     | 2012  | 2014 |---------------|
| small-vessel disease      | 2012 | 6.35     | 2012  | 2015 |---------------|
| follow up                 | 2012 | 6.17     | 2012  | 2014 |---------------|
| white matter change       | 2012 | 5.57     | 2012  | 2016 |---------------|
| infarction                | 2012 | 5.43     | 2012  | 2013 |---------------|
| elderly people            | 2012 | 5.39     | 2012  | 2015 |---------------|
| ladi                      | 2012 | 5.22     | 2012  | 2014 |---------------|
| disability                | 2012 | 4.69     | 2012  | 2016 |---------------|
| brain microbleed          | 2012 | 4.63     | 2012  | 2015 |---------------|
| white matter disease      | 2012 | 4.57     | 2012  | 2015 |---------------|
| cerebral infarction       | 2012 | 4.52     | 2012  | 2013 |---------------|
| cognitive function        | 2012 | 4.5      | 2013  | 2015 |---------------|
| thrombolysis              | 2012 | 4.91     | 2014  | 2016 |---------------|
| vascular disease          | 2012 | 4.5      | 2014  | 2018 |---------------|
| national institute        | 2012 | 5.04     | 2018  | 2022 |---------------|
| scale                     | 2012 | 4.95     | 2018  | 2020 |---------------|
| outcome                   | 2012 | 7.33     | 2019  | 2022 |---------------|
| gut-brain axi             | 2012 | 5.95     | 2019  | 2022 |---------------|
| connectivity              | 2012 | 5.81     | 2019  | 2022 |---------------|
| normative data            | 2012 | 4.76     | 2019  | 2020 |---------------|
| impact                    | 2012 | 4.75     | 2019  | 2020 |---------------|
| cerebrospinal fluid       | 2012 | 4.35     | 2019  | 2020 |---------------|
| cortex                    | 2012 | 5.26     | 2020  | 2022 |---------------|

**Figure 10**

Keyword emergence analysis in the literature on cerebral small vessel disease