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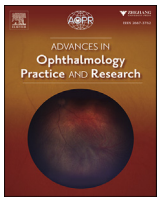

Full Length Article

Global research on artificial intelligence in thyroid-associated ophthalmopathy: A bibliometric analysis

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ABSTRACT

Purpose: To provide an overview of global publications on artificial intelligence (AI) in thyroid-associated ophthalmopathy (TAO) through bibliometric analysis.

Methods: Publications related to AI in TAO from inception until April 2023 were retrieved from the Web of Science database. The trends of publications and citations, publishing performance, collaboration among countries and institutions, and the funding agencies, relevant research domains, leading journals, hotspots and their evolution were identified.

Results: A total of 55 publications were included for analysis. The number of publications and citations continued to grow since 1998, with a significant acceleration of growth after 2020. China is the most productive country with the highest number of productive institutions, followed by the United States. European countries have the most extensive collaboration. The most relevant research domain was radiology, nuclear medicine & medical imaging. The European Journal of Radiology was one of the most productive journals, with the most influential articles published. "Thyroid-associated ophthalmopathy" and "neural network" maintain hotspots during the entire period. Studies were more focused on clinical features during 1998 and 2016, clinical features and medical data during 2017 and 2020, and medical data and AI techniques during 2021 and 2023.

Conclusions: This study summarized the global research status regarding AI in TAO in terms of trends, countries, institutions, research domains, journals, and key topics. AI has shown great potential in TAO. Sponsored by funding agencies such as NSFC, China has become the most productive country in the field of AI in TAO. Our findings help researchers better understand the development of this field and provide valuable clues for future research directions.

1. Introduction

Thyroid-associated ophthalmopathy (TAO) is a disabling and disfiguring autoimmune disorder affecting the orbit and ocular adnexa and is mainly associated with autoimmune thyroid diseases such as Grave's disease.[1] The global prevalence in patients with thyroid-associated ophthalmopathy is 86.2% for hyperthyroidism, 10.36% for hypothyroidism, and 7.9% for euthyroidism.[2] Oftentimes, the diagnosis of TAO is directly based on history and physical examination. Ophthalmic manifestations can be classified as mild (such as dry eye), moderate-to-severe (such as diplopia), and sight-threatening (such as optic neuropathy and corneal decompensation).[3] Due to a broad spectrum of clinical presentations, the treatment options may vary from supportive therapy (such as ocular surface lubrication) to surgery (such as orbital decompression).[4] TAO is detrimental to the visual function and craniofacial appearance of patients, which lowers their quality of life.[5] Screening and early diagnosis of TAO allows timely and effective treatment of the disease, reducing physical and mental burden on the patients.

A wide application of imaging techniques with abundant data resources has been found in TAO, such as magnetic resonance imaging (MRI), computed tomography (CT) and facial photography.[6] Artificial intelligence (AI) is a branch of computer science that has rapidly developed over the past few years. The ability of AI to deal with large sets of data has significantly outweighed human efforts.[7] Due to the advancement of machine learning techniques, particularly deep learning, AI has shown promise in the diagnosis, treatment, and prognosis of TAO.[8–10] There is an urgent need for a comprehensive analysis of research patterns and trends of AI in TAO, considering that academic research on this topic has proliferated in recent years. However, no bibliometric analysis has been conducted in this field yet.

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Bibliometric analysis is an interdisciplinary subject using information visualization methods to qualitatively and quantitatively assess the scientific performance of countries, institutions, authors, and journals, as well as references and keywords of worldwide literature, thus providing an overview of a certain field.[11,12] Bibliometrics has been widely used to analyze scientific literature on AI in ophthalmology, such as diabetic retinopathy,[13] strabismus,[14] and glaucoma.[15] Summarizing the global research situation is critical for future work to promote AI in ophthalmology. Therefore, this study aimed to perform a comprehensive analysis of publications on AI in TAO to provide an overall view and direction for future work in this field.

2. Methods

2.1. Database and search strategy

The Web of Science (WoS) Core Collection is one of the most comprehensive scientific databases covering over 9000 research journals and 12000 academic conferences. Due to standardized and consistent records in multidisciplinary literature research, WoS is the most frequently used database in bibliometric studies.[16] According to the guidance of collecting bibliometric data from only one database,[17] WoS was used as the scientific database for our data collection.

We conducted a search of literature mentioning TAO-related terms and AI-related terms in the title, abstract, and keywords. The complete search string combining keywords with Boolean operators was as follows: TS = ("thyroid-associated ophthalmopathy" OR "thyroid-associated orbitopathy" OR "thyroid eye disease" OR "dysthyroid ophthalmopathy" OR "Graves ophthalmopathy" OR "Graves orbitopathy" OR "endocrine ophthalmopathy" OR "endocrine orbitopathy" OR exophthalmos OR "eyelid retraction") AND TS = ("artificial intelligence" OR "machine learning" OR "deep learning" OR "neural network" OR "decision tree" OR "back propagation" OR "support vector machine" OR "random forest" OR "eXtreme gradient boosting" OR "graph theoretical analysis" OR "principal component analysis" OR "logistic Regression" OR "linear discriminant analysis" OR "Markov chain Monte Carlo" OR "predictive model" OR "generative adversarial network" OR "image segmentation" OR "image processing"). The document types were restricted to journal articles, conference papers and reviews. The timespan was set from 1990 to 2023, and the final search was conducted on April 15, 2023.

The search strategy yielded 140 publications from WoS. The publications included for bibliometric analysis were restricted to those that (i) were written in English, (ii) involved TAO, and (iii) involved AI technologies. Two co-authors (L-XL and XZ) independently reviewed the title, abstract, and keywords of all retrieved studies for possible inclusion. Any disagreements were resolved through discussion with the senior author (X-BZ). After careful screening, 55 publications (41 journal articles, 9 conference papers and 5 reviews) were included for bibliometric analysis.

2.2. Data analysis

The summarized data, including the number of publications and citations of years, countries, institutions, research domains, and journals, were derived from the analytic tool of the WoS database. The bar chart of annual publications and annual citations was plotted using Microsoft Excel 2019. VOSviewer (version 1.6.19) was applied to visually analyze network maps of the collaboration among countries and institutions.[18] The plain text files of the publications and cited references were imported into VOSviewer to generate the initial keyword co-occurrence network. Then, the initial network was adjusted by merging synonyms and deleting meaningless keywords to a final version. The title, abstract and keyword data of publications were sorted into three groups by publication year, and the Word Cloud Python package was used to visualize the evolution of hotspots.[19] Similarly, the word cloud map was adjusted with synonyms merged and meaningless keywords deleted.

3. Results

3.1. Trends of publications and citations

Between 1990 and 2023, 55 publications on the topic of AI in TAO were identified from the WoS database. The trends of annual publications and citations on research on AI in TAO are shown (Fig. 1). The earliest literature in this field was published in 1998. From 1998 to 2016, a few studies were occasionally published, indicating that AI-related research on TAO was in its infancy. Between 2017 and 2020, the research on AI in TAO was at the exploratory development stage. However, the number of publications has increased rapidly since 2020, reaching 18 in 2022, six times that of 2020. In the past three years (January 1, 2021 – April 15, 2023), the cumulative number of publications accounted for 69.09% (38/55) of all publications. The number of citations grew slowly before 2017 but increased rapidly after 2020, showing a similar trend to that of publications.

Moreover, the top 10 publications ranked by annual citation count are listed in Table 1. All of them were journal articles, the majority (90.00%, 9/10) of which were published since 2017. The most influential article was by Wiersinga et al., in 2018, who constructed a predictive score for the development or progression of TAO in patients with newly diagnosed Graves' hyperthyroidism.[20] Meanwhile, the top 10 publications ranked by total citations are also noted in Table 1. The article by Terwee et al., in 2005, which measured disease activity to predict therapeutic outcome in TAO, was the first on the list,[21] followed by the article by Wiersinga et al., in 2018.[20]

3.2. Publishing performance and collaboration

In total, 20 countries and 101 institutions contributed to publications on AI in TAO. To explore the global geographical distribution of publications, the number of publications in each country was ranked. China (63.64%, 35/55) was found to be the most productive country, followed by the United States (12.73%, 7/55) and South Korea (10.91%, 6/55). In regard to institutions, Nanjing Medical University was detected as the most prolific institution (12.73%, 7/55), followed by Shanghai Jiao Tong University (10.91%, 6/55) and Sichuan University (9.09%, 5/55). Table 2 shows the 10 countries and 10 institutions with the most publications.

The collaboration networks among countries (17 countries included) and institutions (22 institutions included) are collected (Fig. 2). Turkiye had the highest number of collaborations with 13 countries, followed by Denmark, which collaborated with 12 countries. Belgium, England, Italy, and Netherlands all collaborated with 10 countries. Meanwhile, the University of Southern Denmark had the highest number of collaborations with 19 institutions, followed by the University Amsterdam, which collaborated with 16 institutions.

China has the most publications on AI in TAO. Thirty-five publications from China are listed in Table S2. The majority of these publications were focused on the diagnosis and prediction of treatment efficacy using CT images, MRI images, facial images, or other relevant clinical information. Four journal articles focusing on the diagnosis of TAO and the removal of patient-identifying information were published in collaboration with other countries. What's more, the data show that NSFC (36.36%, 20/55) was the top funding agency ranked by publication count, followed by National Key Research and Development Program of China (9.09%, 5/55) (Table S1).

3.3. Research domains and targeted sources

WoS subject categories were used to demonstrate the research domains of the included publications, as shown in Table 3. The top research domains of AI in TAO were radiology, nuclear medicine & medical imaging (21.82%, 12/55), endocrinology & metabolism (16.36%, 9/55), and ophthalmology (12.73%, 7/55).

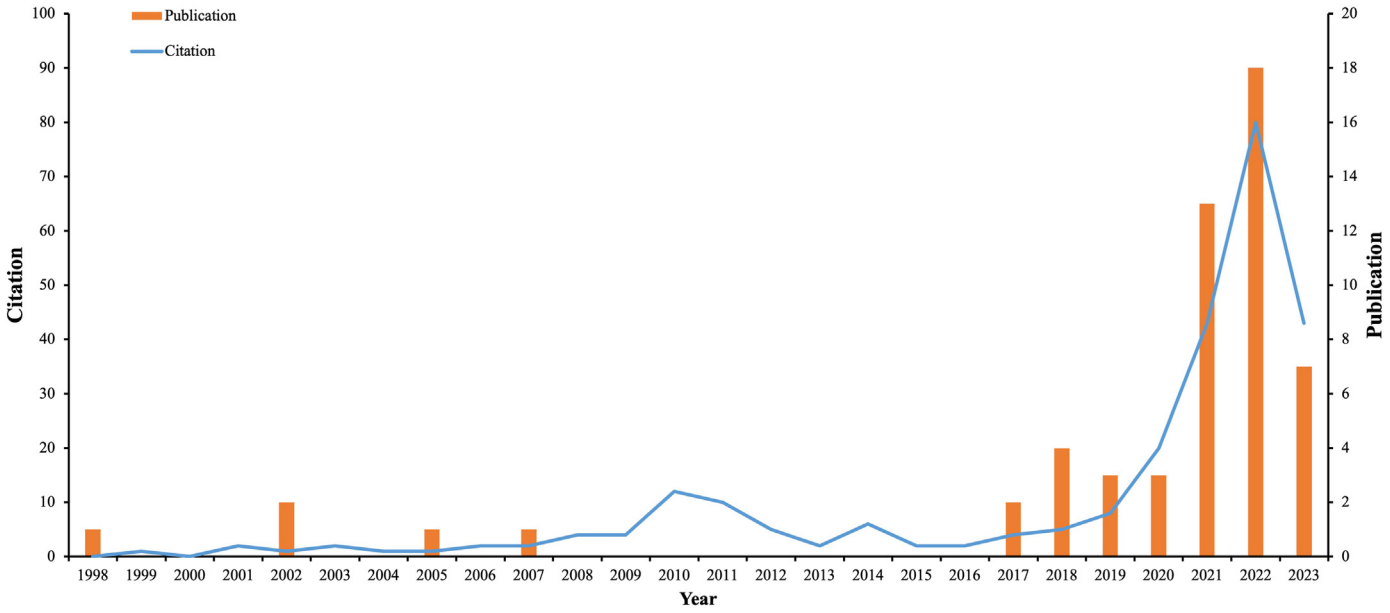

Fig. 1. Trends of publications and citations of artificial intelligence in thyroid-associated ophthalmopathy.

Table 1
Top publications ranked by annual citations and total citations.

References	Title	Year	C/Y	Source
Wiersinga et al.[20]	Predictive score for the development or progression of Graves' orbitopathy in patients with newly diagnosed Graves' hyperthyroidism	2018	5.17	European Journal of Radiology
Yoo et al.[25]	A generative adversarial network approach to predicting postoperative appearance after orbital decompression surgery for thyroid eye disease	2020	5.00	Computers in Biology and Medicine
Lin et al.[26]	Detection of active and inactive phases of thyroid-associated ophthalmopathy using deep convolutional neural network	2021	4.67	BMC Ophthalmology
Song et al.[31]	Artificial intelligence CT screening model for thyroid-associated ophthalmopathy and tests under clinical conditions	2021	3.50	International Journal of Computer Assisted Radiology and Surgery
Terwee et al.[21]	Measuring disease activity to predict therapeutic outcome in Graves' ophthalmopathy	2005	2.95	Clinical Endocrinology
Wu et al.[36]	Disrupted topological organization of the brain structural network in patients with thyroid-associated ophthalmopathy	2021	2.67	Investigative Ophthalmology & Visual Science
Hu et al.[37]	Multiscale attention U-net for segmenting clinical target volume in Graves' ophthalmopathy	2021	2.33	Neurocomputing
Huang et al.[8]	An intelligent diagnostic system for thyroid-associated ophthalmopathy based on facial Images	2022	2.00	Frontiers in Medicine
Wang et al.[32]	A single-center retrospective study of factors related to the effects of intravenous glucocorticoid therapy in moderate-to-severe and active thyroid-associated ophthalmopathy	2018	1.83	BMC Endocrine Disorders
Zhai et al.[33]	Prediction of treatment response to intravenous glucocorticoid in patients with thyroid-associated ophthalmopathy using T2 mapping and T2 IDEAL	2021	1.67	European Journal of Radiology

References	Title	Year	TC	Source
Terwee et al.[21]	Measuring disease activity to predict therapeutic outcome in Graves' ophthalmopathy	2005	56	Clinical Endocrinology
Wiersinga et al.[20]	Predictive score for the development or progression of Graves' orbitopathy in patients with newly diagnosed Graves' hyperthyroidism	2018	31	European Journal of Radiology
Salvi et al.[34]	Classification and prediction of the progression of thyroid-associated ophthalmopathy by an artificial neural network	2002	21	Ophthalmology
Yoo et al.[25]	A generative adversarial network approach to predicting postoperative appearance after orbital decompression surgery for thyroid eye disease	2020	21	Computers in Biology and Medicine
Lin et al.[26]	Detection of active and inactive phases of thyroid-associated ophthalmopathy using deep convolutional neural network	2021	20	BMC Ophthalmology
Song et al.[31]	Artificial intelligence CT screening model for thyroid-associated ophthalmopathy and tests under clinical conditions	2021	14	*International Journal of Computer Assisted Radiology and Surgery*
Wang et al.[32]	A single-center retrospective study of factors related to the effects of intravenous glucocorticoid therapy in moderate-to-severe and active thyroid-associated ophthalmopathy	2018	14	BMC Endocrine Disorders
Wu et al.[36]	Disrupted topological organization of the brain structural network in patients with thyroid-associated ophthalmopathy	2021	8	Investigative Ophthalmology & Visual Science
Hu et al.[37]	Multiscale attention U-net for segmenting clinical target volume in graves' ophthalmopathy	2021	7	Neurocomputing
Grus et al.[38]	Diagnostic classification of autoantibody repertoires in endocrine ophthalmopathy using an artificial neural network	1998	7	Ocular Immunology Inflammation

C/Y: citations per year; TC: total citations.

Table 2
Top countries and institutions ranked by publication count.

Country	Publications	% of publications	Citations	Average citation per publication
China	35	63.64%	107	3.06
USA	7	12.73%	32	4.57
South Korea	6	10.91%	23	3.83
England	4	7.27%	33	8.25
Germany	3	5.46%	94	31.33
Netherlands	3	5.46%	90	30.00
Italy	3	5.46%	54	18.00
Turkiye	3	5.46%	34	11.3
Belgium	2	3.64%	34	17
Denmark	2	3.64%	31	15.5
Institution (Country)	**Publications**	**% of publications**	**Citations**	**Average citation per publication**
Nanjing Medical University (China)	7	12.73%	17	2.43
Shanghai Jiao Tong University (China)	6	10.91%	45	7.50
Sichuan University (China)	5	9.09%	16	3.20
Huazhong University of Science Technology (China)	4	7.27%	9	2.25
Naval Medical University (China)	3	5.46%	22	7.33
Vanderbilt University (USA)	3	5.46%	5	1.67
Chung-Ang University (South Korea)	3	5.46%	3	1.00
University of London (England)	3	5.46%	2	0.67
University of Amsterdam (Netherland)	2	3.64%	87	43.50
Hubei University of Technology (China)	2	3.64%	1	0.50

Journals with no less than 2 publications are listed in Table 4. The most productive journals were the European Journal of Radiology, Frontiers in Cell and Developmental Biology and Scientific Reports. Meanwhile, Frontiers in Medicine and Proceedings of SPIE were remarkable due to their high number of citations.

3.4. Keywords analysis

To deeply understand the research topics and their interconnected network, the hotspots of the included publications were visualized using a keyword co-occurrence network (Fig. 3). Among a total of 189 identified keywords, 39 keywords that occurred at least twice are shown (Fig. 3). These keyworks were grouped into 2 major clusters. One cluster consisted of 23 keywords representing the clinical features and medical data of TAO (such as "therapeutic efficacy", "clinical activity score", "magnetic resonance imaging", and "CT imaging"), indicated by red color. The other cluster consisted of 16 keywords representing the AI techniques and applications (such as "deep-learning", "machine learning",

Table 3
The most related research domains ranked by publication count.

Research Domain (WoS categories)	Publications	% of publications	Citations	Average citation per publication
Radiology, Nuclear Medicine & Medical Imaging	12	21.82%	31	2.58
Endocrinology & Metabolism	9	16.36%	112	12.44
Ophthalmology	7	12.73%	55	7.86
Engineering, Biomedical	5	9.09%	35	7.00
Cell Biology	4	7.27%	3	0.75
Medicine, General & Internal	4	7.27%	3	0.75
Computer Science, Interdisciplinary Applications	3	5.46%	22	7.33
Mathematical & Computational Biology	3	5.46%	22	7.33
Multidisciplinary Sciences	3	5.46%	4	1.33
Developmental Biology	3	5.46%	1	0.33

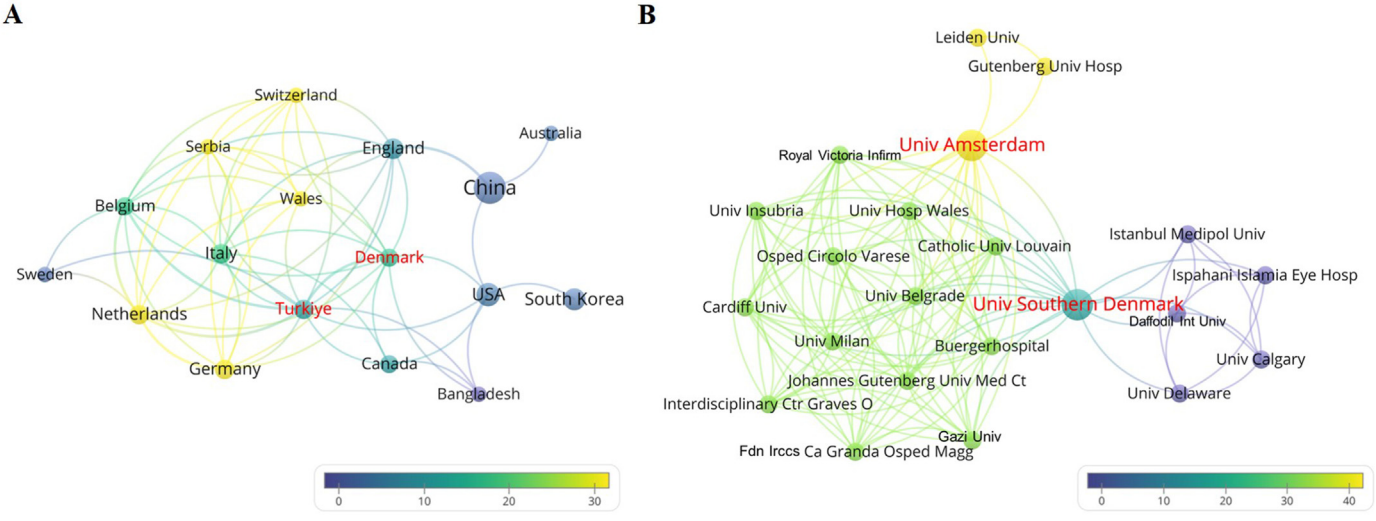

Fig. 2. Collaboration maps among countries (A) and among institutions (B). Circle size represents the number of publications; circle color represents average citations per publication; links represent collaboration.

Table 4
The most productive journals ranked by publication count.

Research Domain (WoS categories)	Publications	% of publications	Citations	Average citation per publication	Journal Citation Reports (2022)
European Journal of Radiology	3	5.46%	11	3.67	Q2
Frontiers in Cell and Developmental Biology	3	5.46%	11	3.67	Q1
Scientific Reports	3	5.46%	1	0.33	Q2
Frontiers in Medicine	2	3.64%	194	97.00	Q2
Proceedings of SPIE	2	3.64%	62	31.00	/
Thyroid	2	3.64%	3	1.50	Q1
Quantitative Imaging in Medicine and Surgery	2	3.64%	3	1.50	Q2
Clinical Endocrinology	2	3.64%	2	1.00	Q3

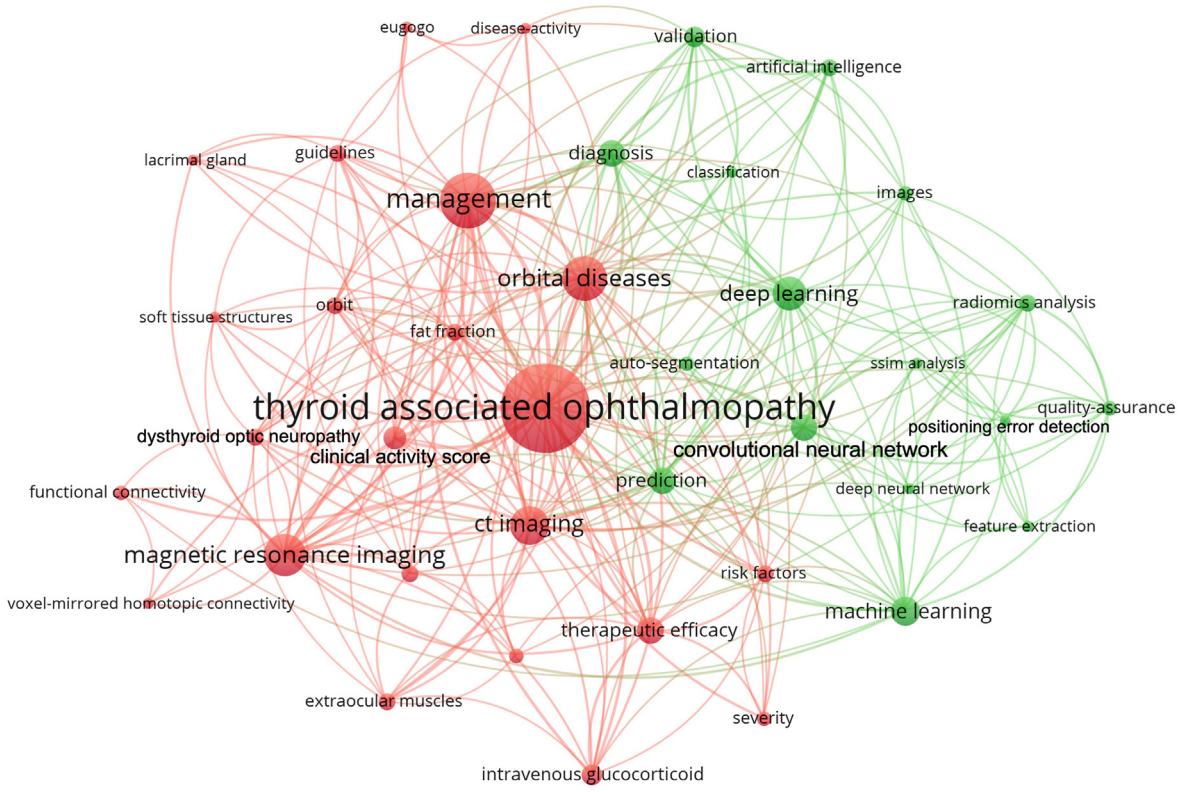

Fig. 3. Network of co-occurrence keyworks. Circle size represents the frequency of occurrence; links represent the co-occurrence; circles in the same color represent similarity among topics.

"diagnosis", and "prediction"), indicated by green. The keywords with closer relevance were identified by more links and shorter distances (Fig. 3).

The research on AI in TAO could be divided into 3 stages by publication date: (i) slow development stage: 1998–2016: (ii) exploratory development stage: 2017–2020; (iii) fast development stage: 2021–2023. Word cloud maps were used to visualize the evolution of hotspots (Fig. 4). Each map included the top 30 keywords ranked by the frequency of occurrence during each stage. "Thyroid-associated ophthalmopathy" was the most frequent keyword during the entire period. From 1998 to 2016, frequent keywords included "neural network", "patients", "extraocular muscle", "eye disease", and "progression". From 2017 to 2020, frequent keywords included "patients", "imaging", "therapy", "eye disease", and "neural network". From 2021 to 2023, frequent keywords included "patients", "neural network", "imaging", "deep learning", and "eye disease".

4. Discussion

A detailed bibliometric analysis of published research on AI in TAO was performed in this study based on the WoS database. Since the earliest literature was published in 1998, the number of publications in this field grew slowly before 2017, but with a significant acceleration of growth after 2020. Meanwhile, the growing number of citations indicated the increasing impact of the publications. The growing trends in publications and citations may be due to breakthroughs in AI technologies (e.g., convolutional neural networks and generative adversarial networks) and their wide applications in health care.[22,23] In addition, the improvements of examination techniques (e.g., MRI and CT) and treatment (e.g., immunotherapy) in recent years also have accelerated the research on AI in TAO.[24] After Wiersinga et al. published the most influential research in 2018,[20] many influential studies emerged, which is consistent with the development of AI technologies. For example, Yoo et al. proposed a generative adversarial network approach to predicting postoperative appearance after orbital decompression surgery in 2020,[25] followed by a deep convolutional neural network-based system for detecting the activity of TAO using MRI, which was proposed by Lin, CY et al., in 2021.[26]

Countries around the world have extensively participated in research on AI in TAO. In recent years, increasing attention has been given to the great potential of artificial intelligence in health care worldwide. The United States released the first version of the national artificial intelligence research and development strategic plan in 2016 and the updated

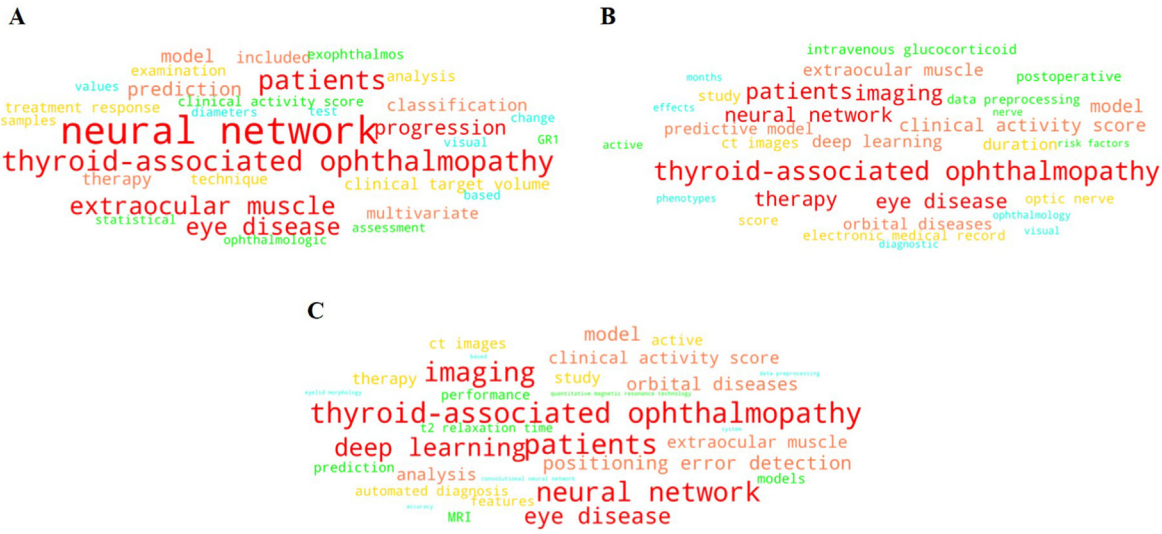

Fig. 4. Cloud maps of keywords during different periods: (A) 1998–2016; (B) 2017–2020; (C) 2021–2023. Font size represents the frequency of occurrence.

version in 2019,[27] with the goal of producing new AI knowledge and technologies that provide a range of positive benefits to society. In 2017, China released a development plan for the new generation of AI to seize strategic opportunities for AI development.[28] The National Natural Science Foundation of China (NSFC) not only supports basic research and fosters talented researchers, but also promotes socioeconomic development. In 2018, AI and cross-disciplinary information sciences were added into the Directorate of Information Sciences of NSFC to address the core scientific issues and key technologies in AI research field, meaning that researchers are eligible to apply funding from NSFC to AIresearch.[29] Sponsored by funding agencies such as NSFC and National Key Research and Development Program of China, China has become the most productive country in the field of AI in TAO, followed by the United States. A majority of the top institutions ranked by the number of publications are located in China. China, the world's most populous country, has a large number of patients with TAO and thus has a much higher number of studies. However, European countries have the most extensive collaboration. One possible reason is that European visa policy makes it easy for institutions to recruit researchers from other European countries. Another reason may be that the European Research Council provides a variety of opportunities for researchers from different European countries to cooperate.[30] AI technology is widely applied to extract ocular parameters and use these results for further assessment, such as diagnosis and predicting the treatment efficacy of TAO.[26,31–33] In addition, AI could predict the progression of TAO,[34] as well as postoperative appearance after orbital decompression surgery.[25] The various types of imaging data for TAO provide a large amount of training data for AI models. Since data are the lifeblood of AI, improving the usability of big data via collaboration between countries and institutions might be the next breakthrough in AI-related research on TAO.

Radiology, nuclear medicine & medical imaging were the top research domains of AI in TAO. It is easy to understand, because imaging techniques (such as MRI,[26] CT[31] and facial photography[25]) produce lots of valuable data on TAO patients, which are useful for developing AI technologies. It is worth noting that orbital MRI is more sensitive than clinical examinations in the evaluation of TAO and could become a biomarker of early asymptomatic inflammation.[35] Not surprisingly, the European Journal of Radiology was one of the most productive journals, with the most influential articles published in the field of AI in TAO. TAO research groups usually consist of endocrinologists, ophthalmologists, and radiotherapists. Thus, AI in TAO is a multidisciplinary research field in which interrelated domains such as endocrinology, ophthalmology, radiology, and computer science have a great contribution. In addition to journals that specialized in these domains, comprehensive journals such as Scientific Reports and Frontiers in Medicine were also productive in this field.

The frequently occurring keywords representing clinical features and medical data of TAO as well as AI techniques and applications always indicate research hotspots. By linking up the co-occurring keywords, the mainstream concepts in the field of AI in TAO are immediately visible, for example, "prediction" of "clinical activity score" based on "magnetic resonance imaging" using "deep-learning". The research on AI in TAO has gone through 3 stages of development. The evolution of hotspots was visualized on the word clouds referring to different stages. "Thyroid-associated ophthalmopathy" and "neural network" maintain hotspots during the entire period. Other hotspots have changed over time, including "extraocular muscle" and "progression" during 1998 and 2016; "imaging" and "therapy" during 2017 and 2020; and "imaging" and "deep learning" during 2021 and 2023. Studies were more focused on clinical features in the slow development stage, clinical features and medical data in the exploratory development stage, and medical data and AI techniques in the fast development stage. However, there are currently few TAO-related AI techniques approved for clinical use. Future research should focus on filling the gap between TAO-related AI research and clinical applications.

Several limitations should be noted in this study. First, WoS was the only scientific database for the collection of bibliometric data. Despite the fact that WoS is a comprehensive database offering a large number of multidisciplinary studies, it is likely that some potential publications indexed by other databases (such as Scopus, PubMed, or Google Scholar) were not included in this study. Second, our bibliometric analysis only covered literature published in English. Although the majority of WoS literature is in English, we might have missed relevant publications in other languages. Third, some keywords ranked as top keywords were not informative enough (such as "patients" and "eye disease") and did not refer to a deeper layer. Fourth, new research on AI in TAO might be published every month due to rapidly evolving AI technologies. Therefore, the results of this study only present the current state of the art in this field. Future studies are needed to explore more relevant research to enrich the literature.

5. Conclusions

This study provided an overview of the global research on AI in TAO. It was the first bibliometric analysis of this field, in which 55 scientific studies published between 1998 and 2023 were analyzed. The research

trends, publishing performance and collaboration among countries and institutions, research domains and targeted sources, and hotspots and their evolution were identified. The application of AI in TAO is a relatively new field, but there is no doubt that this field will rapidly move on driven by clinical demands, technological advances and funding supports. Sponsored by national or regional funding agencies, China has become the most productive country in the field of AI in TAO. NSFC will continue and increase the funding support for basic research and applications of AI in TAO. Our findings help researchers better understand the development of AI in TAO field and provide valuable clues for future research directions.

Study approval

Not Applicable.

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Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.aopr.2023.11.002.

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