REVIEW ARTICLE

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Research trends in brain imaging of mild cognitive impairment in 25 years: a bibliometric analysis

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ABSTRACT

Mild cognitive impairment (MCI) is a condition that is experienced by most elderly in the world. Although there has been a huge rise in research on developing brain imaging tests that can identify and evaluate MCI early on, a bibliometric analysis of this issue is still lacking. The purpose of this review is to determine the pattern and growth of research trends related to MCI and brain imaging using bibliometric analysis, based on Scopus data from 1996 to 2021. The data was converted to Comma Separated Values (CSV) and exported to VOSviewer to bibliometrically analyze the origin by country, keywords, frequently cited articles, author, and journals. Over a 25-year period, 5081 articles were discovered, with the number rising, particularly in the past four years, and significantly in 2022 when 561 articles (11.04%) were found. The Journal of Alzheimer's Disease (19.22%) and Neuroimage Clinical (10.22%) published the largest number of articles on this subject. The United States (24.31%) led all other countries in the number of publications, followed by China (14.84%) and UK (6.5%). The most cited article was by Petersen RC in 1999 (41 citations) about MCI and its clinical characterization. The keywords that appeared the most frequently were mild cognitive impairment (984 occurrences) associated with biomarkers, brain scanning procedures, brain part, age, and human subject. The most frequently cited authors were Petersen RC (1365 citations) and Jack CR (1103 citations). Neuroimage (4164 citations), and Neurology (3268 citations) are the most repeatedly cited journals. This bibliometric study displays the trend in the last 25 years for MCI and brain imaging.

Keywords: Mild cognitive impairment, brain imaging, bibliometric analysis, VOS viewer

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INTRODUCTION

The proportion of the world's elderly population will double from 12% to 22% by 2050 according to the World Health Organization (WHO). Physical and mental abilities may gradually deteriorate as people age and there is also a reduction in cognitive function, manifested as mild cognitive impairment (MCI).[1] Mild cognitive impairment is defined as a neurological disorder in the elderly which is characterized by decreased cognitive functioning, especially in memory, but has no significant impact on daily life and has not met the criteria for dementia.[2] The prevalence rate of MCI in the elderly population varies greatly in various studies around the world ranging from 3% to 42%.[3] Based on Indonesian National Socio-Economic Survey (Susenas) data in 2022, the proportion of the elderly population is 10.48%.[4] According to data from the Directorate General of Medical Services of the Indonesian Ministry of Health in 2010, the prevalence of MCI in the elderly in Indonesia was around 32.4%.[5]

To both identify and protect patients from cognitive deterioration, it is necessary to examine biomarkers that can predict individuals who are predisposed to developing Alzheimer's disease (AD). Various diagnostic and screening techniques are used to detect these biomarkers and evaluate MCI, such as magnetic resonance imaging (MRI), positron emission tomography (PET), and cerebrospinal fluid (CSF) sampling.[6] Brain imaging techniques such as MRI are recommended by various guidelines in Europe and the United States because these techniques can assess structural damage, such as in blood vessels, and changes in parts of the brain. The presence of biomarkers allows pre-symptomatic diagnosis and evaluation of disease progression.[7] However, to determine how well these screening techniques and biomarkers can predict the risk in MCI individuals, further studies are needed in individuals with different levels of risk.[8]

This review was conducted because of the rise in the incidence of MCI and the need to prevent its potentially worsening effect in the elderly.[6] Through bibliometric analysis, researchers can understand the focus of current research, identify widely cited publications, and predict the direction of future research.[9] However, this approach is still lacking in the case of MCI. Therefore, the aim of this review is to conduct a bibliometric analysis of MCI and brain imaging using Scopus and VOSviewer to ascertain the scientific framework (year of publication, articles, authors, countries, keywords, and journal). The findings of this bibliometric analysis are expected to provide an overview of the connections between the two topics and offer recommendations regarding ways to conduct examination for MCI screening, diagnosis and evaluation.

METHODS

This bibliometric analysis has three methodological phases (Figure 1), namely data collection (Phase 1), data visualization (Phase 2), and data analysis with data interpretation (Phase 3).[10]

Data collection

Data collection in the first phase begins by using a search for journals according to keywords and research criteria. The search for bibliometric journals using basic data from the Scopus database with keywords was carried out on April 13, 2023. The keywords used were MCI, brain, imaging, and brain imaging. Keyword intake was associated with Boolean logical functions such as OR and AND which led to the following search topics: [TITLE-ABS-KEY ("mci") AND TITLE-ABS-KEY ("brain" AND "imaging" OR "brain imaging") AND (EXCLUDE (UBYEAR, 2023))]. In phase 1, there are no set criteria for the year of publication to show the trend of these topics, but we omit 2023 because it is still in progress. The types of data are not limited to articles, but also include books, book chapters, reviews, and conference papers. Based on these keywords, 5081 articles were obtained from 1996 to 2021.

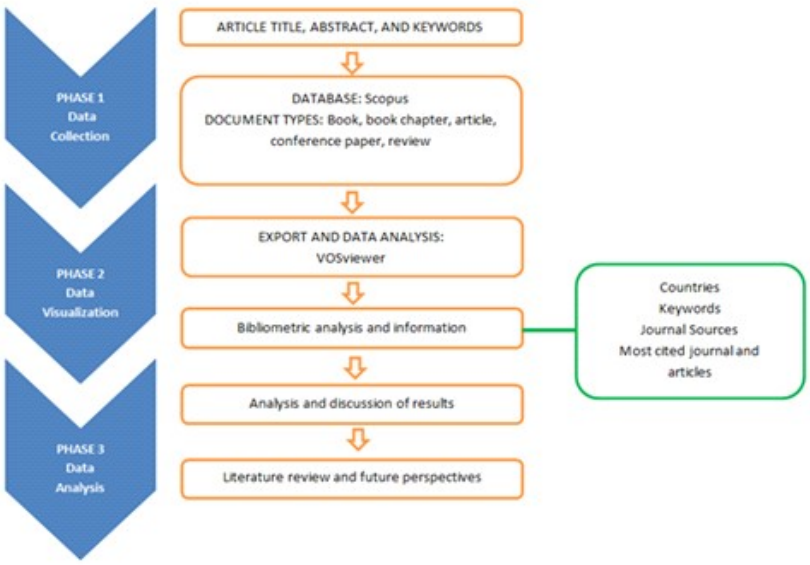

Figure 1. The methodological phases and analytical criteria applied in this study.[10]

Data visualization

In the second phase, the data found in Scopus was subsequently converted to a Comma Separated Value (CSV) file using Microsoft Excel. The CSV file was then extracted using the OpenRefine application so that the number of keywords in the author and index keywords section can be streamlined. After data conversion, the CSV file was exported by VOSviewer software for bibliometric analysis of countries, authors, journals, articles, and keywords.[10] In this study, the bibliometric method was used to visualize MCI and brain imaging through VOSviewer by means of bibliographic coupling (independent articles citing the same article), co-citation analysis (showing linked journals and authors from stored citations) and co-occurrence of keywords (showing frequently repeated author keyword maps). [11]

Data analysis

In the third phase, bibliometric analysis was carried out using the performance analysis approach and scientific structure analysis. Performance analysis is carried out by evaluating trends in year of publication, country, journal, number of articles and most frequent citations. Scientific structure analysis uses scientific mapping of keywords, authors, most frequently cited articles, and co-citation networks of authors and journals. The results will be displayed in the form of interconnected circles.[12] Data interpretation is done by looking at the relationship between circles, color, and size. The closer the distance between the two circles, the greater the strength of the relationship between the terms in these circles. In addition, the larger circle size is correlated with a higher frequency of occurrence of the terms represented. In the end, bibliometric analysis enables the achievement of our research objectives, namely the mapping of scientific structures, patterns and developments in research trends related to MCI themes and brain imaging.[13]

Ethics statement

Ethical approval is not required for this study because it is based on secondary data.

RESULTS

Analysis of annual publications and trend

It was found that there were 5081 articles that matched the criteria. Figure 2 shows that articles on this topic just began to appear in 1996, with yearly increases and decreases until 2005. The increase in articles continues to occur every year from 2006, but there is a sharp increase in

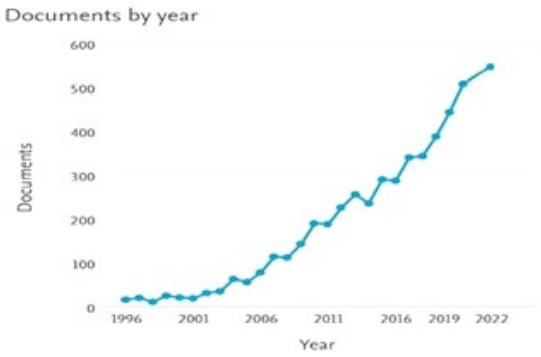

Figure 2. Development of articles on published study topics

the 4 years from 2019 until 2022, with 387 (7.61%), 442 (8.69%), 506 (9.95%), and 561 articles (11.04%), respectively. This indicates the increasing interest of researchers in this topic and the possibility of future advances in imaging examination capabilities.

Sources of scientific publications

When viewed from the number of articles published annually on Scopus, it was found that there were five journals with the highest numbers of articles. The Journal of Alzheimer's Disease publishes the largest number of articles on this topic with 94 articles (19.22%), followed by Neuroimage: Clinical with 50 articles (10.22%). The other three journals that publish articles on this topic are Frontiers in Aging Neuroscience (9.61%), Alzheimer's and Dementia (6.74%), and Alzheimer's Research and Therapy (5.72%).

Country contribution

The more countries that contribute to creating articles and publishing them, the more likely it is to link knowledge on the topic. Bibliographic coupling helps provide a consistent picture, as well as differences in research from different countries over different timescales.[13,14] Using 5 as the minimal number of articles from a country, we found 34 countries that are divided into six clusters. A visualization of the country distribution analysis based on the year of publication regarding MCI and brain imaging is shown in Figure 3.

The country with the largest number of publications in this category is the United States, with 452 articles (24.31%), followed by Asia, with China having 276 articles (14.84%). The next

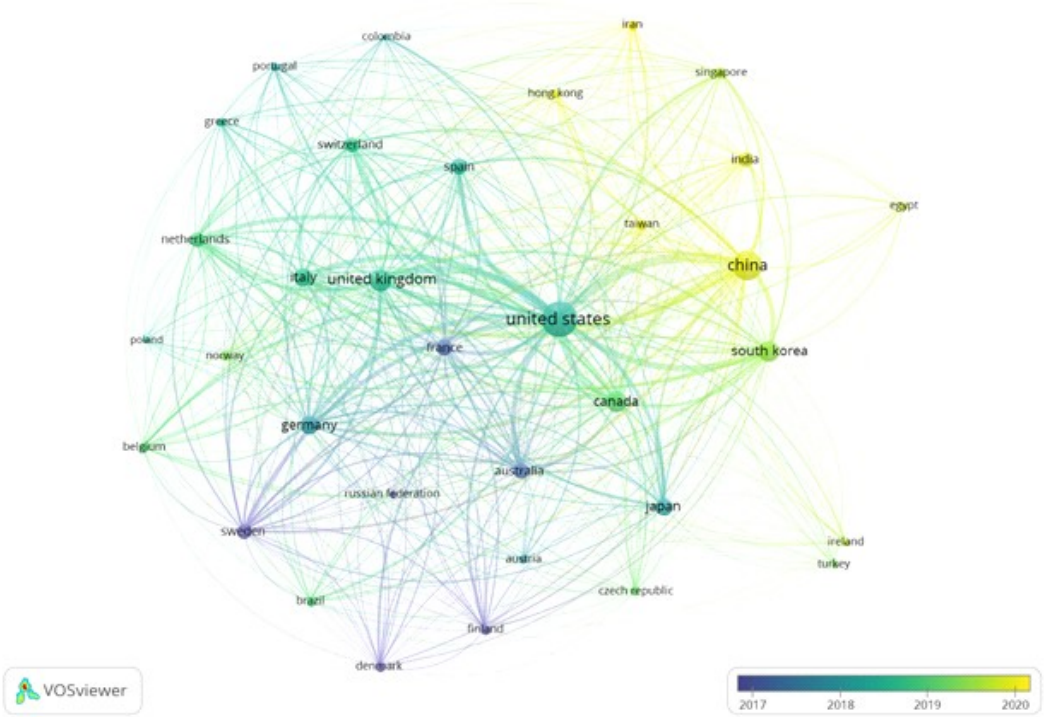

Figure 3. Visualization of country distribution analysis by year of publication

Table 1. The ten most frequently cited articles regarding MCI and brain imaging.[15–24]

Rank	Author	Year	Article	Citations
1	Petersen et al.[15]	1999	Mild cognitive impairment: clinical characterization and outcome	41
2	Petersen [16]	2004	Mild cognitive impairment as a diagnostic entity	40
3	Tzourio-Mazoyer et al. [17]	2011	Automated anatomical labeling of activations in SPM using a macroscopic anatomical parcellation of the MNI MRI single-subject brain	25
4	Albert et al. [18]	2011	The diagnosis of mild cognitive impairment due to Alzheimer's disease: recommendations from the National Institute on Aging-Alzheimer's Association workgroups on diagnostic guidelines for Alzheimer's disease	23
5	Fischl [19]	2012	Freesurfer	15
6	Rathore et al.[20]	2017	A review on neuroimaging-based classification studies and associated feature extraction methods for Alzheimer's disease and its prodromal stages	13
7	Sperling et al.[21]	2011	Toward defining the preclinical stages of Alzheimer's disease: recommendations from the National Institute on Aging-Alzheimer's Association workgroups on diagnostic guidelines for Alzheimer's disease	13
8	Belleville et al. [22]	2014	Predicting decline in mild cognitive impairment: a prospective cognitive study	11
9	Dubois et al.[23]	2014	Advancing research diagnostic criteria for Alzheimer's disease: the IWG-2 criteria	9
10	Besson et al. [24]	2015	Cognitive and brain profiles associated with current neuroimaging biomarkers of preclinical Alzheimer's disease	9

highest contributors are the UK with 121 articles (6.5%), South Korea with 105 articles (5.64%), and Canada with 102 articles (5.48%). There are also Asian and European countries in this distribution. Most studies on this subject were conducted between 2017 and 2020. Articles from the United States and UK are from 2018 (bluish green). Those from Europe are largely from 2017 to 2019 (purple, bluish green and green), and those from China and other Asian nations are the newest ones, from 2020 (yellow).

Most frequently cited articles

The search for the most frequently cited articles aims to see the importance of an article and its discussion.[14] The analysis was carried out by selecting 5 as the minimum number of citations, with a total of 201 articles being found. The results showing the most frequently cited articles can be seen in Table 1.

The 10 most frequently cited articles are the following, sorted in descending order. The first 2 are both on MCI, both were authored by Petersen et al.[15,16] and were published in 1999 and 2004, with 41 and 40 citations, respectively. The next 2 articles with respectively 25 and 21 citations are by Tzourio-Mazoyer et al. [17] and by Albert et al. [18], both published in 2011. Then come 3 articles, the first of which is by Fischl [19] about Freesurfer and published in 2012, with 15 citations, while the next 2 articles are about AD, authored by Rathore et al.[20] and Sperling et al.[21], and published in 2017 and 2011, respectively, both with 13 citations. The next article with 11 citations is by Belleville et al. [22] about MCI and published in 2014. The last 2 articles both have AD as topic and are by Dubois et al.[23] and Besson et al. [24], both having 9 citations.

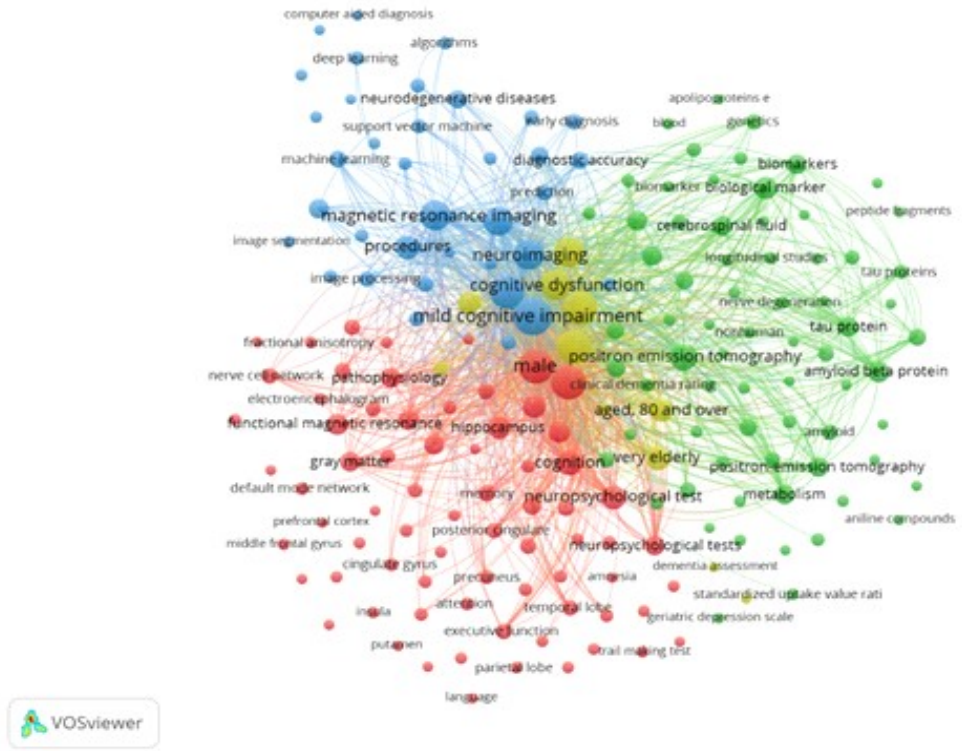

Figure 4. Visualization of keywords used from year to year in Scopus indexed journals

Co-occurrences map by author keyword

Keyword analysis can provide an overview of the concepts that most frequently arise from the research area under investigation.[25] With a minimum of 29 keywords that appear in each article, out of 7,468 keywords, 236 were found. In Figure 4, these keywords are mapped by frequency of occurrence.

Keywords that appeared the most frequently were mild cognitive impairment (984 occurrences), male (822 occurrences), female (815 occurrences), aged (789 occurrences), cognitive defect (704 occurrences), nuclear magnetic resonance imaging (731 occurrences), cognitive dysfunction (579 occurrences), magnetic resonance imaging (547 occurrences), neuroimaging (547 occurrences), and diagnostic imaging (535 occurrences). There are four clusters in the search for publications based on keywords. The red colored cluster mostly highlights human subjects and parts of the brain. The blue cluster shows mild cognitive impairment associated with the procedures of brain scanning, whereas the green cluster is associated with biomarkers and the yellow cluster with age.

Co-citation map by most frequently cited author

This kind of analysis emphasizes outstanding authors which are linked using citation records. There are 69.231 cited authors who are the references of this study. By using the criterion of 20 as the number of authors, the study found 2250 authors who met the criterion. Six clusters are created here using the default setting of 1000 authors. Shen D (758 citations) is the most frequently referenced author in the red cluster, and many other Chinese authors are listed as being associated with studies on imaging of brain anatomy and medical image analysis. Morris JC (538 citations) and Klunk WE (346 citations) in the green cluster, whose research focuses on the role of biomarkers in aging and AD as well as brain amyloid imaging. The author with the most citations overall in the blue cluster is Petersen RC (1365 citations) with numerous studies about MCI and dementia, from guidelines up to biomarkers to detect the disease and it's progression. The blue cluster linking up with other authors whose research focuses mostly on aging and dementia. The authors who are most

Table 2. Top 10 authors co-cited in references on MCI and brain imaging

Ranking	Author	Citations	Links	Total Link Strength
1	Petersen RC	1363	999	170.174
2	Jack CR	1103	999	141.981
3	Shen D	758	970	78.147
4	Blennow K	674	997	91.941
5	Knopman DS	665	997	91.941
6	Scheltens P	626	999	92.606
7	Morris JC	538	998	82.523
8	Fox NC	528	996	70.542
9	Fischl B	520	990	74.320
10	Weiner MW	495	999	69.126

frequently cited in the yellow cluster are Jack CR (1103 citations), Knopman DS (665 citations) and Scheltens P (626 citations) who are associated with other authors whose research focuses on CSF and inflammatory biomarkers in AD. The author with the most citations in the purple cluster is Blennow K (674 citations), associated with authors whose studies are about risk of AD from plasma biomarkers and genetic factors. Aarsland D (320 items) is the most prominent author in the light blue cluster, related with other authors whose studies are about the diagnosis, risk factors, and clinical manifestations of AD and other related dementia. The top 10 most co-cited authors on MCI and brain imaging are shown in Table 2.

Co-citation map of scientific journals

A map of the co-citation journal was conducted to emphasize direct observation of source that have been cited repeatedly by a particular discipline.[26] This analysis shows scientific journals that are repeatedly cited in studies on MCI and brain imaging. It was found that there were 10.283 scientific journals and with a minimum criterion of 20 citations, there were 437 journals that met the criterion. Table 3 shows the top 10 scientific journal sources co-cited on the subject of MCI and brain imaging.

The cluster analysis of journal sources is divided into four groups with high similar properties. The red cluster consists of the journal Alzheimer's & Dementia (1308 citations) and other journals on geriatrics and psychiatry in this network. Neuroimage (4164 citations) is the most prominent journal in the green cluster and is associated with additional imaging and neurobiology journals. The blue cluster is dominated by the journal Neurology (3268 citations), which is linked to other interdisciplinary journals that deal with neurological disorders. The yellow cluster has Plos One (946 citations) as the most well-known publication associated with journals broadly discussing science and medicine.

Table 3. Top 10 scientific journals co-cited on MCI and brain imaging

Ranking	Journal Source	Citations	Links	Total Link Strength
1	Neuroimage	4164	435	159.938
2	Neurology	3268	435	155.258
3	Brain	1410	435	73.700
4	Alzheimer's & Dementia	1308	424	55.796
5	Plos One	942	435	41.556
6	Journal of Alzheimer's Disease	903	339	40.880
7	Neurobiology of Aging	829	337	46.145
8	Archives of Neurology	690	321	37.015
9	The Lancet Neurology	652	398	31.954
10	Annals of Neurology	605	292	31.471

DISCUSSION

According to the analysis of scientific production, there has been an increase in research output on MCI and brain imaging since 2006, but there has been a strong increase particularly since 2019, with production hitting a peak of 561 articles (11.04%) in 2022. It is indisputable that over the past four years, it has become crucial that the topic of MCI and brain imaging has generated a great deal from both research and clinical perspectives. The growing knowledge about this topic can also signal a greater need for newer alternative approaches to imaging tools and techniques that are developed to detect, treat, prevent, and evaluate MCI globally. The country with the greatest number of publications in this category is the United States, followed by China, the UK, South Korea, and Canada. When sorted by year, articles from the United States are largely from 2018, those from Europe are from 2017 to 2019, and those from China and other Asian nations are the newest ones from 2020.[27–29] The growing number of studies on this subject coming from various countries demonstrates the need for the ability to deal with cognitive issues in both developing and developed countries, especially with the use of brain imaging technique that can then be taken into consideration.[30,31] Due to Asia's prominence as the world's most populous region and its fast expanding societies, there has been a rise in research on this subject recently in the Asian region.[32,33] According to recent studies, the prevalence of MCI is almost the same in the East and the West, at 3–42%, but Asia has a very dense population, and particularly the number of people who are aging and at risk of developing MCI would rise in this region.[34,35] The rapid rise in the prevalence of MCI causes significant issues for the healthcare system that can be influenced by factors such as culture, economics, education, social conceptions of aging, and geographic location.[36,37]

According to the source of scientific publications as well as the co-citation map of scientific journals, the majority of MCI and brain imaging journals are multidisciplinary, including journals about geriatrics, psychiatry, imaging, neurobiology, neuropsychology, neurology, science, behavior, and medicine. There are various ways to look at this issue, therefore it is possible that all parties involved will need to work together to find a solution. (38,39) With a multidisciplinary team, broad approaches to MCI are required, encompassing pharmaceutical and non-pharmacological interventions from prevention to rehabilitation.[40–42] To improve patient-centered care and present a viable strategy for providing patients and families with integrated health and medical care, the collaborative care model should be established and put into practice concurrently.[43–45] The foundation of a successful collaboration is built on open communication among team members, teamwork, trust and respect for each team member's knowledge, collegiality, and understanding of the area of medical practice.[46] According to the research that has received the most citations on this subject, Petersen RC's 1999 publication emphasizes that clinical traits that fit the requirements for MCI can be distinguished from mild AD and from cognitive domain deficits in more severe AD.[15] Petersen RC's research from 2004 that also featured a similar topic on improving the MCI criteria and making the therapy target more apparent was the second-most-cited study.[16] Articles from 2011 to 2017 have also received many citations in other studies. Based on the discussion of prior research, studies from before 2015 continue to focus more on diagnostic criteria that are clinically evaluated using tests of memory and cognition.[15–19] It appears that numerous studies from 2015 and later have started to talk about brain profiles and biomarker methods using neuroimaging techniques to detect MCI and other cognitive issues. To forecast cognitive decline, early detection, diagnostic guidelines, and the goal of an extensive early treatment, neuroimaging techniques using MRI and PET scans for the detection of A_{1-42} and tau have started to be used.[20–24]

The keyword that appears the most frequently in each article is mild cognitive impairment which is connected to the procedures of brain scanning. The other keywords that tend to come up frequently are male and female, which is related to human subjects, brain structure, and function. Moreover, positron emission tomography is frequently used and connected to biomarkers. The keywords age and those connected to it are the most prevalent. The correlation between keywords demonstrates a connection between MCI, imaging methods, and biomarkers as aging progresses. According to the visual analytical findings, there has been considerable research done on the topic of brain scanning techniques because keywords related to these techniques are frequently discovered. This highlights the fact that more studies are examining the use of neuroimaging as a test to diagnose and evaluate cognitive impairment by looking at specific biomarkers, potentially because it is easier and provides data more rapidly.[47,48]

In the co-citation map by most frequently cited author, Petersen RC is the most prominent cited author, followed by Jack CR, Shen D, Blennow K, Knopman DS, Scheltens P, Klunk WE, and Aarsland D. Petersen RC, a professor in neurology[49] has began to write articles in 1974 and since 2002 has produced numerous articles related to MCI, dementia, and Alzheimer's disease.[50–52] He produces a lot of research and interestingly, starting in 2013, he began to concentrate more on biomarkers and neuroimaging methods.[53–57] It is not surprising that he is the author who is most commonly cited considering the approximately 1000 publications on this subject and the continual yearly development of those numbers.[49] This is in contrast with Shen D, a professor of radiology,[58] who began writing articles in 2002 on a variety of subjects, including genetics, anatomical brain networks, medical image analysis, and others on topics ranging from infants to elderly people who suffer from dementia.[59–61] Because of the broadness of his writing, although not as a first author, Shen D has received numerous citations for his work. The writers who are commonly referenced here come from a variety of institutions, nations, and fields of study, indicating that the distribution of authors on this subject is quite diverse.[62–66]

This 25-year trend can be seen by looking bibliometrically at the top productive authors, countries, keywords, most cited articles, and journals. According to the trend of the discussions, this subject started to be popular around 2015, its popularity increased until 2022, and this mapping supports the premise that brain imaging approaches to look for distinctive biomarkers seem promising for future directions in building guidelines for diagnosis and treatment of MCI. Arguably it cannot be the only test used to diagnose cognitive impairments, but its significance is obviously important given the increased discussion about this topic. The weakness of this research is that the data were limited to the Scopus database, therefore it is possible that some overview from a different angle was not included in the study. In addition, bibliometric analysis also cannot be used to measure the validity and quality of scientific publications, and the number of citations to an article is highly dependent on various factors. Although the results of this bibliometric analysis can be used for further study and for developing the topic of MCI and brain imaging, these limitations need to be considered in interpreting the results of this study.

CONCLUSIONS

This review provides a research trend related to MCI and brain imaging through bibliometric analysis over a period of 25 years. This theme is getting more popular by looking at the growing articles, particularly in the past four years. Since 1996, there has been research on mild cognitive impairment alone. However, since 2015 and beyond, there has been a rise in interest in the topic in relation to brain imaging techniques and biomarkers, with Asia in 2020 receiving particular emphasis. The mapping's findings

provide more evidence for the relationship between aging, MCI, and numerous biomarkers and brain imaging procedures. The primary method used in the research is brain imaging to identify A_{1-42} and tau as biomarkers for MCI and other cognitive diseases, as well as for diagnostic guidance and treatment. The results of journals that are frequently cited and clearly shown suggest that there is a relationship between various multidisciplinary fields, necessitating team collaboration with a patient focus to achieve better results in preventing MCI and its deterioration. However, until now, brain imaging cannot be used as a single examination in diagnosis and therapy for MCI. Hence, more thorough analysis and research are needed to determine how to apply brain imaging in clinical practice.

CONFLICT OF INTEREST

We know of no conflicts of interest associated with this publication.

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CONTRIBUTORS

DS: majorly participated in drafting the article, critical revision and final approval of the manuscript to be published.
ATWR: majorly participated in article conception and design and in data acquisition, analysis and interpretation. All authors have read and approved the final manuscript.

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