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Bibliometric analysis of research trends and prospective directions in geographic atrophy secondary to Age-related macular degeneration

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Running title: Bibliometric analysis on GA in AMD

Abstract

Background: Age-related macular degeneration (AMD) is a leading cause of irreversible vision loss among middle-aged and older adults worldwide. Its dry late stage, geographic atrophy (GA), involves progressive loss of photoreceptor and retinal pigment epithelial cells in the central retina. This study presents a bibliometric analysis of current research on GA in AMD, examining publication trends, global collaboration patterns, and key topics.

Methold: Publications from 1975 to 2025 were retrieved from the Web of Science Core Collection (WoSCC) database.

Results: Among 2,623 publications, 66.26% were published between 2015 and 2025. The top institution was Rheinische Friedrich-Wilhelms-Universität Bonn (142 publications), followed by the National Eye Institute of the NIH (140) and the University of California, Los Angeles (129). Frank G. Holz was the most prolific author (534 papers). *Investigative Ophthalmology & Visual Science* was the most influential journal (272 publications). The most frequent search term was "retina" (149), followed by "optical coherence tomography" (139) and "drusen" (123).

Conclusion: This analysis maps the research landscape of GA secondary to AMD and highlights priority areas for future investigation. Although only WoSCC publications were included, its broad coverage and citation tracking ensured reliable results. These findings provide a foundation for future research and clinical applications.

Keywords: age-related macular degeneration, geographic atrophy, bibliometric analysis, VOSviewer, CiteSpace

1 Introduction

Age-related macular degeneration (AMD) is a leading cause of irreversible decline in vision among middle-aged and older people worldwide. In AMD, the choroid or pigment epithelium in the macular area of the fundus undergoes senescent changes due to aging, associated degeneration by inflammation, oxidative stress, smoking, retinal pigment epithelium (RPE) dysfunction, ultraviolet rays, and multiple other pathological mechanisms[1]. More than 190 million people worldwide are estimated to be affected by the disease, and this number is expected to double by 2050[2]. AMD is classified into two types: neovascular AMD (also called wet AMD [w-AMD]) and dry AMD (also called geographic atrophy [GA]), the latter representing the dry late stage of the disease and

characterized by the progressive loss of photoreceptor cells and retinal pigment epithelial cells in the fovea[3].

Blindness due to w-AMD has become much less common since the introduction of anti–vascular endothelial growth factor (VEGF) therapy in 2006[4], but GA continues to cause irreversible vision loss. Current treatment methods for GA include anti-VEGF intravitreal treatment, laser therapy, vision correction, medication, and surgery[5,6]. However, limitations such as limited therapeutic effects and high costs remain.

The severe vision impairment caused by AMD impacts patients' quality of life, resulting in a significant economic burden to society. Nevertheless, there has been a significant increase in research focusing on AMD throughout the years, warranting a comprehensive analysis. In this regard, "bibliometrics" refers to conducting quantitative analysis of publications using mathematical and statistical methods to explore the structure of scientific knowledge of a topic, development trends, and research hotspots[7]. Recently, Sun et al.[8] conducted bibliometric analysis in the field of neovascular AMD, including publication trends, keyword co-occurrence, international collaborations, and the top 10 most cited articles in the field. However, their review primarily concentrated on VEGF and anti-VEGF treatment in neovascular AMD; no study has conducted a bibliometric analysis of GA in AMD. Therefore, this analysis focused only on GA, and revealed the topics, research trends and knowledge map in GA .

2 Methods

2.1 Data collection and retrieval strategy

This study used the method of bibliometrics to analyzed the publications collected in the Web of Science Core Collection (WoSCC) database. The search was performed on April 20, 2025 using the following search strategy: [Topic (TS) = ("Macular Degeneration*" OR "Age Related Macular Degeneration" OR "Macular Dystrophies") AND TS = ("Geographic Atrophy" OR "Atrophy, Geographic")]. This process yielded 3,201 records for 1975–2025. After limiting the search to include only original articles and reviews written in English, 2,623 valid publications were included in the analysis. For next bibliometric analysis, we saved these documents in plain text file format. The analyzed content included titles, keywords, author information, abstracts, and references. The

data collection and retrieval strategy is illustrated in Fig.1.

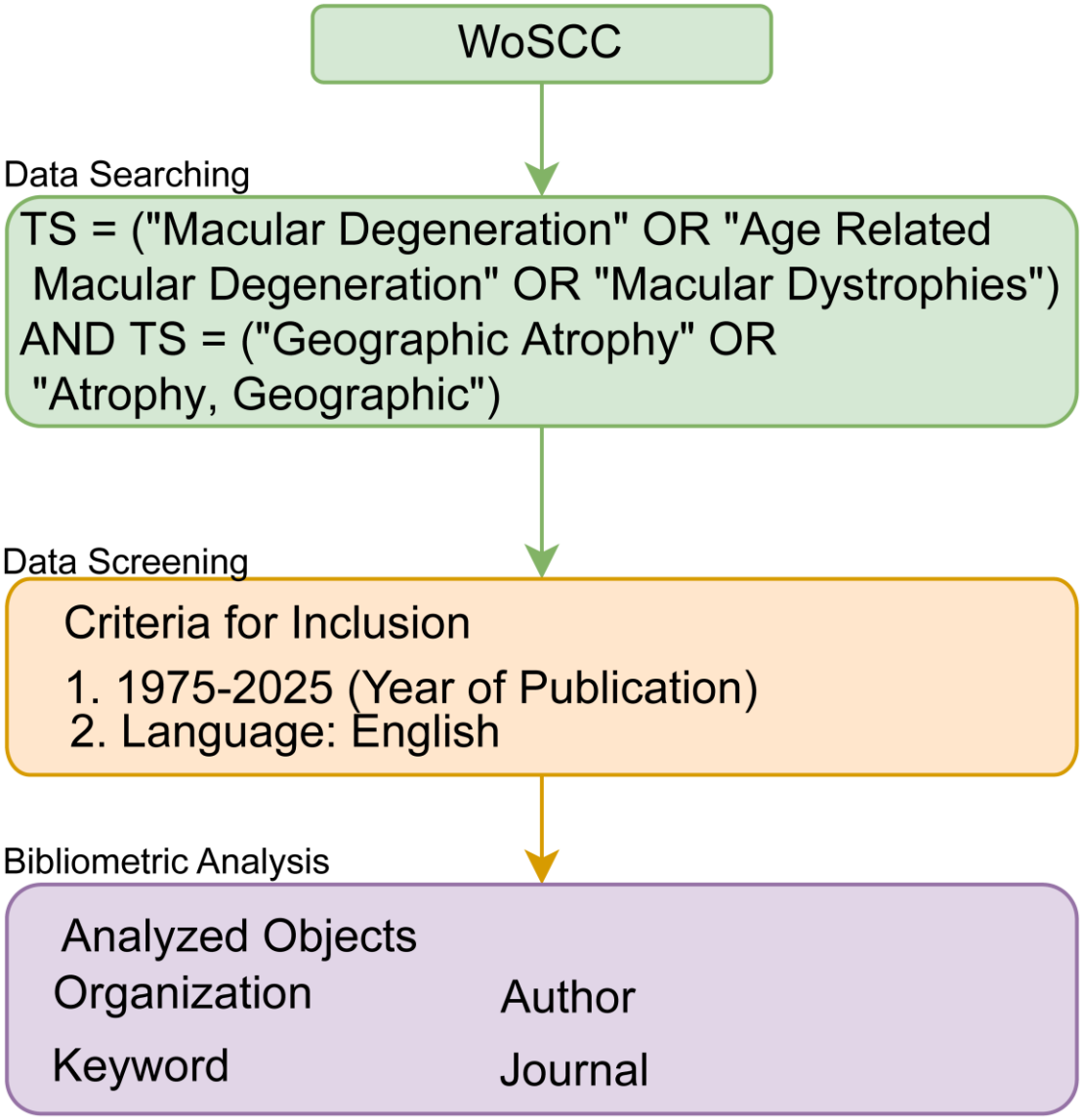

Fig.1 Flowchart for comprehensive analysis of age-related macular degeneration and geographic atrophy

WoSCC, Web of Science Core Collection; TS, Topic Search.

2.2 Data analysis

This study performed bibliometric analysis and visualization using VOSviewer (version 1.6.20)[9]. the number of publications and citations were counted based on the authors and the years by WoSCC. A visual bar chart was created by ggplot2 (version 3.5.1)[10]. Data extraction, author visualization, journals, institutional influence and collaborations, and keywords were analyzed using VOSviewer.

Set the method parameters to the association strength. The minimum publication thresholds for institutional influence and collaboration, author influence and collaboration, journals, and keywords were set at 15, 10, 5, and 10, respectively.

3 Results

3.1 Annual publication trends in GA

A total of 2,623 publications regarding GA in AMD, published between 1975 and 2025, were retrieved. Fig.2 shows the cumulative annual publications and annual publications in the field of GA in AMD. From 1975 to 2025, the cumulative annual number of publications increased from 1 to 2,623, with 66.26% of these published within the past 10 years (2015–2025). This indicates that researchers are paying increasing attention to GA.

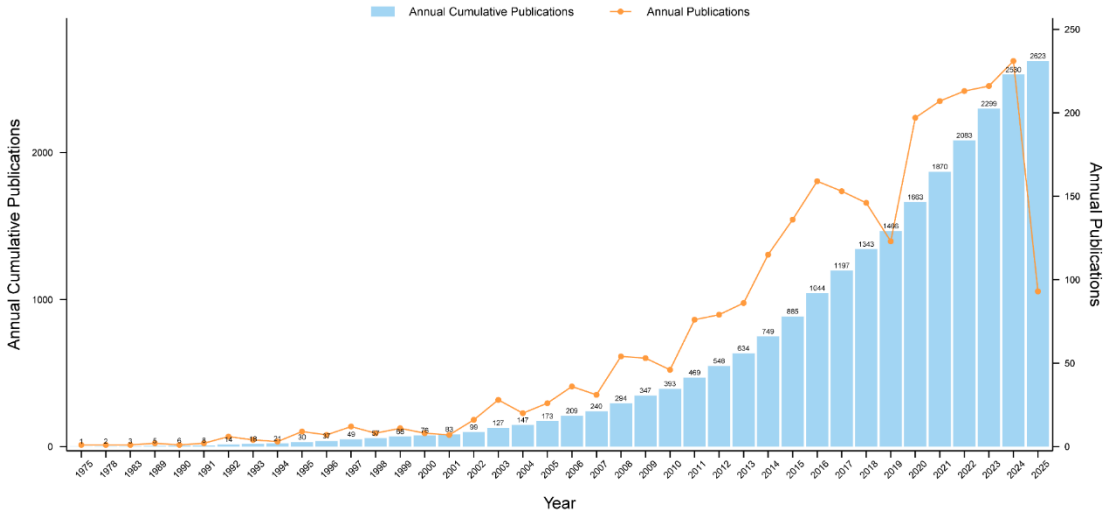

Fig.2 Analysis of annual publication trends in geographic atrophy

The annual cumulative number of publications (bar graph) and annual number of publications (dot plot) in the literature on GA in AMD. AMD, Age-Related Macular Degeneration; GA, Geographic Atrophy.

3.2 Institutional influence and collaboration analysis

We used VOSviewer (version 1.6.20) to conducted a bibliometric analysis and to identify institutions with significant influence and activity in research on GA in AMD. A total of 2,549 institutions contributed studies on GA, among which 90 met the minimum publication standards. Table 1 and Fig.3**a** show the top 10 institutions by publication volume. The top institution was

Rheinische Friedrich-Wilhelms-Universität Bonn, followed by the National Eye Institute of the National Institutes of Health and University of California, Los Angeles, with 142, 140, and 129 publications, respectively. In terms of total link strength (TLS), the top institution was University of California, Los Angeles (TLS = 381), followed by Rheinische Friedrich-Wilhelms-Universität Bonn (TLS = 338) and the National Eye Institute of the National Institutes of Health (TLS = 316). These institutions maintain close links with each other in research on GA (Fig.3**b**).

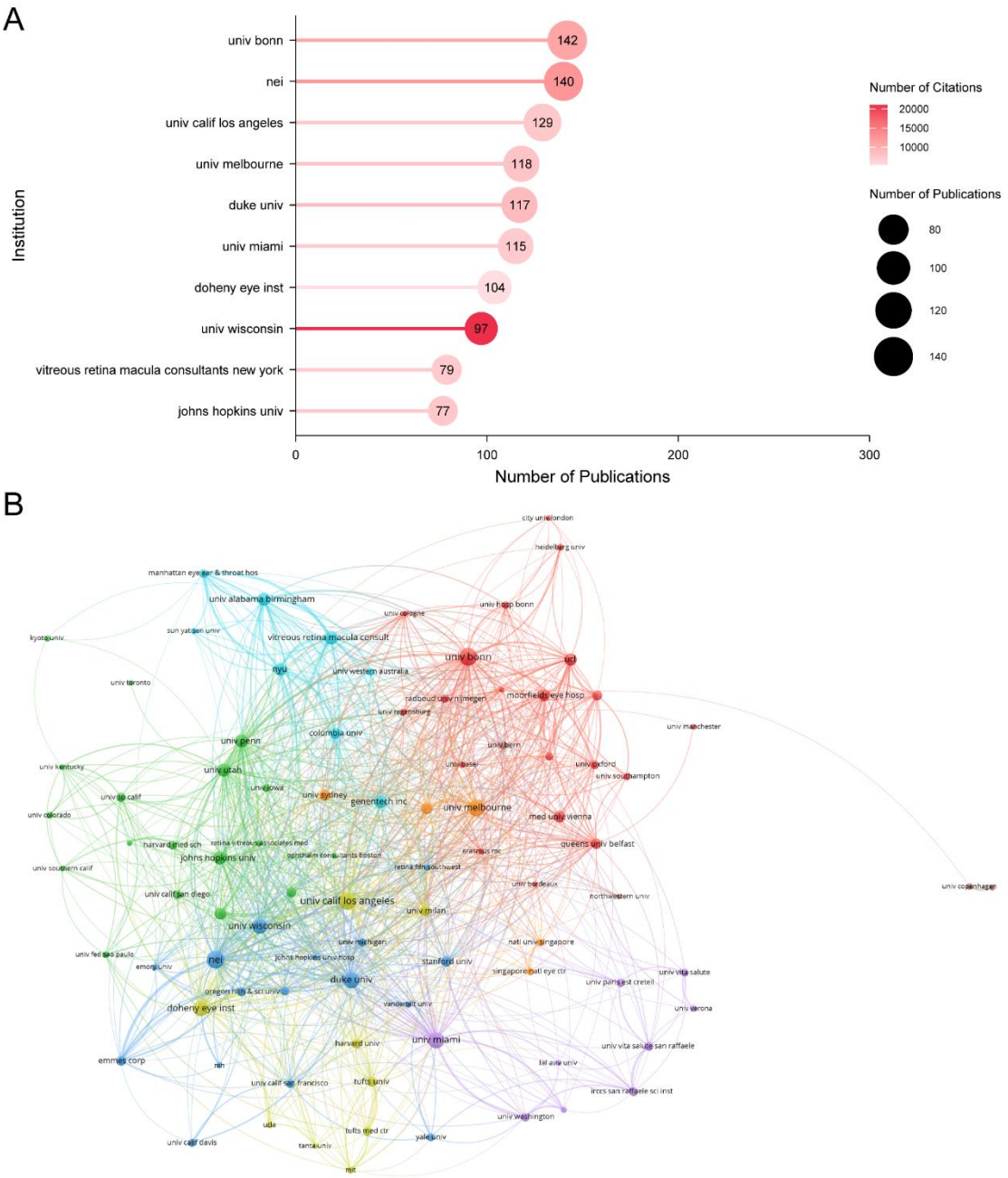

Fig.3 Analysis of institutional influence and collaboration

(a) Lollipop chart of the top 10 institutions in terms of publication volume. The size of the circle is

proportional to the number of publications: the redder the circle, the higher the citation frequency. (**b**) Cooperation network of universities with more than 15 publications. Nodes represent institutions, and node size corresponds to the number of publications of each institution. The node and line color represent a clustering relationship between institutions, and the thickness of the lines represents cooperation strength. Univ Bonn, Rheinische Friedrich-Wilhelms-Universität Bonn; NEI, National Eye Institute of the National Institutes of Health; Univ Calif Los Angeles, University of California, Los Angeles; Univ Melbourne, University of Melbourne; Duke Univ., Duke University; Univ Miami, University of Miami; Doheny Eye Inst, Doheny Eye Institute; Univ Wisconsin, University of Wisconsin; Vitreous Retina Macula Consultants New York, Vitreous Retina Macula Consultants of New York; Johns Hopkins Univ, Johns Hopkins University.

Table 1 Top 10 Institutions by Publication Volume

Rank	Institution	Number of publications	Number of citations	Total link strength
1	Rheinische Friedrich-Wilhelms-Universität Bonn	142	11,020	338
2	National Eye Institute of the National Institutes of Health	140	12,588	316
3	University of California, Los Angeles	129	7,554	381
4	University of Melbourne	118	7,885	269
5	Duke University	117	8,702	303
6	University of Miami	115	7,190	266
7	Doheny Eye Institute	104	5,322	258
8	University of Wisconsin	97	21,034	202
9	Vitreous Retina Macula Consultants of New York	79	7,201	274
10	Johns Hopkins University	77	7,353	148

3.3 Author influence and collaboration analysis

A bibliometric analysis was conducted to evaluate authors working on GA using VOSviewer (version 1.6.20), enabling the identification of prominent researchers and basic research trends. The

top 10 authors, as well as the number of publications and citations, are shown in Table 2 and Fig.4**a**. A total of 9,215 authors published studies on GA, of whom 194 met the minimum publication threshold, forming a collaborative network of 194 authors. Frank G. Holz had the highest number of publications, with 534 papers accounting for 20.36% of all publications. This author also had the highest number of citations, at 121 citations in total. Meanwhile, Srinivas R. Sadda had the highest link strength (TLS = 78) with other authors (Fig.4**b**).

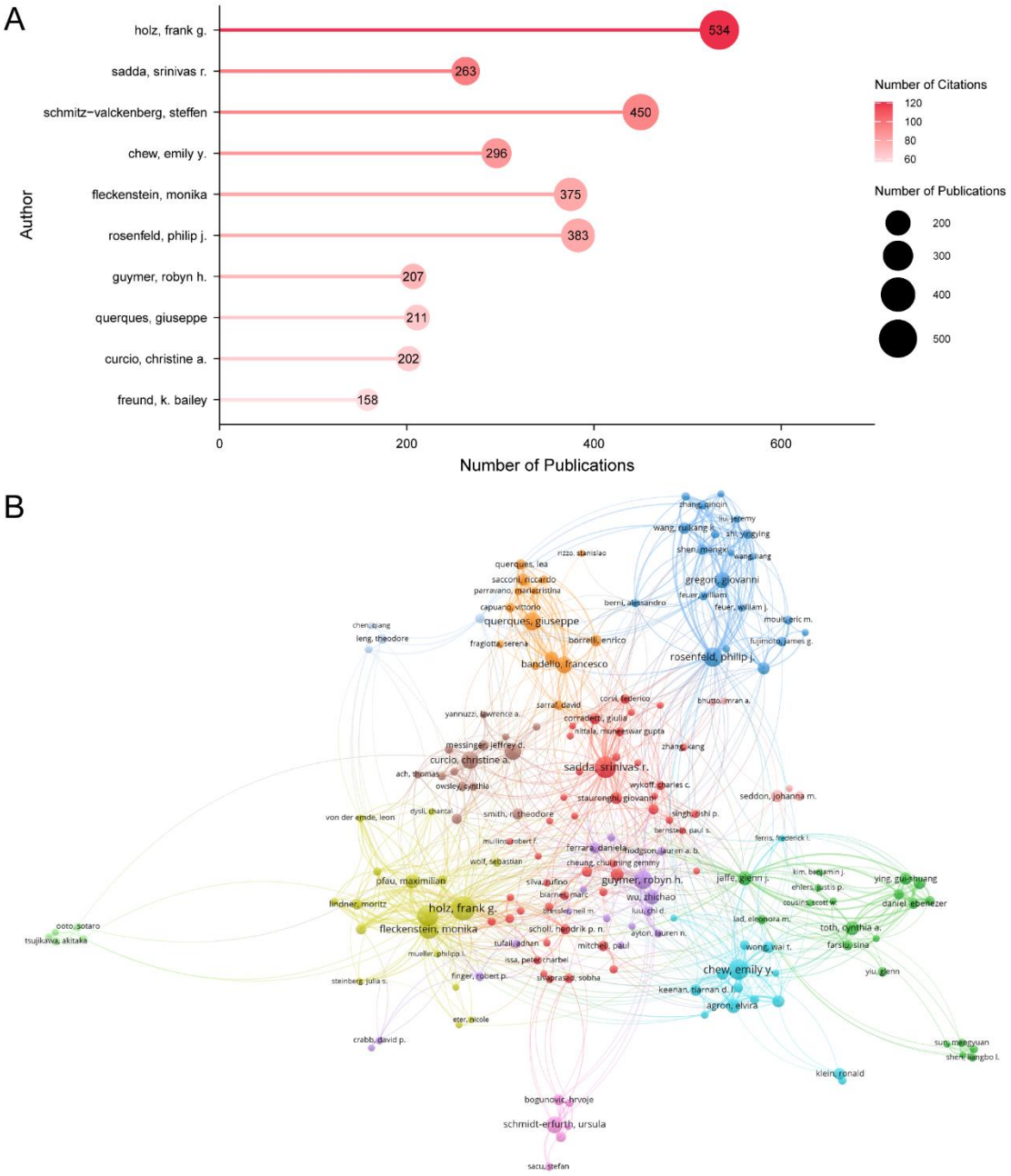

Fig.4 Analysis of author influence and collaboration

(a) Lollipop chart of the top 10 authors in terms of publication volume. B The size of the circle is

proportional to the number of publications; the redder the circle, the more frequently it is cited. (**b**) Cooperative networks of authors with more than 10 publications. The node represents the author, and the node size corresponds to the number of papers published by each author. The color of the node and the lines between represent the clustering relationship between authors, with the thickness of the line represents the link strength.

Table 2 Top 10 Authors by Publication Volume

Rank	Author	Number of publications	Number of citations	Tota llink strength
1	Holz, Frank G.	534	121	73
2	Sadda, Srinivas R.	263	96	78
3	Schmitz-Valckenberg, Steffen	450	93	62
4	Chew, Emily Y.	296	86	47
5	Fleckenstein, Monika	375	79	55
6	Rosenfeld, Philip J.	383	79	72
7	Guymer, Robyn H.	207	73	59
8	Querques, Giuseppe	211	66	27
9	Curcio, Christine A.	202	64	39
10	Freund, K. Bailey	158	57	47

3.4 Core journal analysis

We conducted a bibliometric analysis of journals to present an overview of journals' publication volume and influence in the field of GA using VOSviewer (version 1.6.20). As a result, there were 393 journals published articles related to GA, 69 journals had the publication volume greater than the minimum publication standards. Table 3 and Fig.5**a** present the top 10 journals in terms of publication volume. *Investigative Ophthalmology & Visual Science* had the largest number of

publications, followed by *Ophthalmology* and *Retina - The Journal Of Retinal And Vitreous Diseases*, with 272, 196, and 185 publications, respectively. The journals are color-coded based on their founding year. The yellow nodes represent journals with high publication volumes and high influence in recent years, such as *Nature Communication and Biomedicines* (Fig.5**b**).

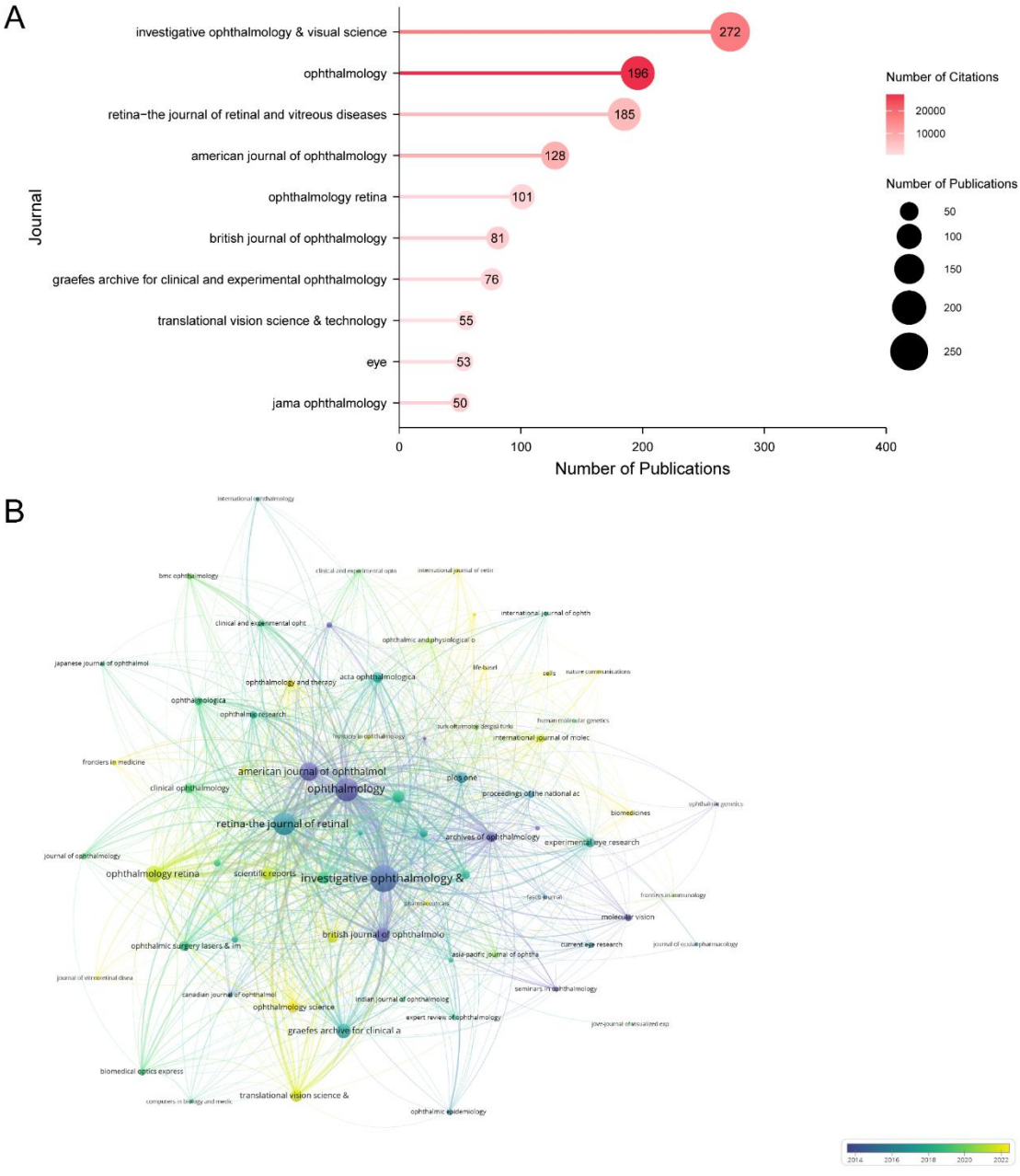

Fig.5 Impact analysis of journals

(a) Lollipop graph of the top 10 journals by publication volume. The size of the circle is proportional to the number of articles published; the redder the color, the higher the citation frequency. (**b**) Literature time distribution network graph of journals with more than five publications. The node

size is proportional to the number of articles published, and the colors of nodes and lines represent different publication years.

Table 3 Top 10 Journals by Publication Volume

Rank	Journal	Number of publications	Number of citations	Total link strength
1	*Investigative Ophthalmology & Visual Science*	272	17,003	6,160
2	*Ophthalmology*	196	27,209	8,047
3	*Retina - The Journal Of Retinal And Vitreous Diseases*	185	6,793	3,812
4	*American Journal Of Ophthalmology*	128	8,557	3,449
5	*Ophthalmology Retina*	101	2,043	2,338
6	*British Journal Of Ophthalmology*	81	3,438	1,529
7	*Graefes Archive For Clinical And Experimental Ophthalmology*	76	1,600	1,106
8	*Translational Vision Science & Technology*	55	620	881
9	*Eye*	53	1,183	1,075
10	*JAMA Ophthalmology*	50	2,835	1,233

3.5 Keywords analysis

We conducted a bibliometric analysis of keywords related to GA using VOSviewer (version 1.6.20) to depict research topics and future trends. A total of 2,950 keywords were identified, among them 116 met the minimum frequency threshold. The top 20 keywords were ranked in terms of frequency in Table 4 and Fig.6**a**. The most frequent search term was “retina” (N = 149), followed by “optical coherence tomography” (N = 139) and “drusen” (N = 123). Keywords in different node colour represent different domain,. The same color represents the same type of research content (Fig.6**b**).

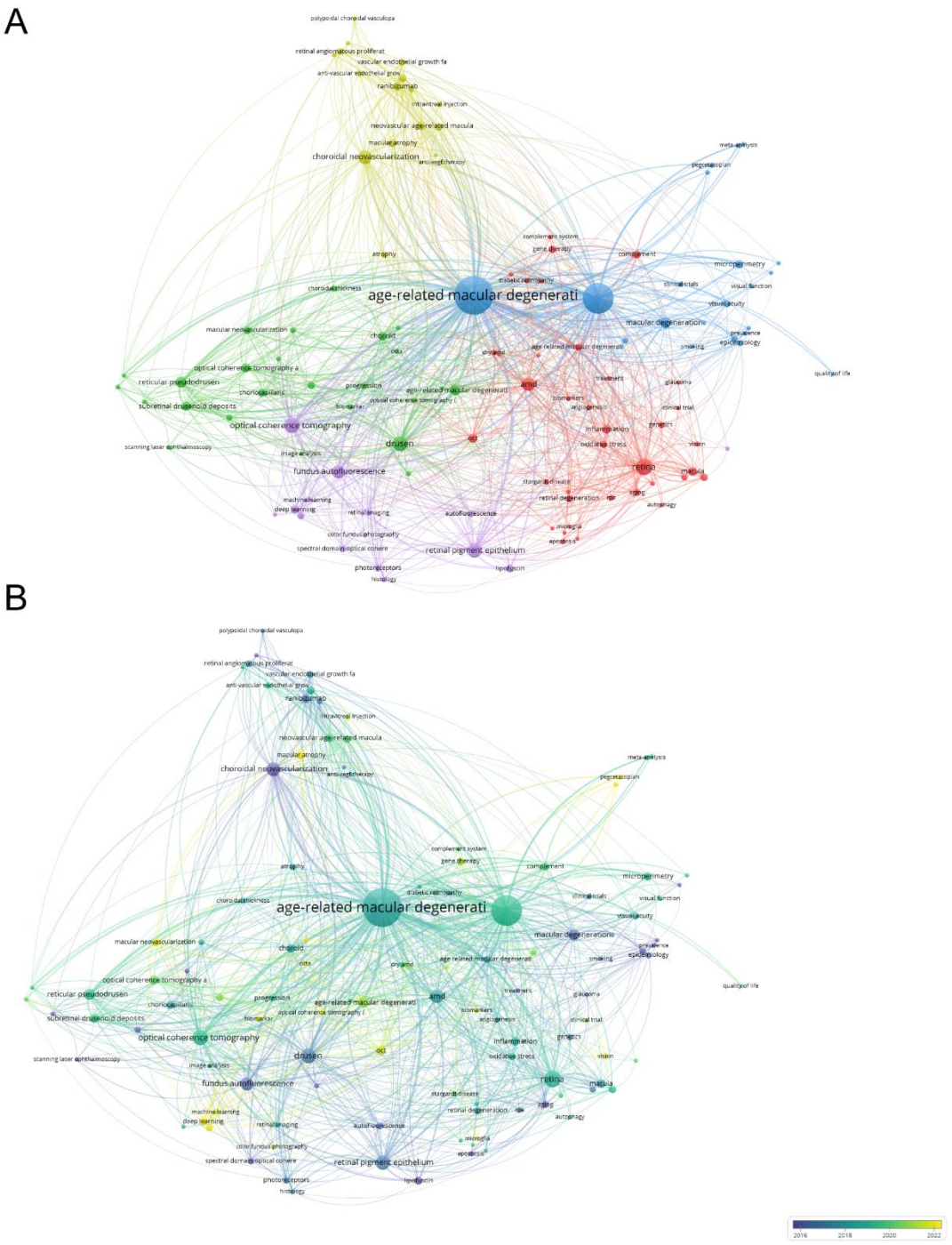

Fig.6 Keyword co-occurrence analysis

(a) Thermodynamic map of keyword co-occurrence network and (**b**) temporal distribution network with frequency > 10. Color intensity is directly related to the frequency of keywords in thermodynamics. Node size is proportional to the frequency of occurrence, and the node and line colors represent different domain.

Table 4 Top 20 Keywords in terms of Frequency

Rank	Keyword	Number of publications	Total link strength
1	Age-Related Macular Degeneration	842	1913
2	Geographic Atrophy	525	1,336
3	Retina	149	390
4	Optical Coherence Tomography	139	452
5	Drusen	123	412
6	Retinal Pigment Epithelium	118	349
7	Choroidal Neovascularization	107	339
8	Amd	103	238
9	Fundus Autofluorescence	102	282
10	Reticular Pseudodrusen	73	243
11	Macular Degeneration	70	135
12	Age-Related Macular Degeneration (amd)	56	89
13	Optical Coherence Tomography Angiography	49	160
14	Subretinal Drusenoid Deposits	45	169
15	Microperimetry	44	98
16	Neovascular Age-Related Macular Degeneration	44	120
17	Ranibizumab	44	154
18	Choroid	43	142
19	Inflammation	42	110
20	Oct	42	143

4 Discussion

This review focused on publications in the field of GA in AMD, a major cause of blindness among middle-aged and older adults and a significant public health challenge[11]. From 1975 to 2025, the annual publication rate of articles focusing on GA steadily increased. The cumulative annual number of publications increased to 2,623, among which 66.26% were published within the past 10 years (2015–2025). This indicates an increasing focus on GA, which could be attributed to the intensifying focus on drug and mechanism research.

According to our research, Western countries contribute the most studies on AMD. The top 10 institutions were all located in Western countries, and these leading institutions maintain close collaborations in AMD research. AMD, particularly cases resulting in visual impairment, is a common and frequently occurring disease in Western countries, especially in the United States. In

early 2004, approximately 54% of blindness cases in the United States were attributed to AMD[12]. Notably, the United States has registered a large number of randomized clinical trials on AMD and therefore holds a leading position in terms of publication volume[13,14]. Epidemiological studies have demonstrated significant differences in the incidence of AMD among ethnic groups, with a higher risk seen among White people compared with Black people[15]. The incidence of advanced AMD also significantly increases with age, as demonstrated by a meta-analysis of follow-up data from approximately 135,000 White people in Europe, Australia, and the United States[16].

A total of 9,215 authors published studies related to GA. Among them, Frank G. Holz was the most prolific, with the highest number of publications and citations. His team primarily focuses on machine learning, imaging diagnosis, and treatment of AMD, particularly the therapeutic effects on GA. He presented the 12-month results of the GALE open-label extension study (NCT04770545), which evaluated the 36-month intravitreal pegcetacoplan treatment for GA in AMD. The results showed that pegcetacoplan could reduce the growth rate of GA by 45%, and the efficacy increased after 30 months, with good safety[17]. Srinivas R. Sadda had the most close collaboration with other authors on GA according to our research. He focused on advanced retinal imaging and its applications for GA. He also studied the therapeutic effects of GA, a meta-analysis on the effect of complement C3 or C5 inhibition on GA secondary to AMD revealed that C3 and C5 inhibition likely to prevent the development of GA in a longtime observision[18].

A total 393 journals published articles on GA, among which 69 journals met the minimum publication threshold. In terms of publication volume, the highest-ranking journals were *Investigative Ophthalmology & Visual Science*, *Ophthalmology*, and *Retina - The Journal Of Retinal And Vitreous Diseases*. Therefore, these three classic ophthalmology journals represent indispensable resources for AMD studies. The content of these classic ophthalmology journals covers various aspects, including the pathogenesis, clinical diagnosis, and treatment of GA. They provide an excellent source for obtaining the latest research advancements.

Keywords are highly condensed expressions that summarize the research topic and core content of a research paper. Co-occurrence is defined as when two or more keywords appear in the same publication, and higher frequencies of keyword co-occurrence indicate stronger correlation between them. According the keywords analysis, we could clear the research directions and topics

of GA.Clustering analysis of VOSviewer's keywords produced five clusters, each cluster had a distinct color and represented different reasearch domian.

The red cluster's co-occurring keywords focus on diagnosis, autoimmune aspects, and various pathogenic mechanisms related to AMD. At present, diagnosing AMD is a relatively straightforward task,while the pathogenic mechanisms is still under investigation.The pathogenic mechanisms of AMD is multifactorial, including RPE dysfunction, oxidative stress, associated degeneration, chronic inflammatory responses, genetic susceptibility, and metabolic disorders [19-22]. These intricate interactied mechanisms highlight the necessity of continuing research to clarify the potential pathogenesis of AMD and to develop effective treatment methods.

The yellow cluster's keywords predominantly focus on the relationships among management, treatment, risk assessment, and various complications associated with AMD treatment. The conventional treatments for AMD include oral medication, photodynamic therapy, laser therapy and intravitreal injection...The research focuses echo these developments, focusing mainly on anti-VEGF therapy[23,24], anti-inflammatory therapy[25], stem cell therapy[26], gene therapy[27], and nanotechnology[11]. Intravitreal injection of anti-VEGF therapy is currently the most effective and widely used treatment for AMD. Most patients can improve their vision after 3 to 5 treatments. Some patients may experience recurrence after discontinuation of the medication. AMD cannot be cured completely, the best outcome would be to delay or prevent its progression[28]. Anti-VEGF therapy has limited efficacy due to AMD's diverse pathogenic mechanisms and the currently treatments only target one or two of these mechanisms, Furthermore the damaged visual cells that have already undergone apoptosis and necrosis cannot regenerate. Accordingly, recent research has focused on developing new therapies, such as higher concentration anti-VEGF drugs which can be long-acting, implantable devices similar to drug delivery ports that facilitate non-invasive multiple administrations, and gene-based treatments[28]. The purpose of these innovative treatments is to achieve better therapeutic effects while reducing the number of injections required by patients and minimizing the possible surgical complications. These advancements represent promising avenues for long-term treatment of AMD. Meanwhile, drugs used for treating other diseases such as metformin and fenofibrate have showed potential effects to slow the progression of AMD . However, the specific effectiveness and mechanisms still requires further experimental verification[29]. However, these have a limited therapeutic effect on GA because atrophy of the outer layer of the

retina, choroid, and RPE, as well as other physiological barriers, result in decreased drug permeability, reduced bioavailability, and shortened drug residence time. Nevertheless, other novel therapies (e.g., gene therapy, stem cell therapy, etc.) have all shown potential. In GA, research increasingly focuses on therapeutic effects. For instance, intravitreal pegcetacoplan treatment and C3 and C5 inhibitior for GA can reduced the GA growth rate[17-18]

In AMD, drug delivery is usually limited by the intraocular barrier (i.e., blood–retinal barrier, RPE, choroid, and sclera), which greatly prevented the drugs from reaching the affected area. The current administration routes mainly included local eye drops; intravitreal, subretinal, and microneedle injection; systemic administration. However, these traditional routes have limitations in terms of targeting and efficacy[30-31]. Consequently, designing an improved drug administration method represents a crucial research hotspot.

The green and purple clusters' keywords predominantly focus on advanced retinal imaging and its applications for AMD. With technological advancements, ophthalmic equipment has become increasingly sophisticated. Currently, several instruments can be used in clinical practice for fundus examination, including optical coherence tomography, fundus fluorescein angiography, optical coherence tomography angiography, and fundus autofluorescence. These modalities are not only used for diagnosing AMD but can also serve as screening tools for detecting certain biomarkers at an early stage[32].

The blue cluster's keywords predominantly focus on disease classification, quality of life, social burden, and some of the treatment methods currently under investigation. Blindness due to neovascular AMD has become much less common since the introduction of anti-VEGF therapy in 2006[33], but GA remains one of the more common causes of irreversible vision loss. Although no treatment for GA has been approved to date in Europe, intravitreal complement inhibitors—approved and available in the United States since 2023—can significantly slow the progression of the GA area[34]. This treatment, however, cannot halt the disease or improve vision. Furthermore, the need for repeated long-term treatments is burdensome for patients and their families and poses a challenge for physicians and the healthcare system.

The treatment of GA in AMD faces numerous challenges. Aside from concerns regarding the development of novel intravitreal injection drugs and innovative remedies, there are also challenges posed by treatment effectiveness, economic pressure, and social pressure. This review

comprehensively summarizes the status and progress of research on this topic, providing insights for future research in the field.

5 Limitations

Our study conducted a bibliometric analysis of GA in AMD, revealing cooperative relationships among authors, institutions, journals, topics and clarifying development trends,,and future directions in this field. However, the study is limited due to the following factors.

First, this study only utilized publications from the WoSCC database, excluding other databases such as PubMed and Scopus . This concern is mitigated by the high coverage rate of the WoSCC database, with the overall trends not significantly affected. Second, as this study only included articles written in English, valuable insights from studies written in other languages may have been overlooked. Third, although bibliometric analysis is considered objective, the researchers' understanding of diseases may influence the results of the data. To overcome these comprehension limitations, the inputs of other researchers are needed as well.

6 Conclusion

This study conducted a bibliometric analysis of research on GA from the WoSCC database, providing an overview of the global scientific research landscape from 1975 to 2025. The increasing annual publication rate and the leading research bodies indicate that this field is in a stage of vigorous development. Nevertheless, to reach even greater heights, it is necessary to overcome obstacles such as uneven resource distribution and actively explore new opportunities for interdisciplinary integration.

Declarations

Ethics approval and consent to participate

I confirm that all methods were performed in accordance with the relevant guidelines. This work has been carried out in accordance with the Declaration of Helsinki (2000) of the World Medical Association. This study was approved by the Medical Ethics Committee of Nanchong Central Hospital (Ethics Approval Number: 2023 Review No.

089), and all participants provided written informed consent.

Consent for publication

Not applicable.

Availability of data and materials

All data generated or analyzed during this study are included in this article and supplementary information files.

Competing interests

The authors declare that they have no competing interests.

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Authors' contributions

Lan Wang carried out the studies, participated in collecting data, and drafted the manuscript. Yi Lu performed the statistical analysis and participated in its design. Lan Wang, Yi Lu and Hui Tang participated in acquisition, analysis, or interpretation of data and draft the manuscript. All authors read and approved the final manuscript.

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