• Bibliometric Research •

A bibliometric and visualized analysis of choriocapillaris from 2013 to 2023

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Abstract

● **AIM:** To assess the current research status and emerging trends of the choriocapillaris (CC) by bibliometric analysis.

● **METHODS:** Publications spanning from January 2013 to May 2023 were retrieved on June 27th, 2023, using the Web of Science Core Collection. Bibliometric and visualized analyses were performed employing the bibliometrix, CiteSpace and VOSviewer.

● **RESULTS:** A total of 1563 papers met the inclusion criteria, and a publication growth trend was observed. The United States was the leading country in the CC field. *Retina* and *Investigative Ophthalmology & Visual Science* stood out as highly impactful and prolific journals. Research topics in the CC field encompassed choroidal neovascularization, choroidal thickness, central serous chorioretinopathy, age-related macular degeneration, myopia, choroidal vascularity index, and diabetic retinopathy, based on the co-citation analysis. The keyword "high myopia" experienced a burst lasting until 2023.

● **CONCLUSION:** In the past decade, research in the field of CC has flourished due to recent advancements in choroidal imaging; with focus shifting towards elucidating its role in various diseases. This will provide novel insights into managing chorioretinal diseases and vision-preserving interventions.

● **KEYWORDS:** bibliometric; choriocapillaris; age-related macular degeneration; optical coherence tomography angiography

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INTRODUCTION

The choriocapillaris (CC), a dense vascular network located in the innermost layer of the choroid, features lumens that exceed the intercapillary septa in volume. The endothelial cells of CC exhibit fenestrations, especially on their inner surface. The retinal pigment epithelium (RPE)/Bruch's membrane (BM)/CC complex is considered an indissociable unit. The CC plays a pivotal role in vision by nourishing outer retinal cells and facilitating their function through waste removal[1]. In animal models, modifications of the CC potentially involved in choroidal thickening as a compensatory mechanism for myopic defocus[2].

The alteration of CC is implicated in the pathogenesis of various chorioretinal diseases. The recent increase in CC-related publications is partially attributed to advancements in imaging technologies, including optical coherence tomography (OCT) and OCT angiography (OCTA). These innovations provide novel possibilities for evaluating CC and improving diagnosis and management in clinical practice[2-3].

Bibliometric analysis is widely used to explore and analyze vast scientific data, uncovering evolutionary nuances and emerging trends within specific fields. It employs two primary techniques: performance analysis to evaluate the contributions of research entities, and science mapping to discern the interconnections among these entities[4]. The past decade has witnessed the emergence of bibliometrics as an essential tool for analyzing scientific research in the field of ophthalmology[5-6]. However, no bibliometric investigations have focused on the CC. Our objective was to conduct a comprehensive bibliometric analysis to evaluate the present status and trends of this field.

MATERIALS AND METHODS

Data Collection Literature retrieval was conducted using the Web of Science Core Collection (WoSCC). To minimize the impact of database updates, the retrieval and data extraction were performed on June 27th, 2023. The search formula employed was: TS="choriocapillar*" OR TS="choroidal capillar*". Publications dated from January 1, 2013 to May 31, 2023, were included. Articles or review articles written in English were included, excluding early access, proceeding papers, and book chapters. Relevance to the study was

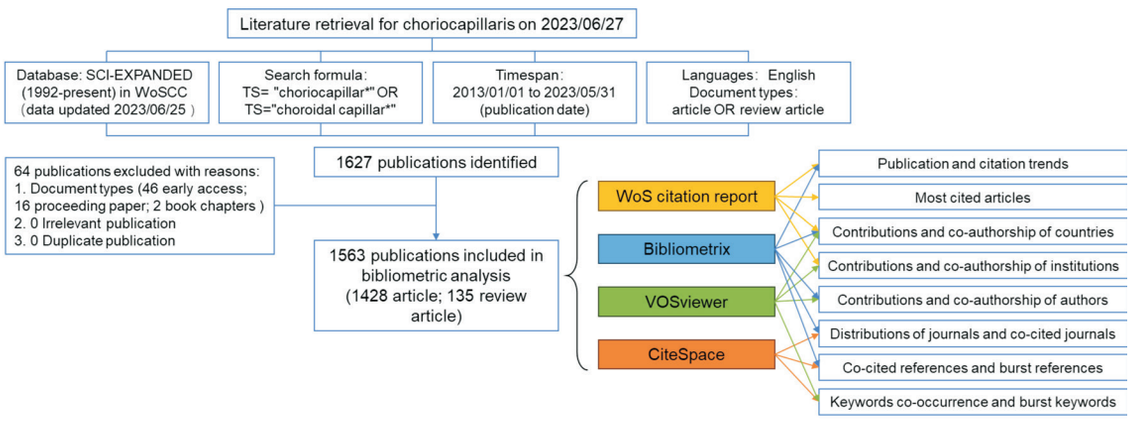

Figure 1 Flowchart of literature retrieval, screening, bibliometric analysis and data visualization.

assessed by screening titles, abstracts and keywords. The relevant literature was exported as full record and references, in plain text file format for subsequent analysis. The flowchart of literature retrieval, screening, bibliometric analysis and data visualization is shown in Figure 1.

Data Analysis The bibliometrix R package (4.1.2)[7], CiteSpace (version 6.2.R4 Advanced)[8] and VOSviewer (version 1.6.18)[9] were used to conduct the bibliometric analysis and data visualization. The bibliometrix R package, an open-source tool for comprehensive science mapping analysis that can be integrated with other statistical R packages[7], was utilized to analyze publication trends, article citations, contributions of countries and authors, distributions of journals, as well as co-citation of journals and references. The citation trend, countries' publication trend, most cited articles, and institutions' contributions were generated from the citation reports of Web of Science. Additionally, the journal impact factor (JIF) was obtained from Journal Citation Reports 2022.

VOSviewer is a software tool for constructing and visualizing bibliometric networks[9]. It was utilized to visualize the co-authorship network and keywords co-occurrence network. CiteSpace, a Java-based bibliometric software, designed for analyzing emerging trends within a knowledge domain[8], was applied to generate dual-maps overlay of journals, detect bursts in keywords and references, and conduct co-citation analysis of references.

The aforementioned analysis was preceded by the removal of duplicates using CiteSpace and cleaning the data. Regions within a country were manually merged. Synonymous keywords were merged, and variations in names referring to the same author, institution, or country were integrated. These steps were carried out independently by two researchers (Wei PY and Wang XZ). Any discrepancies that arose during data processing were resolved through discussion and consensus-building facilitated by a third researcher (Han JM).

RESULTS

Publication and Citation Trends A total of 1563 papers met the inclusion and exclusion criteria, accumulating a total of 29 704 citations (22 095 without self-citations) and yielding an H-index of 76. From 2013 to 2022, both the number of publications and citations within WoSCC has increased, as illustrated in Figure 2A. The average citations of the articles in each year and those adjusted by the citable year are shown in Figure 2B. Furthermore, 57 papers were published in 2015 garnering 3145 citations, boasting the highest average article citations (55.2) and average article citations per year (6.9).

Most Cited Articles Among 1563 documents on CC, 1428 were articles and 135 were review articles. The 10 most cited articles are listed in Table 1, with Jia *et al*'s[10] publication leading the list. This article demonstrated the ability of OCTA to detect and measure diverse vascular pathologies, boasting 480 total citations (TC; citations within WoSCC) and 76 local citations (LC; citations within the current dataset on choriocapillaris from 2013 to 2023).

Contributions and Co-authorship of Countries A total of 59 countries contributed to the CC field. The top 15 most productive countries are presented in Table 2, with USA leading in the number of publications and H-index, followed by Italy. The trend of annual publications for the top 8 most productive countries is shown in Figure 3A. The country co-authorship overlay visualization map is shown in Figure 3B. In VOSviewer, the node size reflects the number of documents or keyword occurrences, while the link width indicates link strength, measured by the number of co-authorships or co-occurrences. Notably, USA exhibited the highest total link strength, followed by Italy and China. The link strengths between these two countries and USA were the strongest. Additionally, USA had a relatively early average publication year.

Contributions and Co-authorship of Institutions Figure 4A displays institutions with at least 36 publications and the top 10 with the highest TC. Vita-Salute San Raffaele University led in the number of publications, followed by University of California Los Angeles (UCLA) and Doheny Eye Institute.

Table 1 The 10 most cited articles

Title	First/corresponding author	Journal	Year	TC	LC
Quantitative optical coherence tomography angiography of vascular abnormalities in the living human eye	Jia YL/Huang D	*P Natl Acad Sci U S A*	2015	480	76
The impact of oxidative stress and inflammation on RPE degeneration in non-neovascular AMD	Datta S/Handa JT	*Prog Retin Eye Res*	2017	379	17
Pachychoroid disease	Cheung CMG	*Eye*	2019	318	51
Retinal vascular perfusion density mapping using optical coherence tomography angiography in normals and diabetic retinopathy patients	Agemy SA/Rosen RB	*Retina*	2015	318	47
Ginsenoside Rg-1 protects retinal pigment epithelium (RPE) cells from cobalt chloride ($CoCl_2$) and hypoxia assaults	Li KR/Jiang Q	*PLoS One*	2013	302	0
En face imaging of pachychoroid spectrum disorders with swept-source optical coherence tomography	Dansingani KK/Freund KB	*Retina*	2016	254	61
Choriocapillaris flow features follow a power law distribution: implications for characterization and mechanisms of disease progression	Spaide RF	*Am J Ophthalmol*	2016	237	189
A paradigm shift in imaging biomarkers in neovascular age-related macular degeneration	Schmidt-Erfurth U	*Prog Retin Eye Res*	2016	219	4
Choriocapillaris and choroidal microvasculature imaging with ultrahigh speed OCT angiography	Choi W/Fujimoto JG	*PLoS One*	2013	215	93
Quantitative retinal optical coherence tomography angiography in patients with diabetes without diabetic retinopathy	Dimitrova G	*Invest Ophth Vis Sci*	2017	214	36

RPE: Retinal pigment epithelium; AMD: Age-related macular degeneration; OCT: Optical coherence tomography; TC: Total citations; LC: Local citations.

Table 2 Top 15 countries with the most publications

Countries	*n*	MCP rate	LC	TC	H-index
USA	521	51.1%	4408	15499	61
Italy	269	46.1%	1518	4485	36
China	268	33.6%	866	3996	31
Germany	124	58.1%	1034	3818	34
Türkiye	117	6.0%	115	583	13
Japan	106	29.2%	586	2592	27
UK	101	74.3%	478	2200	27
South Korea	89	18.0%	364	1574	21
France	65	63.1%	360	1416	22
India	61	54.1%	139	839	17
Switzerland	57	93.0%	164	864	15
Spain	47	36.2%	113	633	15
Singapore	44	88.6%	231	1214	18
Australia	34	73.5%	67	686	12
Austria	33	72.7%	161	857	14

n: Number of publications; MCP: Multiple-country publication; LC: Local citations; TC: Total citations.

Regarding citations, Vitreous Retina Macula Consultants of New York ranked first, trailed by UCLA and Massachusetts Institute of Technology (MIT). VOSviewer generated institutions co-authorship maps (Figure 4B-4C). UCLA emerged with largest total link strength and number of links, followed by Vitreous Retina Macula Consultants of New York. Notably, institutions from USA and Europe tend to cooperate more extensively with domestic or international institutions.

Contributions and Co-authorship of Authors Figure 5A presents the important scholars who have published at least 30 publications or are among the top 10 with the highest TC or LC. The three most prolific scholars were Bandello F, Querques G, and Borrelli E from Vita-Salute San Raffaele University, followed by Sadda SR from UCLA and Wang RK from University of Washington, Seattle. In terms of TC, Duker JS from Tufts University ranked first, followed by Freund KB from Vitreous Retina Macula Consultants of New York and Fujimoto JG from MIT. For LC, Sadda SR ranked first, followed by Duker JS and Borrelli E. VOSviewer was used to generate authors co-authorship maps and categorize authors into clusters (Figure 5B-5C). Authors primarily affiliated with American institutions such as UCLA (Cluster 1), along with those from Vita-Salute San Raffaele University and other European institutions (Cluster 2 and 5), demonstrated strong collaborations. Centrally positioned, Borrelli E had numerous links with these authors as well as those from University of G. D'Annunzio (Cluster 6). Freund KB had established connections across most clusters. Authors from Tufts University and MIT (Cluster 7) also engaged in productive cooperations. In contrast, some authors from University of Washington, Seattle, University of Miami (Cluster 3), University of Iowa (Cluster 8), Johns Hopkins University (Cluster 9), and Asian institutions (Cluster 4) tended to collaborate with local or specific research teams over global partners.

Distributions of Journals and Co-cited Journals The articles were published in 226 academic journals. The top 10 most productive and cited journals are presented in Table 3, with the majority falling under the category of ophthalmology.

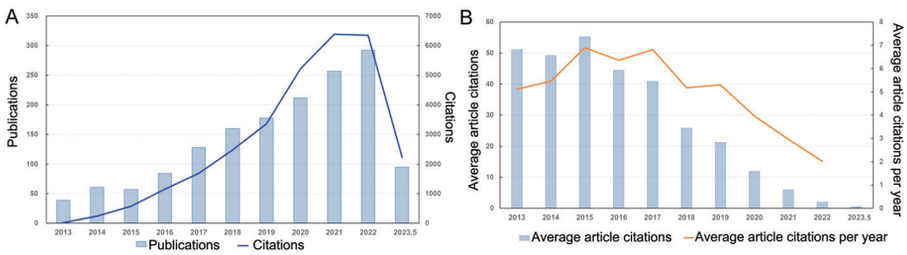

Figure 2 Publication and citation trends A: Trend of yearly publications and citations; B: Average article citations and average article citations per citable year. Citable year is calculated by subtracting the publication year from 2023.

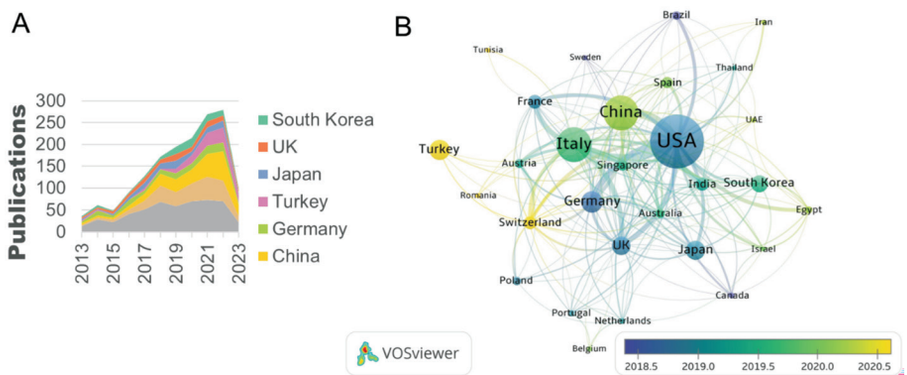

Figure 3 Contributions and co-authorship of countries A: The annual publications of the top 8 productive countries; B: Countries co-authorship overlay visualization map based on the average publication year of countries with at least 6 articles. Layout parameters: Attraction=2, Repulsion=-1.

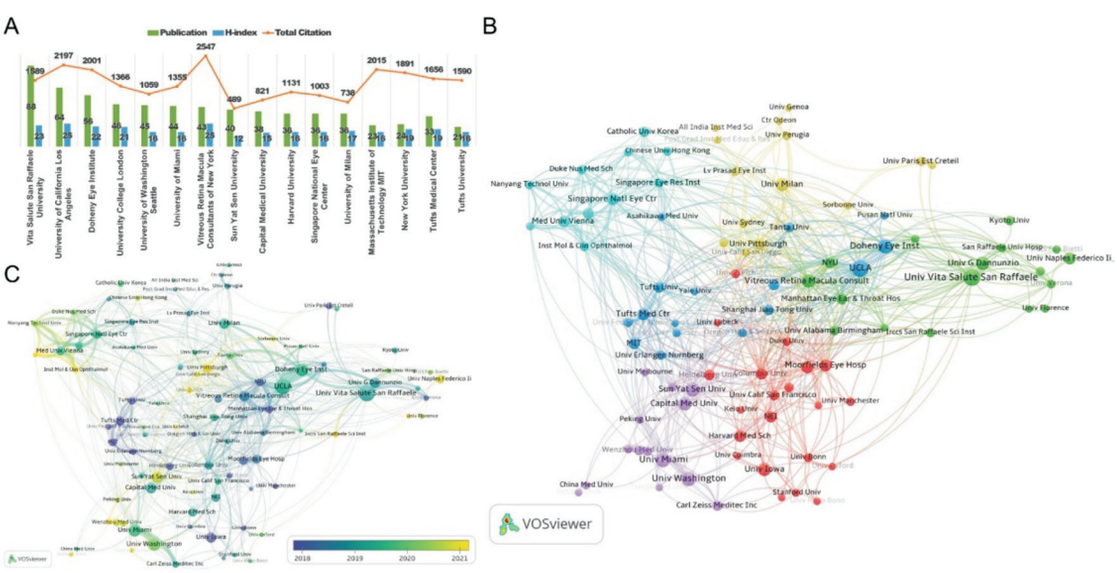

Figure 4 Contributions and co-authorship of institutions A: The publications, H-index and total citations of important institutions. B: Clustering institutions co-authorship network visualization map of institutions with at least 8 articles. Layout parameters: Attraction=2, Repulsion=0; Clustering parameters: resolution=1, Min. cluster size=8. C: Institutions co-authorship overlay visualization map based on the average publication year.

Retina and *Invest Ophthalmol Vis Sci* exhibited the largest numbers of publications and citations, and were the most frequently referenced journals in the CC field. *Prog Retin Eye Res* and *Ophthalmology* ranked among the top 10 most cited journals, boasting a high JIF. A dual-map overlay revealed three core citation paths in the distribution of academic disciplines and their citation relationships (Figure 6).

Co-cited References and Burst References The top 10 cited references are presented in Table 4, with the study by Spaide *et al*[11] published in 2016 ranking first, cited 189 times in the current dataset. Co-cited references refer to the literature cited together in the reference list of another article. Analysis of co-citation references was generated by CiteSpace (Figure 7). CiteSpace uses the time slicing technique to construct a series

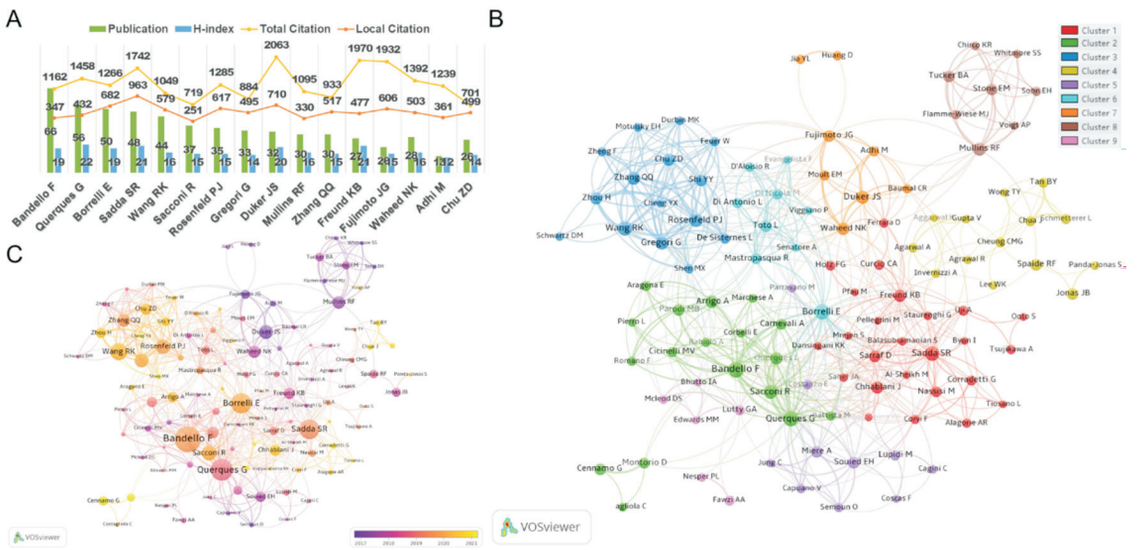

Figure 5 Contributions and co-authorship of authors A: The publications, H-index, total citations and local citations of important authors. B: Clustering authors co-authorship network visualization map of authors with at least 7 articles. Layout parameters: Attraction=4, Repulsion=-3; Clustering parameters: resolution=1, Min. cluster size=5. C: Authors co-authorship overlay visualization map based on the average publication year.

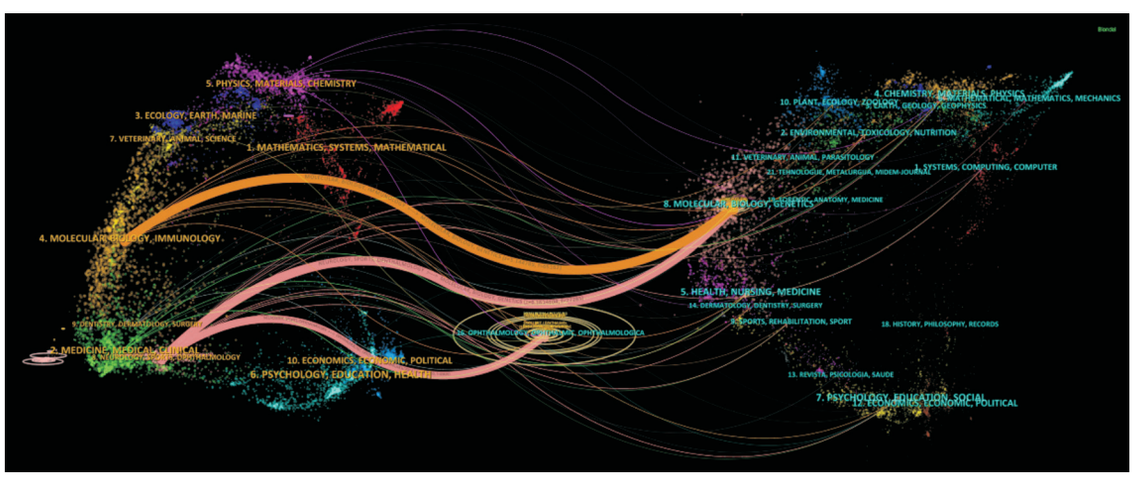

Figure 6 Dual-map overlay analysis of journals The citing journals are on the left, and the cited journals are on the right. The thick lines represent the core citation paths.

Table 3 Top 10 most productive journals and top 10 most cited journals of publications

Journal	*n*	TC	H-index	JIF2022	Cited journal	Citation	JIF2022
Retina	131	3126	32	3.3	*Invest Ophthalmol Vis Sci*	7645	4.4
Invest Ophthalmol Vis Sci	100	3508	32	4.4	*Retina*	4818	3.3
Graefes Arch Clin Exp Ophthalmol	83	1241	22	2.7	*Am J Ophthalmol*	4503	4.2
Am J Ophthalmol	63	2280	29	4.2	*Ophthalmology*	4127	13.7
Sci Rep	62	687	16	4.6	*Br J Ophthalmol*	2405	4.1
Ophthalmic Surg Lasers Imaging Retina	53	794	14	1.0	*Prog Retin Eye Res*	1607	17.8
Br J Ophthalmol	51	1404	24	4.1	*Graefes Arch Clin Exp Ophthalmol*	1586	2.7
PLoS One	50	1420	20	3.7	*Arch Ophthalmol*	1501	-
J Clin Med	46	210	8	3.9	*PLoS One*	1368	3.7
Eur J Ophthalmol	42	193	9	1.7	*Eye*	1131	3.9

n: Number of publications; TC: Total citations; JIF: Journal impact factor.

of networks of cited references over time and then combines them into an overview network. The synthesized network is further divided into clusters. Citers to these references are considered as the research fronts associated with these clusters. Each cluster represents the intellectual base of the underlying specialty[8]. The eight largest clusters are illustrated in Figure 7B. The cluster labels, extracted through the LLR algorithm from keywords, encapsulate the research themes in

Table 4 The 10 most cited references

Title	Citations	First/corresponding author	*Journal*	Year
Choriocapillaris flow features follow a power law distribution: implications for characterization and mechanisms of disease progression	189	Spaide RF	*Am J Ophthalmol*	2016
Split-spectrum amplitude-decorrelation angiography with optical coherence tomography	180	Jia YL	*Opt Express*	2012
Relationship between RPE and choriocapillaris in age-related macular degeneration	176	McLeod DS/Lutty GA	*Invest Ophth Vis Sci*	2009
Retinal vascular layers imaged by fluorescein angiography and optical coherence tomography angiography	165	Spaide RF	*JAMA Ophthalmol*	2015
Optical coherence tomography angiography	164	Spaide RF	*Prog Retin Eye Res*	2018
Morphometric analysis of Bruch's membrane, the choriocapillaris, and the choroid in aging	155	Ramrattan RS/de Jong PT	*Invest Ophth Vis Sci*	1994
Choriocapillaris vascular dropout related to density of drusen in human eyes with early age-related macular degeneration	150	Mullins RF	*Invest Ophth Vis Sci*	2011
Image artifacts in optical coherence tomography angiography	149	Spaide RF	*Retina*	2015
A novel strategy for quantifying choriocapillaris flow voids using swept-source OCT angiography	138	Zhang QQ/Wang RK	*Invest Ophth Vis Sci*	2018
The multifunctional choroid	131	Nickla DL	*Prog Retin Eye Res*	2010

RPE: Retinal pigment epithelium; OCT: Optical coherence tomography.

this field, encompassing choroidal neovascularization (CNV), CC, choroidal thickness (CT), central serous chorioretinopathy (CSC), age-related macular degeneration (AMD), myopia, choroidal vascularity index (CVI), and diabetic retinopathy (DR). Betweenness centrality highlights potential pivotal points of paradigm shift over time[8]. The reference published by Mullins *et al*[12] in 2011, located in Cluster 4, had the highest betweenness centrality. The timeline view in Figure 7C illustrates clusters depicted horizontally over time, with "myopia" cluster emerging relatively late. Citation burst detection can identify emerging trends. Cluster 0, 2 and 1 had the most burst references, indicating that they were active topics[8]. The article "Relationship between RPE and choriocapillaris in age-related macular degeneration"[13] ranked first among the top 20 references with the strongest citation bursts (Figure 7D). Furthermore, the papers "Quantification of choriocapillaris with Phansalkar local thresholding: pitfalls to avoid"[14] and "Correlations between choriocapillaris flow deficits around geographic atrophy and enlargement rates based on swept-source OCT imaging"[15] had sustained bursts until 2023.

Keyword Co-occurrence and Burst Keywords Based on Author Keywords and WoSCC-identified Keywords Plus, we analyzed the keywords to reveal research hotspots. Co-occurrence visualization of both Author Keywords and Keywords Plus is illustrated in Figure 8A-8B, highlighting the three most prevalent ones: CC, OCTA and OCT. The keywords were divided into four groups, as depicted in Figure 8A. The large clusters concentrated on imaging and treatment of chorioretinal diseases (Cluster Red), the application of OCTA (Cluster Green), and the pathobiology underlying macular degeneration (Cluster Blue). The overlay visualization map indicated that the green cluster was relatively emerging (Figure 8B). Additionally, the Author Keywords burst detection identified eighteen bursts. As shown in Figure 8C, "AMD" demonstrated the greatest strength, while the burst for "high myopia" persisted until 2023.

DISCUSSION

CC supplies oxygen and nutrients to the outer retinal cells, playing a role in the pathogenesis of chorioretinal diseases. With the help of bibliometrics, comprehensive research status and potential trends can be noted. To our knowledge, this is the first bibliometric investigation dedicated to exploring CC-related research.

General Information In the past decade, there has been a surge in publications and citations regarding CC, with 1563 papers being published across 226 academic journals. Average annual citations reveal an extensive impact of articles published between 2015 and 2017. During this period, 7 out of the 10 most cited articles were published, covering topics such as quantitative vascular analysis[10,16], CC flow characteristics on OCTA[11], and novel OCT technologies[17]. We propose that recent increase in publications can be partially attributed to the advancements in imaging technology.

USA maintained a prominent position in CC research, evidenced by the highest number of publications and citations. Although USA initially dominated the field overwhelmingly, Asian and European countries including Italy, China and Germany have gradually caught up. China and Turkey, despite high productivity, exhibited relatively lower H-index, highlighting a need to improve research quality. Meanwhile, USA has fostered strong international collaborations, particularly with China, Italy, and Germany.

USA has numerous renowned universities. UCLA has engaged in extensive collaborations, yielding significant research on CC from various perspectives[2-3,18]. Similarly, the Vitreous Retina Macula Consultants of New York has fostered

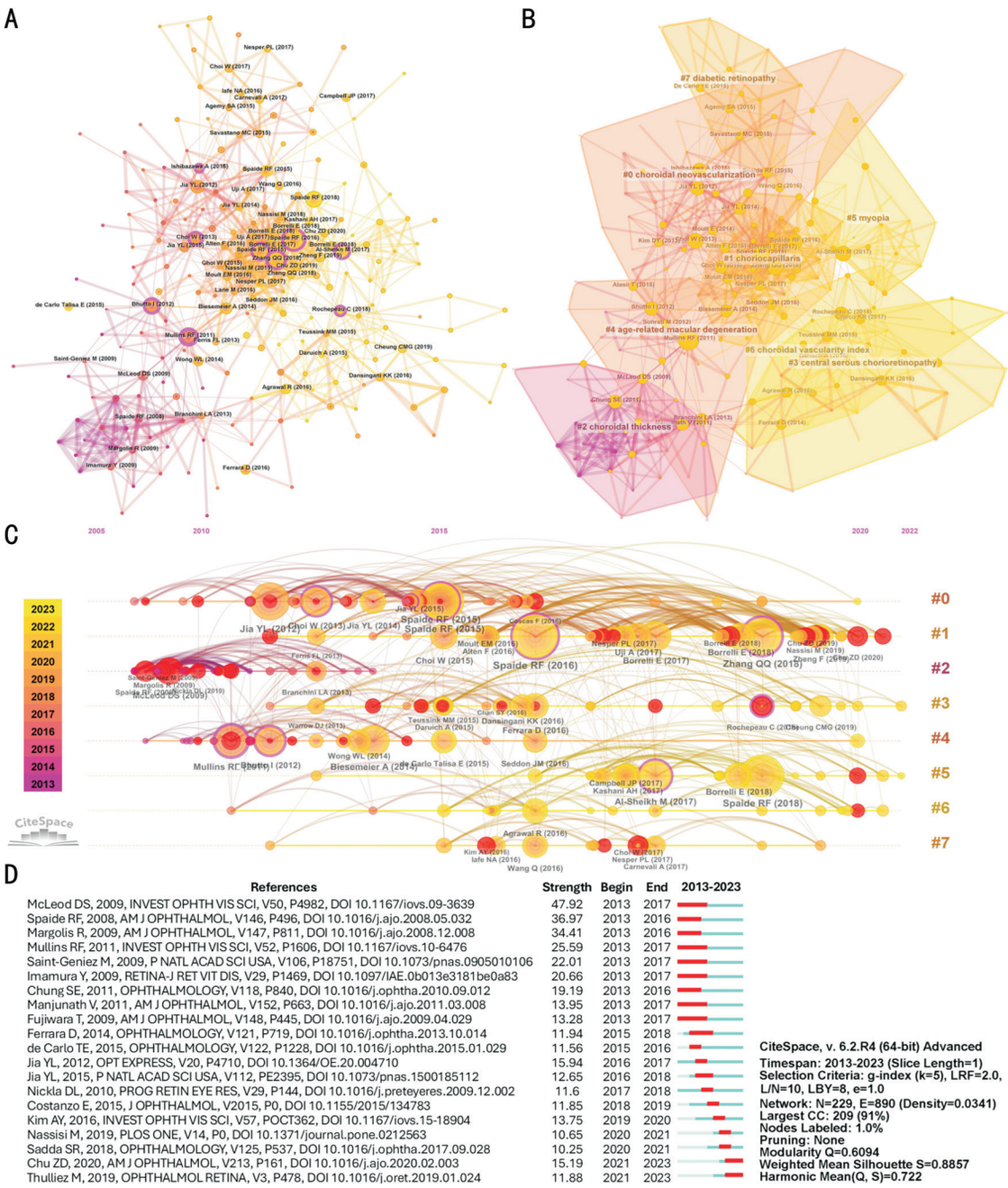

Figure 7 Analysis of co-citation references A: Network visualization map of co-citation references. Link color signifies the year of first co-citation. Node size reflects citation frequency, and tree rings depict the citations over time. Nodes with high betweenness centrality are outlined in purple. B: Clustering visualization map of the co-citation references. Node size reflects betweenness centrality. C: Timeline visualization map of the co-citation references. Nodes exhibiting burst characteristics are highlighted in red on the corresponding ring. Burstness parameters: α1/α0=3, with default settings for other parameters. D: Top 20 references with the strongest citation bursts. Parameters for the co-citation analysis are listed on the right.

global collaborations, achieving numerous citations, with contributions from scholars such as Freund[2,17,19]. Scholars from University of Iowa have extensively studied CC in normal health and aging, including employing single-cell RNA sequencing to characterize gene expression patterns specific to CC[1,20]. Pioneering research in angiography of CC using OCT has been conducted by scholars from Tufts University and Fujimoto JG from MIT[21-23]. Some noteworthy studies have been conducted by scholars from University of Washington, Seattle and University of Miami recently[14-15,24]. Moreover, an Italian institution, Vita-Salute San Raffaele University has conducted extensive research focusing on the application of OCTA to study retinal and choroidal vessels[25-26].

Other institutions from Europe or Asia, including University College London, Sun Yat-Sen University, Capital Medical University, Singapore National Eye Center, and University of Milan, have demonstrated interest in this field. Chinese scholars rarely appeared in the co-authorship network,

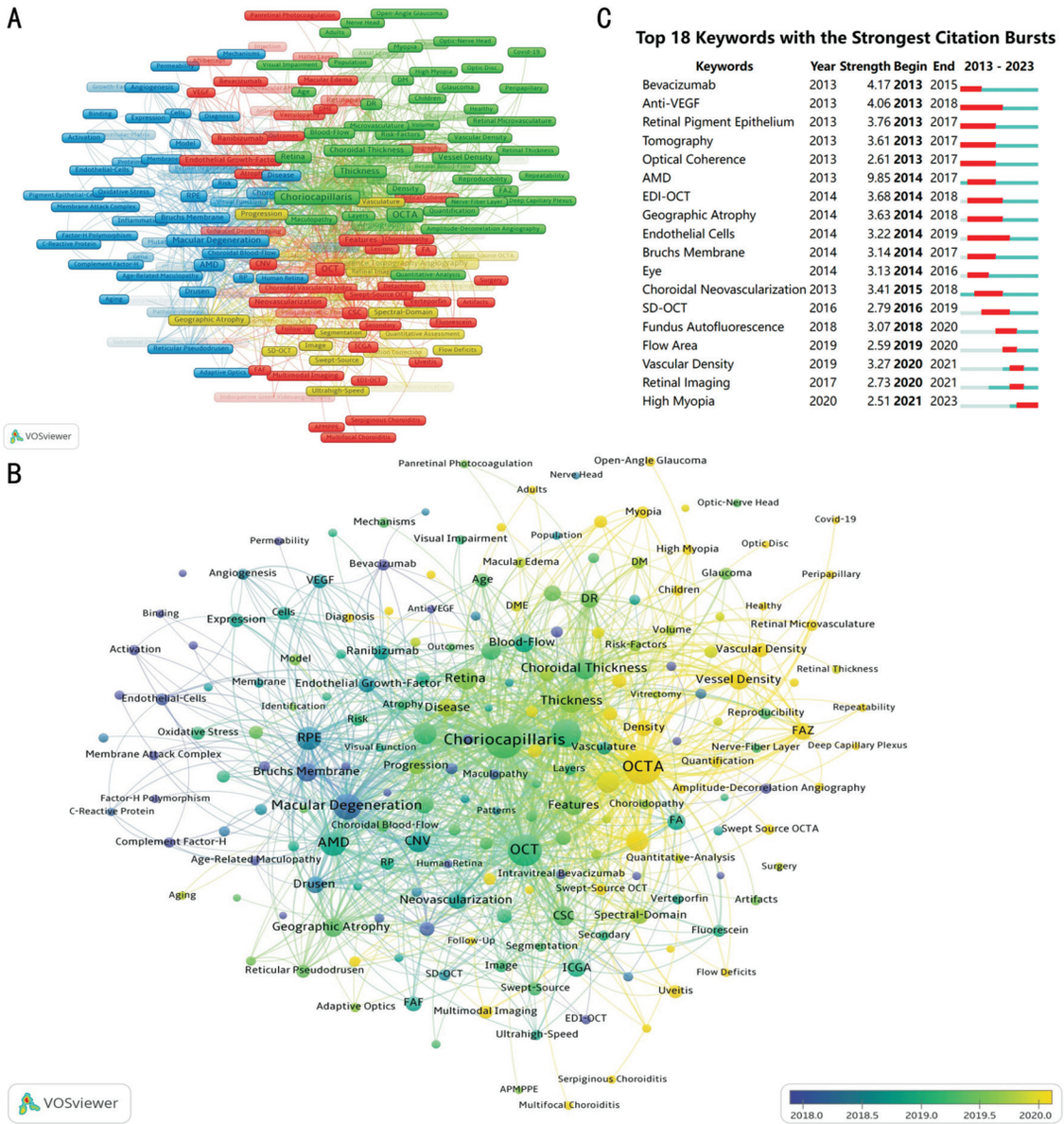

Figure 8 Keyword co-occurrence and burst keywords A: Clustering co-occurrence network visualization map of the all keywords occurring at least 10 times. Layout parameters: Attraction=3, Repulsion=-1; Clustering parameters: resolution=0.85, Min. cluster size=1. B: Overlay visualization map based on the average time of occurrence. C: Top 18 keywords with the strongest citation bursts of the author keywords. Selection criteria: g-index (k=20), with default settings for others parameters.

indicating a need for expanded international collaboration to improve research quality. Nonetheless, the formation of dominant academic teams and collaboration among research communities has propelled significant progress in the field. To foster further development, researchers exploring related topics should intensify their cooperation.

Among the top 10 journals with the most publications of CC, seven of them had a JIF greater than 3, but none surpassed 5. Most of these journals are specialized in ophthalmology. Ophthalmological journals typically have a lower JIF than other disciplines due to the limited readership as a clinical secondary discipline. *Retina* and *Invest Ophthalmol Vis Sci* are recognized as authoritative journals in fundus diseases and ophthalmic basic research, respectively. They are representative journals in this field, serving as primary platforms for disseminating groundbreaking research findings. *Prog Retin Eye Res* and *Ophthalmology* are two ophthalmic journals with a JIF exceeding 10, making them highly referenced in this field.

Research Hotspots and Frontiers By integrating references and keyword analyses, we have summarized the research hotspots and trends in the field of CC, including advancements *in vivo* choroidal imaging and exploration of CC in diseases.

***In vivo* choroidal imaging** Fluorescein angiography and indocyanine green angiography (ICGA) are conventional techniques for visualizing the choroid *in vivo*. However, fluorescein obstructs fine details of CC by the penetrating through fenestrations, whereas ICGA encounters challenges

in isolating the CC signal from the entire choroid. OCT advancements have greatly facilitated *in vivo* research on the choroid and CC. Before 2019, enhanced depth imaging (EDI) OCT and spectral-domain (SD) OCT emerged as burst keywords, indicating the research hotspots. CT has been an early active area in this field, while the topic of CVI has been ongoing until recently. Initially, OCT struggled to clearly image the choroid; however, EDI SD-OCT provided detailed and measurable images of the choroid to evaluate CT[27]. CVI, initially derived from B-scans using EDI SD-OCT to assess vascular status of the choroid, was later examined through swept-source (SS) OCT structural scans, showing less variability with age compared to CT measurements, suggesting its potential as a robust disease marker[28]. En face imaging with SS-OCT enables a fast and reproducible method for visualizing the choroid and analyzing its individual layers, providing superior visualization of the CC layer[22].

OCTA offered a safe and routine method for *in vivo* imaging of CC, utilizing repeated B-scans to contrast blood motion within static tissue[10,21]. Previously, Choi *et al*[21] employed the long-wavelength, ultrahigh speed SS-OCTA to noninvasively visualize the CC lobules, which is consistent with previous observations. The CC images consisted of bright regions indicating blood flow and dark regions suggesting complete vessel loss, reduced blood flow, or image artifacts. Pathological changes, including large drusen or RPE detachments, can attenuate the signal, obscuring the CC imaging[29]. OCTA instruments, limited by their lateral resolution, may not visualize flow in individual CC; yet regions without flow signals remain visible[11]. Therefore, quantifying the CC mainly relied on flow deficits (FD) rather than the actual vasculature. Reliable quantification hinged on selecting an appropriate slab position and thickness[3,29]. FD segmentation involves binarization, often achieved by a global threshold technique where pixels exceeding this threshold represent vasculature, while those below indicate FD. To enhance CC imaging and mitigate signal attenuation caused by RPE or BM abnormalities, Zhang *et al*[24] proposed incorporating structural information to compensate for such attenuation. Another popular approach is to locally ascertain the binarization threshold using the Phansalkar method in Image J with a small optimized window radius[11,14]. From 2019 to 2021, flow area and vascular density were identified as research hotspots. CC parameters, such as those derived from newly developed frame averaged OCTA slabs, can be utilized to quantitatively evaluate the flow within the CC vessels[30]. Before integrating these quantitative CC measurements into clinical practice, improved imaging techniques with greater lateral resolution are needed. Nonetheless, OCTA remains the foremost device for CC investigation in humans[2]. Other imaging modalities also provide distinct advantages, such as the digital subtraction ICGA technique, which highlights the difference between consecutive frames in high-speed video, enabling the evaluation of dynamic CC filling[31].

AMD Research in the field of CC has been consistently focused on macular degeneration from various perspectives. AMD is attributed to alterations in the photoreceptor/RPE/BM/CC complex and has been recognized as a multifactorial disease[32]. The density of CC decreases with age[33]. In early AMD eyes, a correlation was observed between the extent of sub-RPE deposits and CC loss[12]. The choroids of early AMD, stained with Ulex europaeus agglutinin lectin, revealed a loss of viable CC and the presence of incipient neovascular buds at the borders of CC dropout regions[34]. CC drops in early AMD, accompanied by retinal hypoxia, caused an up-regulation of vascular endothelial growth factor-A, which may confer a predisposition to wet AMD[20]. CC dropout was observed adjacent to active CNV in wet AMD, in the absence of RPE atrophy[13]. The loss of CC in geographic atrophy (GA) is more pronounced compared to early AMD[20]. The vascular area exhibited a 50% reduction in regions of RPE atrophy in GA eyes compared to regions with intact RPE, while there was not a complete loss of CC. The surviving capillaries were highly constricted with loss of fenestrations in their endothelium. It was believed that the RPE atrophy decreased the vascular endothelial growth factor supply and preceded the secondary degeneration of CC[13]. However, the exact sequence of events remains unclear; CC degeneration may be a primary event, and complement-mediated injury to the CC is considered a plausible mechanism[20].

OCTA facilitates in vivo assessments, corroborating prior histological findings and highlighting the crucial role of CC in neovascular AMD pathogenesis[26]. Type 3 macular neovascularization, despite originating from the deep plexus, exhibits reduced CC perfusion on OCTA compared to intermediate AMD, suggesting that impaired CC perfusion may contribute to Type 3 macular neovascularization development[35]. Regional variations in CC FD may predict progression from intermediate AMD to specific forms of late. In cases progressing to GA, CC impairment is diffuse across the macula, while in cases progressing to macular neovascularization, CC in the peripheral macula is relatively preserved[18]. The severity of CC FD in eyes with GA has been shown to correlate with the rate of enlargement of these lesions[15]. The application of novel approaches, such as *in vivo* functional imaging, single cell sequencing analysis, and induced pluripotent stem cell modeling techniques may provide new insights into the field of CC[1].

Diabetes Diabetic choroidopathy is characterized by BM thickening, causing a significant narrowing of the CC

capillary lumens[36]. OCTA studies have revealed focal or diffuse impairments in CC flow in diabetic eyes with or without DR[23]. Quantitative analyses have revealed that CC impairment progressively increases with the severity of DR[16,37]. A longitudinal study confirmed that a higher baseline CC FD percentage reliably predicted increased risks of referable DR in diabetic patients, suggesting that CC FD percentage may serve as a novel biomarker for DR onset and progression[38]. Photoreceptors primarily rely on the CC for oxygen demand. CC perfusion density has been identified as a critical vascular variable that significantly impacts the photoreceptor structure in eyes with non-proliferative DR[39]. Notably, the severity of choroidopathy may be underestimated, as current measurements and imaging focus mainly on the posterior pole, whereas the condition primarily affects the mid-circumference[36].

Pachychoroid disease Pachychoroid disease is a spectrum of conditions characterized by thickened choroid, dilated vessels in Haller's layer, and thinning of the CC and Sattler's layer, with or without overlying RPE abnormalities[19]. In chronic disease, *en face* SS-OCT has revealed focal CC atrophy and inward displacement of deep choroidal vessels, which can stimulate the RPE-BM complex and lead to focal ischemia, potentially causing serous retinal detachment or neovascularization[17]. Kishi and Matsumoto[40] observed significant overlap between geographic filling delay in the CC on ICGA images and dilated dominant vortex veins regions in acute CSC, suggesting that congestion within these veins may result in delayed blood flow into the CC. They proposed that chronic stasis leads to the formation of anastomoses across the watershed zone, which dilate and become hyperpermeable, making them recognizable as pachyvessels. Ischemia secondary to occlusion of the CC triggers the development of CNV.

The introduction of OCTA has prompted new insights, revealing that CC is disturbed in CSC, characterized by greater flow void areas and mixed flow patterns[41]. In fellow eyes of unilateral CSC patients, the CC FD percentage was higher compared to healthy controls and correlated with pachychoroid pigment epitheliopathy signs, highlighting the importance of CC in the pathogenesis of CSC and pachychoroid disease[25]. No significant differences were observed in the vascular characteristics of CC derived from frame averaged OCTA images between pachychoroid without a history of disease and normal eye[30]. Limited information on CC in polypoidal choroidal vasculopathy has been reported[42]. Its involvement may differ from that in CSC, with a higher vessel density compared to normal controls, indicating distinct underlying pathological mechanisms[43].

Subthreshold micropulse laser therapy and half-dose photodynamic therapy both improve CC blood flow in chronic CSC eyes. Photodynamic therapy exhibits a more significant effect and has been reported to induce choroidal vascular remodeling[44].

Myopia The choroid undergoes thinning with advancing age and degree of myopia in highly myopic eyes, potentially contributing to myopic degeneration[45]. Recently, research on choroidal circulation in high myopia has gained attention due to the advancement of *in vivo* evaluation techniques. Studies utilizing SS-OCTA to investigate the relationship between CC perfusion and axial elongation yielded contrasting results[46-50]. In more myopic eyes of anisomyopes, lower choroidal vascularity and a higher CC FD percentage were observed[46-47]. In cases with smaller anisometropic differences, changes in FD percentage were not significant; however, a decrease in FD number was noted[48]. These findings suggest that reduced choroidal blood flow may contribute to myopia development[46-47], and that a reduction in FD number may be an early event during myopia progression[48]. A study of highly myopic individuals revealed that the CC FD percentage increased with axial elongation in the perifovea, but not in the fovea, suggesting that CC perfusion may initially be affected in the outer macular region[49]. CC perfusion defects may also play a critical role in myopic macular degeneration. Novel automated methodologies to quantify CC alterations reveal lower CC thickness and higher FD percentage in patients with macular diffuse chorioretinal atrophy compared to controls[50]. Further longitudinal studies are essential to clarify the causal relationship between CC perfusion and both myopia development and macular degeneration.

Our study has several limitations. First, the extraction process was restricted to English articles and reviews from the WoSCC, potentially resulting in incomplete and biased study inclusion. Although standardized procedures were followed, manual data cleaning and dynamic nature of the WoSCC database may cause potential bias.

In conclusion, our bibliometric analysis offers a comprehensive perspective on the current status of CC research, revealing a growing trend in article publications. USA maintains a dominant position in this field, and international cooperation is needed. With the advancement in choroidal imaging, the spotlight gradually moves to the role of CC in various diseases, which represent potential areas for future investigation. This will lead to a paradigm shift in the management of chorioretinal diseases and vision-preserving interventions.

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