Research Trends in Application of Artificial Intelligence in Alzheimer's Disease: Bibliometric and Visualization Analysis

Xin Yang[1,2,3]*
1. Fudan University Library
2. Fudan University Intellectual Property Information Service Center
3. Big Health Informatics Research Center, Fudan university
Shanghai, China
yang_xin@fudan.edu.cn

Xuan Xu[1,2,3]
1. Fudan University Library
2. Fudan University Intellectual Property Information Service Center
3. Big Health Informatics Research Center, Fudan university
Shanghai, China
xuanxu@fudan.edu.cn

Jun Ying[1,2,3]
1. Fudan University Library
2. Fudan University Intellectual Property Information Service Center
3. Big Health Informatics Research Center, Fudan university
Shanghai, China
junying@fudan.edu.cn

***Abstract*—The remarkable performance of Artificial Intelligence (AI) in the diagnosis and prediction of Alzheimer's disease (AD) has attracted considerable attention in recent years. This study intends to outline the development trends and research focus in the AI-Alzheimer field. The VOSviewer and bibliometrix R software package are employed for bibliometrics and visualization analysis of literature obtained from the Web of Science Core Collection database. There are 5,991 affiliations from 104 countries/regions that published 5,675 articles in this field by 2023. Results demonstrate that the number of AI-Alzheimer-related publications has experienced slow progress for over twenty years before entering a period of exponential growth in 2016. The United States and China, contributing over 54% of the publications, stand out as leaders in technological innovation and international cooperation. The clustering analysis of keywords indicates that the major research domains are the utilization of machine learning and deep learning algorithms for AD and mild cognitive impairment (MCI) classification, early diagnosis of disease, and drug discovery. Generative adversarial networks (GANs), transfer learning, and Transformers are the emerging AI algorithms applied in the field of Alzheimer's research, which also represent promising directions for future investigation. The findings provide a comprehensive summary of the AI-Alzheimer field and identify research frontiers, offering valuable references for scholars.**

Keywords—bibliometrics, visualization, research trend, artificial intelligence, Alzheimer's disease

I. Introduction

Alzheimer's disease (AD) is one of the most common neurodegenerative disorders, accounting for approximately 70% of global dementia cases [1]. The main clinical features of AD include cognitive dysfunction, language impairments, memory loss, and other behavioral disorders. According to a recent report by Gustavsson et al. [2], it is estimated that 32 million people are living with AD worldwide. Age is the primary risk factor for AD. Projections from the Alzheimer's Association [3] reveal that the population of individuals aged 65 and older with AD in the United States is expected to reach nearly 12.7 million by 2050. Given the acceleration of the global aging population, it is anticipated that the number of AD patients will continue to rise, imposing a heavy burden on healthcare systems and society. This disease has been considered as a significant threat to global public health by the World Health Organization (WHO).

Currently, there is no effective treatment for AD, however, early-stage diagnosis holds vital importance for timely intervention and disease management. Research implies that clinical data, genetics, medical imaging, including magnetic resonance imaging (MRI), positron emission tomography (PET), electroencephalogram (EEG) et al., cerebrospinal fluid (CSF) biomarkers (e.g., beta-amyloid (Aβ) and tau), and plasma biomarkers have been proposed for AD diagnosis [5-8]. In recent years, the application of artificial intelligence (AI) in Alzheimer's research has shown enormous potential in analyzing these diverse types of data to uncover intricate patterns associated with AD.

Bibliometrics is a quantitative method adopted to analyze scientific data that contains publications, citations, authorship patterns, international cooperation, et al. It is available to gain an integrative view, identify knowledge gaps, detect developing trends, and derive novel research ideas [8]. Nevertheless, there is few research on bibliometric analysis about the AI -Alzheimer. Most study focus on the bibliometric analysis of AI in health care [9, 10], Parkinson's disease detection [11], neuroimaging biomarkers [12, 13]. YU et al. [14] utilized Excel, CiteSpace, and VOSviewer software to conduct bibliometric analysis of relevant literatures on the application of AI to AD from 2004 to 2023, with a primary emphasis on English papers from the 4 sub-databases of Web of Science core database (WoSCC). Therefore, the purpose of this paper is to summarize the AI-Alzheimer research, and data set is sourced from all sub-databases of WoSCC database (no language or publication time restrictions). The R tool and VOSviewer are conducted for bibliometric and visualization analysis of pertinent literature, elucidating the development tendency, evolution of hotspots, and putting forward future research prospects in this field.

II. DATA AND METHODS

A. Data Collection and Cleaning

The publications were retrieved from the WoSCC database on October 20, 2023. The search strategy was presented as follows: TS=(alzheimer*) and TS=("artificial intelligen*" or "depth learning*" or "deep learning*" or "natural language processing*" or "speech recognition*" or "computer vision*" or "gesture control* " or "smart robot*" or "video recognition*" or "voice translation*" or "image recognition*" or "machine intelligen*" or "machine learning*" or “support vector machine*” or “SVM” or “random forest*” or “neural network*” or “artificial neural network*” or “convolution* neural network*” or “deep neural network*” or “adversarial network*” or “fully convolution* network*” or “k-nearest neighbor*” or “transfer learning” or “ generative adversarial network*” or chatgpt or “large language model$”). A total of 5,675 publications were ultimately obtained (articles and reviews only). All data was exported from the WOSCC database as plain text files with record content of the full record and cited references. Subsequently, synonymous terms, abbreviations, singular and plural forms of author’s keywords were merged.

B. Analysis Tools

The VOSviewer software, R packages of bibliometrix and Rcircos are implemented for bibliometric analysis. The Bibliometrix is used to analyze geographic distribution, core authors, major affiliations, and topic trends. The international collaboration map of the AI-Alzheimer field is visualized using Rcircos. VOSviewer is conducted to generate the co-occurrence map of authors’ keywords (word frequency over 25 times).

III. RESULTS AND ANALYSIS

A. Annual Publications

Based on the literature retrieval from the WoSCC database, there are 5,675 documents published in the AI-Alzheimer field (5,026 articles and 649 review articles). The annual distribution and trend forecast of AI-Alzheimer-related publications are presented in Fig. 1.

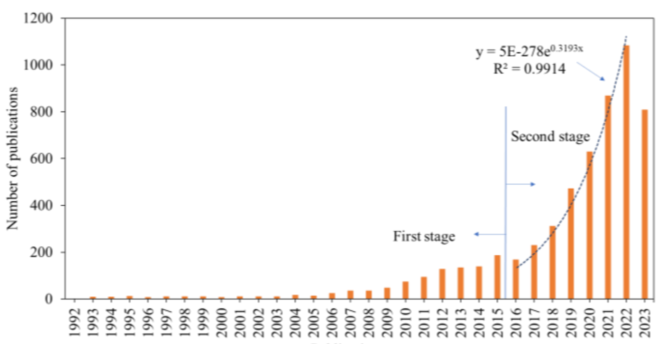

Fig. 1. Annual distribution of publications.

From the WoSCC database, the earliest publication in this domain can be traced back to 1992 [15, 16]. Then the number of publications entered a period of slow growth lasting nearly twenty years, until 2016, there was a rapid surge. The growth trend from 2016 to 2022 aligned with an exponential trajectory, characterized by the fitting curve index $y=5E\text{-}278e^{0.3193x}$ ($R^2=0.9914$). This means that since 2016, the AI-Alzheimer research has gained continuously intense concern, and will be in the high-speed growth stage for the long term. It is important to note that the decline in quantity after 2022 is caused by incomplete data collection for 2023, as the literature search was conducted on October 20, 2023. Therefore, the number of AI-Alzheimer-related publications in 2023 is provided for reference only.

B. Contribution by Authors

Over the last 30 years, 24,198 researchers have contributed to the application of AI technology in the Alzheimer's field. The top 10 authors by H-index ranking are listed in Table I. Shen Dinggang from ShanghaiTech University (China) is tied for first place and also has the highest publication output (69). Górriz Juan M. and Ramírez Javier, both from the University of Granada (Spain), take the second and third positions, respectively. Among the top 10 authors, Bruce L. Miller from the University of California San Francisco (USA) has the highest value of citation frequency per publication (189.1). In terms of the M-index, the most influential newcomer is Liu Mingxia from the University of North Carolina (USA).

TABLE I. THE MOST PRODUCTIVE AUTHORS IN THE FIELD OF AI-ALZHEIMER

No	Authors	H-index[a]	M-index[b]	Publications	AC[c]
1	Shen Dinggang	39	1.95	69	101.1
2	Górriz Juan M.	30	2.00	55	46
3	Ramírez Javier	30	2.00	53	47.04
4	Adeli Hojjat	27	1.59	28	105.9
5	Wang Shuihua	27	2.50	41	70.15
6	Zhang Daoqiang	25	1.92	36	95.61
7	Liu Mingxia	23	2.56	35	50.66
8	Zhang Yudong	23	2.09	31	81.42
9	Segovia Fermín	21	1.40	30	50.13
10	Bruce L. Miller	20	1.33	24	189.1

a. The Hirsch index (H-index) is the number of publications (h) with citation frequency at least h times [17], which can be used to evaluate the research productivity and impact.

b. The M-index is the H-index divided by academic career duration since the researcher’s first published paper, identifying high-potential researchers at the early stage [18].

c. Average citation per article.

C. Regional Distribution

Publications related to AI-Alzheimer research originate from 104 countries/regions. Table II lists the top countries/regions with publication numbers over 150.

The United States contributes to approximately 31.8% of publications, followed by China with a contribution of 22.8%. The publication number in these two countries is much higher than in other countries/regions. Whereas, the average citation of AI-Alzheimer-related publications in China is less than half of that in the United States. The Netherlands has the highest average citation frequency (47.6), before France (44.4) and the USA (44.1). These illustrate the United States is at the forefront in both the quantity and quality of publications, China may need to further heighten the quality and impact of its research in the AI-Alzheimer field. Despite India's relatively high publication number, its citation frequency per document lags far behind that of other productive countries/regions (13.0), revealing less impact on this field as well.

TABLE II THE MOST PRODUCTIVE COUNTRIES/REGIONS WITH PUBLICATION NUMBERS OVER 100

No	Countries/Regions	Publication	AC	Degree[d]
1	USA	1803	44.1	71
2	China	1293	21.5	55
3	United Kingdom	583	40.6	69
4	India	456	13.0	63
5	South Korea	371	26.9	48
6	Italy	350	37.2	55
7	Germany	344	33.9	52
8	Spain	298	28.3	53
9	Canada	278	25.4	59
10	Australia	229	28.9	60
11	France	203	44.4	56
12	Japan	187	19.4	42
13	Netherlands	149	47.6	39

[d] Number of cooperative countries/regions.

The international collaboration network of countries/regions is depicted in Fig. 2, with edges representing cooperation relations between them. The top three countries/regions involved in international collaboration are the United States, the United Kingdom, and India. Additionally, the most frequent cooperations occur between the United States and China (273 publications), followed by the United Kingdom and the United States (139 publications). This also exhibits the enormous influence of the United States in the AI-Alzheimer field.

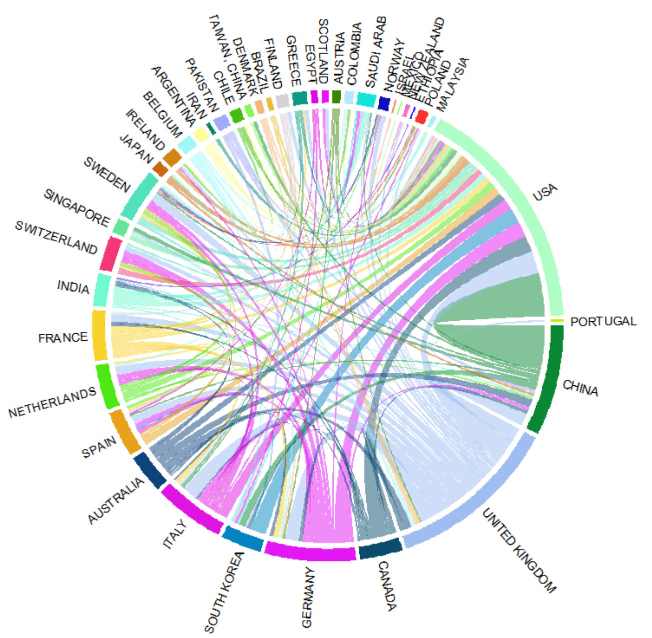

Fig. 2. Collaboration network of countries/regions (edge strength over 10).

D. Keyword Analysis

Keywords are the core extractions of publications. In general, high-frequency keywords can be utilized to detect prominent topics in a certain research field [19]. Thematic clustering of keywords in the AI-Alzheimer field is conducted through correspondence analysis. As presented in Fig. 3, the research trends are divided into 3 clusters.

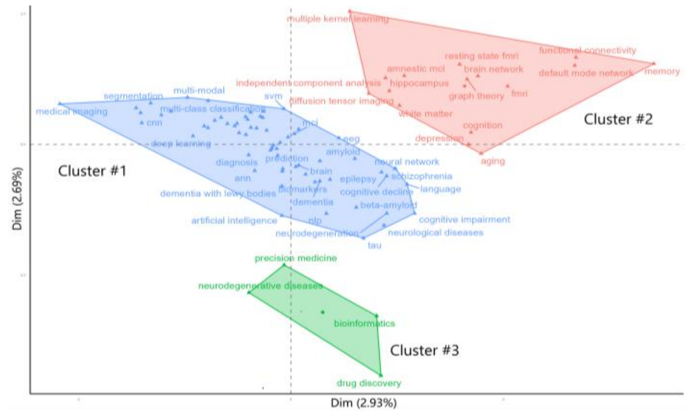

Fig. 3. Factorial map of keywords in the AI-Alzheimer field

The timeline graph of the keywords' co-occurrence network for each cluster is visualized through VOSviewer (Fig. 4). The depth of color signifies the early or late appearance of the keyword by year, while the node size is associated with the keyword frequency.

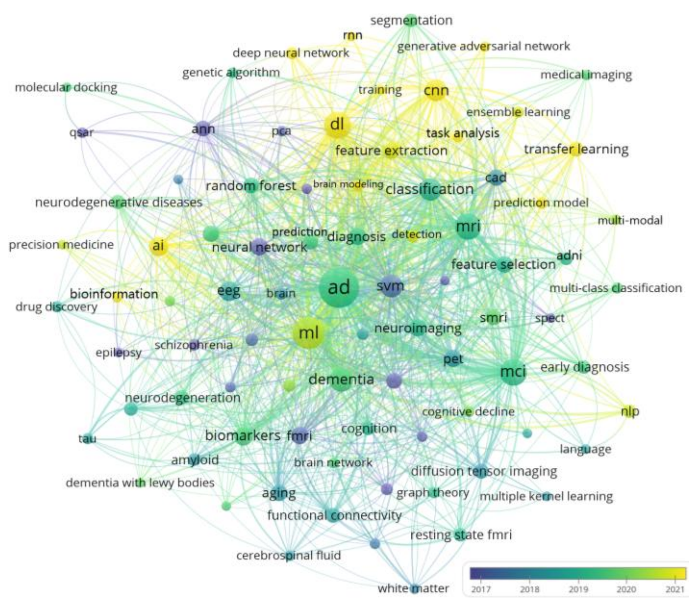

Fig. 4. Co-occurrence map of keywords in the AI-Alzheimer field

The R-package bibliometrix is implemented to track the dynamic evolution of topics within the literature and recognize innovative research areas. Fig. 5 illustrates the developing tendency in the AI-Alzheimer domain during the past two decades. The circles stand for the median emergence year of topics, with their size proportional to the square root of word frequency, and the line length denotes the duration of the topic occurrence.

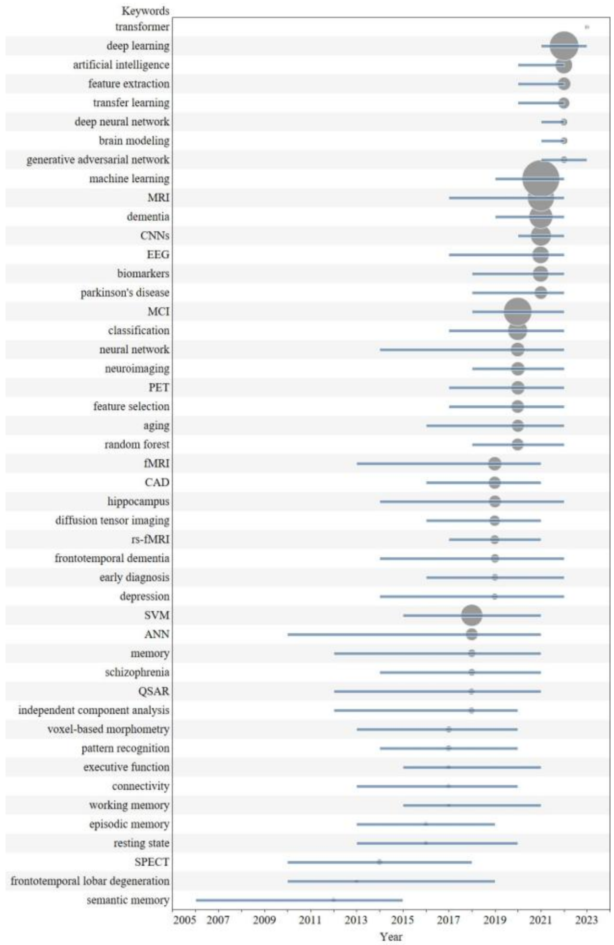

Fig. 5. Topic trends of the AI-Alzheimer field (word frequency > 15 times)

IV. Discussion

The main objective of this paper is to give a systematic review of the application of AI technologies in the AD field through bibliometrics and visual analysis. The related research has undergone a slow 24-year development since its emergence in 1992, experiencing a swift increase phase starting from 2016. The United States stands out leader in both the number of publications and international cooperations.

The keywords clustering analysis reveals that the central to AI-Alzheimer research is the utilization of deep learning and machine learning algorithms for the classification of AD and mild cognitive impairment (MCI), early diagnosis of disease, and drug discovery. “deep learning”, “machine learning”, “MRI”, “CNNs”, “MCI” and “classification” have markedly gained concern in recent years, suggesting that they represent frontier topics in the AI-Alzheimer field.

According to the guidelines of the National Institute on Aging and Alzheimer's Association (NIA-AA), AD progression is composed of three stages: preclinical AD, MCI due to AD, and AD with dementia. MCI is a prodromal stage of AD, however, not all cases of MCI progress to AD. Hence, the accurate classification of AD and MCI is crucial for effective disease prevention and treatment. The earliest keywords in Cluster #1 include neural network, ANN (artificial neural network), and SVM (support vector machine), while CNN (convolutional neural network), deep learning, multi-modal, et al. are the latest research targets. Studies indicate that machine learning and deep learning algorithms has shown remarkable performance in the analysis of neuroimaging data [20-21], such as structural MRI (sMRI), functional MRI (fMRI), EEG, PET, FDG-PET, et al. These imaging modalities provide detailed information about the structural and functional changes in the brain related to AD and MCI. AI techniques can effectively address the integration of complex, large-scale, and high-dimensional neuroimaging data [22-24], thereby promoting classification accuracy. Several AI algorithms, like SVM, CNNs, neural networks, random forests, and ANNs, are considered to hold great potential for early detection and prediction of AD. In particular, CNNs have demonstrated high accuracy in predicting the conversion from MCI to AD. Findings reported by Grueso and Viejo-Sobera [25] also illustrate that while the most commonly used AI algorithm for AD classification is SVM, with a mean accuracy of 75.4%, CNNs obtain a higher mean accuracy of 78.5%.

The conjunction of multiple imaging data from MRI and PET is conducive to increasing the detection and classification accuracy of AD and MCI, as they offer mutually complementary information [26, 27]. Li et al. [28] proposed a VGG-style 3D CNN model to extract feature information from MRI and PET images, achieving 72.55% accuracy in AD: NC: MCI three-group classification. Moreover, AI algorithms can integrate information from various neuroimaging modalities (e.g., sMRI, fMRI, PET) along with other biomarkers, such as clinical data, genetic information, and CSF markers, to further enhance the accuracy of classification models [29-31]. These multiple data across different modalities are more informative for disease diagnosis or prognosis than individual biomarkers. Spasov et al. [32] built a DL architecture based on dual learning and an ad hoc layer for 3D separable convolutions, employing both sMRI images and clinical features (demographic, neuropsychological, and APOe4 data) to increase the average AUC to 0.925 and accuracy to 86%. Venugopalan et al. [33] presented a DL architecture to predict the AD stage from different multi-modality data that includes imaging (MRI), clinical test data, and genetic information (single nucleotide polymorphisms).

Cluster #2 is about the early diagnosis of AD through the combination of brain functional connectivity and AI algorithms. Keywords such as Functional connectivity and resting-state fMRI are the research frontiers. Functional connectivity can reflect functional interaction among different brain regions [34], and it has become a key measure for investigating the functional architecture of the brain in neurodegenerative disorders [35]. Machine learning and deep learning algorithms can extract functional connectivity features of the brain and distinguish between normal controls and subjects with neurodegenerative disorders in brain images, thereby improving diagnostic accuracy and predicting disease progression. In neuroimaging techniques, resting-state fMRI is a valuable tool for exploring functional connectivity networks across brain regions, which can serve as a significant biomarker for AD detection at an early stage. The synergistic utilization of resting-state fMRI with diverse types of data, such as sMRI and genetic information, enhances the classification accuracy between control group individuals and patients with AD [34, 36]. Ju et al. [37] proposed a framework to conduct early detection of AD based on deep neural networks with resting-state fMRI data and clinical examination information (age, gender, and genetic data), and its prediction accuracy was 31.21% higher than that of traditional classifiers. Zhang et al. [38] employed graph theory and random subset feature selection algorithm using sMRI and resting-state fMRI metrics, to distinguish MCI non-converters/AD from MCI converters, with accuracies of 84.71%, and 89.80%.

Another application of AI in Alzheimer field is drug discovery. In May 2021, DSP-0038, the first AI-designed Alzheimer's drug, entered the initiation of Phase 1 clinical trial in the United States. DSP-0038 is a dual-targeted 5-HT1A receptor agonist and 5-HT2A receptor antagonist [39]. This finding offers a promising outlook, particularly given the more than 200 AD therapeutic candidates that have proven unsuccessful or abandoned in the last decade [40, 41]. However, it's important to note that the research of DSP-1181 (the first AI-designed drug candidates developed by the company of Exscientia and Sumitomo Dainippon Pharma to go into human clinical trials) [42] was discontinued in 2022 because the Phase 1 study did not meet the expected criteria for the treatment of the obsessive-compulsive disorder (OCD) [43, 44]. Although AI techniques can accelerate the drug discovery process, there is no guarantee of success in clinical trials. However, this does not diminish the potential prospect of AI in drug development.

The themes of "SPECT", "frontotemporal lobar degeneration" and "semantic memory" have obtained less concern since 2015, which may be due to that they have been thoroughly analyzed. From 2015 to 2021, several algorithms, like "ANN", "SVM", "random forest", and "neural networks" progressively attracted the interest of researchers. These four topics have both strong frequencies and long occurrence durations of 11, 6, 4, and 8 years, respectively, showing their lasting influence on this domain. "Transfer learning", "feature extraction", "deep neural network", "brain modeling", and "generative adversarial networks" (GANs) are the breakout terms in the field from 2021 to 2022, showcasing rapid development within a single year.

A key bottleneck for deep learning algorithms is the requirement for a substantial number of annotated datasets for training. Transfer learning with the augmentation technique can help address this data scarcity by leveraging knowledge obtained from models trained on larger datasets in the relevant fields, leading to high classification accuracy with a smaller dataset [33]. The utilization of data augmentation techniques may mitigate overfitting problems associated with small training data. Statistics display that approximately 68.22% of articles related to transfer learning techniques are based on CNNs by 2021 [45]. Mehmood et al. [46] exploited layer-wise transfer learning and tissue segmentation of MRI images to diagnose the early AD stage on account of 300 ADNI (Alzheimer's Disease Neuroimaging Initiative) subjects, obtaining a testing accuracy of 98.73%. Chen et al. [47] proposed a multi-auxiliary domain transfer learning (MaDTL) method to enhance the classification accuracy of MCI-to-AD conversion to 80.37%, using MRI and CSF data of 409 subjects from the ADNI database.

GANs are a kind of deep learning architecture that is considered a promising avenue in the realm of AI-driven disease diagnosis. Consisting of two neural networks (a generator and a discriminator), this algorithm is capable of generating synthetic data to deal with data scarcity issues, thus mitigating the reliance on real data. Pan et al. [48] adopted 3D cycle-consistent GAN to generate missing PET data from corresponding MRI data, illustrating the beneficial impact of synthetic PET images on improving the classification accuracy of brain disease. Ye et al. [26] utilized the attention layer in both the generator and discriminator to better preserve the structure of the extracted features, which boosts the stability of GANs.

In 2023, there is a new research hotpot occurred in the AI-Alzheimer field: Transformer-based deep learning models for AD diagnosis. The Transformer architecture, proposed by Vaswani et al. [49], is based on a self-attention mechanism to capture long-range dependencies and extract global information features. Studies have indicated that the combination of Transformer and CNN-based architectures can lead to higher performance in AD classification using MRI images. This is because the hybrid network can leverage CNNs to extract low-level features and utilize a Transformer to process remote features [50]. Hu et al. [51] developed a VGG-TSwinformer model based on CNNs and Transformer for early AD prediction. In this model, CNNs were conducted to extract features from longitudinal sMRI image slices, while the Transformer performed feature fusion between these slices.

V. LIMITATIONS

There are several limitations in this study. Firstly, in terms of data collection, this paper retrieved AI-Alzheimer-related literature only from one database (WOSCC), without literature indexed in other databases such as PubMed and Scopus, which inevitably led to some omissions. Secondly, this study did not include literature from preprint repositories, so it is possible that some of the latest research findings were not captured. Future research could incorporate the above several databases to provide a more comprehensive analysis, and make use of preprint literature to track the latest research progress.

VI. CONCLUSION

This study carries out bibliometric and visualization analyses on scientific publications in the AI-Alzheimer sphere to provide insights into the research situation and development trends. The number of publications in this area has increased dramatically since 2016, indicating a favorable foreground. The robust international collaboration reveals that high-income developed countries/regions play the principal roles in driving the AI-Alzheimer research forward. The primary focus areas identified through clustering analysis include early diagnosis of AD, classification of AD and MCI, as well as drug discovery. The applications of AI algorithms such as transfer learning, Transformers, and GANs to facilitate the accuracy of AD diagnosis, prediction, and classification are currently active areas of research and potential direction for future research. Study results can help researchers better grasp the overall trends and track research hotspots within the field.

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