• Bibliometric Research •

Global trends in retinal vein occlusion studies from 2004 to 2023: a bibliometric analysis

Meng-Sha Sun, Hong-Ping Cui, Jian-Cen Tang

Department of Ophthalmology, Shanghai East Hospital, Tongji University School of Medicine, Shanghai 200120, China
Correspondence to: Hong-Ping Cui and Jian-Cen Tang. Department of Ophthalmology, Shanghai East Hospital, Tongji University School of Medicine, Shanghai 200120, China. hpcui@vip.163.com; tangjiancen@sina.com
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Abstract

● **AIM:** To analyse the research status and explore global trends in retinal vein occlusion (RVO) studies.

● **METHODS:** Publications related to RVO from 2004 to 2023 were extracted from the Web of Science Core Collection (WoSCC). Variables including the number of publications, as well as countries, organizations, authors, journals, references and keywords were analysed using Bibliometrix-BilioShiny. Data visualization was performed using VOSviewer and CiteSpace.

● **RESULTS:** A total of 4848 publications were retrieved, and generally, the number of publications showed an overall increasing trend with slight fluctuations over the past 20y. The country with the most publications was the United States. The journal with the most publications was *Retina*, and the most cited journal was *Ophthalmology*. The most prolific organization was the University of California, Los Angeles. The most productive author was Noma H, and the most cited author was Campochiaro PA. The top co-cited references mainly focused on the prevalence of RVO and the therapies used in clinical trials. According to the co-occurrence analysis, the keywords formed 3 clusters: 1) risk factors and pathogenesis of RVO, 2) treatments of RVO, and 3) imaging diagnosis of RVO. Anti-vascular endothelial growth factor (VEGF) treatments and artificial intelligence have recently become popular research topics.

● **CONCLUSION:** Bibliometric analysis of the research status and trends of RVO could provide researchers and clinicians with valuable insights for further collaboration, future research directions, and clinical practice.

● **KEYWORDS:** retinal vein occlusion; bibliometric analysis; macular edema; anti-vascular endothelial growth factor

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INTRODUCTION

Retinal vein occlusion (RVO) is a major retinal vascular disease that obstructs the retinal venous system and is often accompanied by increased capillary permeability, retinal haemorrhage, hypoperfusion and high levels of vascular endothelial growth factor (VEGF)[1]. Some patients can develop vision-threatening complications, such as macular edema (ME), retinal ischemia, neovascularization and neovascular glaucoma[2]. According to the occurrence of retinal ischemia, RVO can be divided into ischemic and non-ischemic RVO. Depending on the occlusion site, RVO mainly consists of central retinal vein occlusion (CRVO) and branch retinal vein occlusion (BRVO).

A large population with different races/ethnicities has been affected by RVO, and the prevalence of BRVO is greater than that of CRVO[3]. The pathological mechanism of RVO is multifactorial and complex and includes hypertension, arteriosclerosis, hyperlipidemia and thrombophilia[4]. It is believed that research on evaluation and treatment strategies is still needed. The evaluation of retinal impairment is commonly performed using fundus photography, fluorescein angiography (FA), optical coherence tomography (OCT) and optical coherence tomography angiography (OCTA). There is currently no high-quality evidence to support the use of antiplatelet or anticoagulation drugs to manage RVO[2]. Clinically, laser therapy, intravitreal steroid injections and anti-vascular endothelial growth factor (VEGF) therapy are the major treatments available[5]. Many novel approaches such as photobiomodulation, gene therapy and stem cell therapy are under development[4].

Numerous academic studies on RVO have been published in the last two decades. Bibliometric analysis is a statistical and mathematical method used to analyse a large number of documents. It is of great importance to explore the research status and trends of academics. Bibliometrix-BilioShiny,

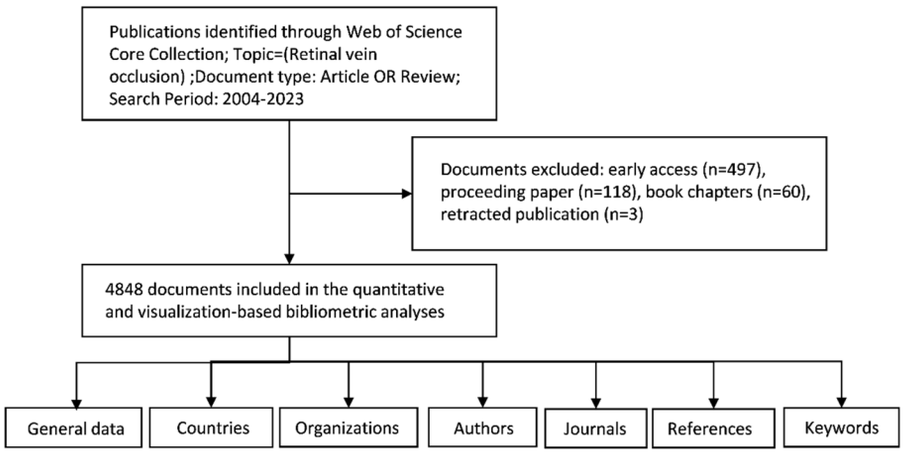

Figure 1 Study flow chart showing the selection criteria and bibliometric analyses of RVO studies RVO: Retinal vein occlusion.

VOSviewer and CiteSpace are used to analyse and reveal the current research status and trends. Specifically, the distribution of publications, authors' productivity and international cooperation could be assessed. Co-authorship and co-occurrence data could present the complex associations of research items. There have been few previous bibliometric analyses related to RVO. In this research, we conducted bibliometric analysis in the field of RVO from 2004 to 2023.

MATERIALS AND METHODS

Data Source and Search Process Data from bibliographic information were searched from The Web of Science Core Collection (WoSCC). "Retinal vein occlusion" was used as the search keyword. "Articles" and "reviews" published from 2004 to 2023 were considered. The data were collected on March 7, 2024, and exported as "plain text" with "full records and cited references" selected. The search process was shown in Figure 1.

Data Analysis The most productive countries, authors, journals, and institutions were summarized. The open-source bibliometrix R package was used to perform comprehensive analyses[6], including research trend information such as countries, journals, organizations, authors and references. VOSviewer (1.6.20, Leiden University, Leiden, the Netherlands) was used for visualization of collaborative data in which items were represented as nodes and links. CiteSpace (6.3. R1, Drexel University, PA, United States) was applied for the co-occurrence and citation burst of keywords. The clustering of keywords was considered to capture the research hotspots in this field, and burst keywords were used to explore research frontiers.

RESULTS

Distribution of Publications and Countries Totally 4848 documents related to RVO from 2004 to 2023 were identified. There was a general upwards trend with small fluctuations in the number of publications in the RVO field over the last two decades (Figure 2).

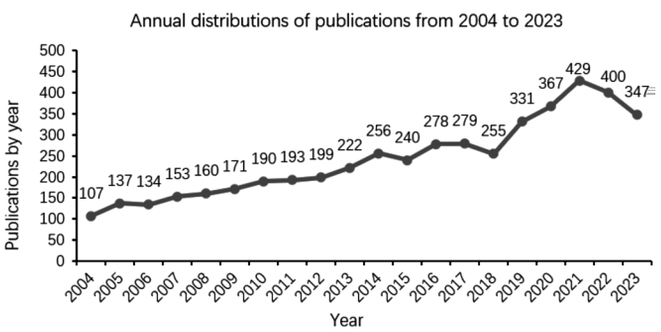

Figure 2 Publication trends in RVO studies for the past 20y RVO: Retinal vein occlusion.

Table 1 Top ten most productive countries in the RVO field from 2004 to 2023

Rank	Country	Publications (%)	Citations
1	USA	1231 (25.4)	46266
2	China	598 (12.3)	7962
3	Japan	587 (12.1)	12239
4	Germany	464 (9.6)	13176
5	Italy	293 (6.0)	9245
6	South Korea	293 (6.0)	4809
7	England	275 (5.7)	7733
8	France	228 (4.7)	6042
9	Turkey	225 (4.6)	2315
10	India	201 (4.1)	2620

The percentages were calculated by dividing the number of a country's publications by the total number of publications (*n*=4848). RVO: Retinal vein occlusion.

Based on the retrieved results, the top 10 countries published 4395 documents, accounting for 90.7% of the total. The United States (25.4%) contributed the most publications, followed by China (12.3%), Japan (12.1%) and Germany (9.6%; Table 1). For citations, the United States (46266 citations) ranked first, followed by Germany (13176 citations), Japan (12239 citations), Italy (9245 citations) and China (7962 citations).

Country co-authorship analysis reveals the degree of cooperation among countries. The node size reflects the

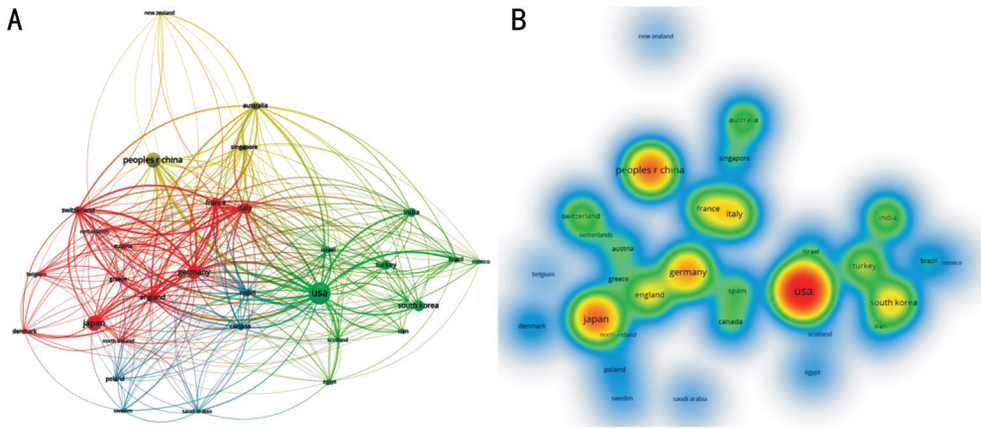

Figure 3 Distribution of the main research countries involved in RVO studies from 2004 to 2023 A: The country co-author network with four clusters; B: The density visualization analysis. The minimum number of documents of a country was set as 20. A total of 32 countries met the threshold of 97 countries involved in RVO research. RVO: Retinal vein occlusion.

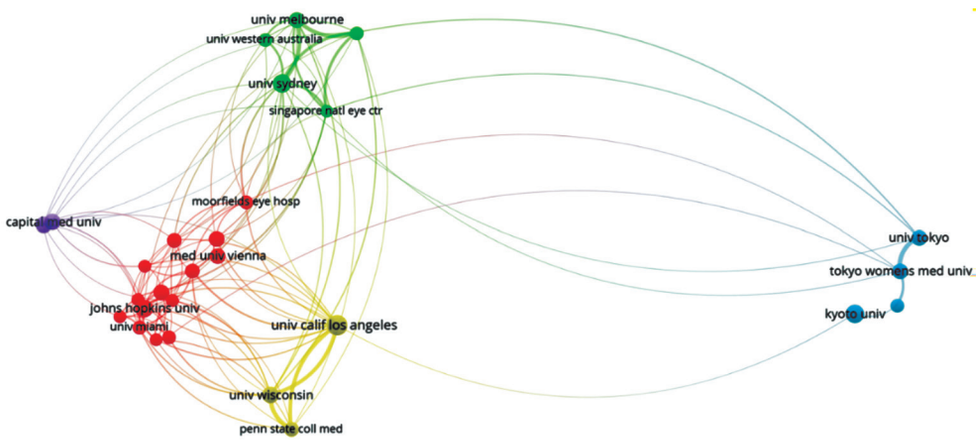

Figure 4 Distribution of the main research organizations involved in RVO studies from 2004 to 2023 The minimum number of documents of an organization was set as 35. A total of 29 organizations met the threshold of 4142 organizations involved in RVO research. RVO: Retinal vein occlusion.

number of publications, and the link strength represents the closeness of connections. The minimum number of documents of a country was set as 20. A total of 32 countries met the threshold of 97 countries involved in RVO research. Figure 3A represented the country co-author network with four clusters. The United States (n=31) and France (n=31) had the largest number of collaborating partners, followed by Germany (n=30), Italy (n=29) and England (n=28). In the density visualization analysis, Figure 3B showed the results consistent with those of the Table 1, in which countries in red had more publications.

Distribution of Organizations The top 10 most productive organizations publishing 666 retrieved documents were shown in Table 2, accounting for 13.7% of the total. The most productive organizations were the University of California Los Angeles (1.9%, 3615 citations), Kyoto University (1.7%, 2015 citations), and the University of Sydney (1.5%, 5240 citations). Figure 4 represented the cooperation between organizations. The minimum number of documents of an organization was set as 35. A total of 29 organizations met the threshold of 4142 organizations involved in RVO research. The co-author network included 28 organizations and formed five clusters. The University of California Los Angeles (n=16) had the largest number of collaborating partners, followed by the University of Sydney (n=14) and Johns Hopkins University (n=14).

Distribution of Authors and Co-cited Authors The top 10 most productive authors publishing 575 retrieved documents were shown in Table 3. The top ranked publishing author was Noma H (75 publications), followed by Tsujikawa A (70 publications) and Jonas JB (62 publications). Co-citation analysis was used to reveal the authors' relative influence in this field. The most co-cited author was Campochiaro PA (2811 citations; Table 3).

Author co-authorship analysis revealed the degree of cooperation among authors, which could provide advice to individual researchers seeking cooperation. The minimum number of documents of an author was set as 20. A total of 40 authors met the threshold of 17 299 authors who were involved in RVO research. The co-author network included 34 authors and formed four clusters (Figure 5).

Table 2 Top ten most productive organizations in the RVO field from 2004 to 2023

Rank	Organization	Country	Publications (%)	Citations
1	University of California Los Angeles	USA	90 (1.9)	3615
2	Kyoto University	Japan	80 (1.7)	2015
3	University of Sydney	Australia	74 (1.5)	5240
4	Johns Hopkins University	USA	70 (1.4)	4628
5	Capital Medical University	China	61 (1.3)	1221
6	Heidelberg University	Germany	61 (1.3)	2684
7	University of Wisconsin-Milwaukee	USA	59 (1.2)	2398
8	Medical University of Vienna	Austria	58 (1.2)	2887
9	Tokyo Women's Medical University	Japan	58 (1.2)	2037
10	University of Melbourne	Australia	55 (1.1)	4222

The percentages were calculated by dividing the number of an organization's publications by the total number of publications (*n*=4848). RVO: Retinal vein occlusion.

Table 3 Top ten most productive authors and co-cited authors from 2004 to 2023 in the RVO field

Rank	Author	Publications	Co-cited author	Citations
1	Noma H	75	Campochiaro PA	2811
2	Tsujikawa A	70	Haller JA	1906
3	Jonas JB	62	Brown DM	1769
4	Mimura T	57	Rubio RG	1765
5	Murakami T	57	Heier JS	1688
6	Bandello F	56	Noma H	1481
7	Feltgen N	54	Saroj N	1411
8	Scott IU	54	Wong TY	1333
9	Muraoka Y	46	Vitti R	1219
10	Ip MS	44	Berliner AJ	1215

RVO: Retinal vein occlusion.

Distribution of Journals and Co-cited Journals The top 10 journals publishing 1621 retrieved documents were shown in Table 4, accounting for 33.4% of the total. The top-ranked publishing journal was *Retina* (7.4%). Co-citation analysis was used to determine which journal played an important role in this field. The most co-cited journal was *Ophthalmology* (20 500 citations; Table 4).

Distribution of Co-cited References Reference co-citation analysis was used to reveal the relative influence of publications and research trends in this field. The top 10 co-cited references were shown in Table 5. The publication titled "The prevalence of retinal vein occlusion: pooled data from population studies from the United States, Europe, Asia, and Australia" was ranked first by Rogers S in 2010. Notably, the top-ranked co-cited references mainly focused on the prevalence of RVO and the therapies used in clinical trials.

Distribution of Keywords The research hotspots of RVO were explored through co-occurrence analysis of high-frequency keywords. The minimum number of occurrences of a keyword was set as 25. Among the 5635 keywords that were involved in RVO research, 66 met this threshold (Figure 6). Based on the network, the three main clusters were represented using the colours red, green and blue according to the similarities of the keywords: 1) risk factors and pathogenesis of RVO, 2) treatments of RVO, 3) imaging diagnosis of RVO. The top 15 keywords for each cluster were listed in Table 6.

We also used CiteSpace's burst detection function to explore the top 20 keywords with the most citation bursts (Table 7). "OCTA" was the strongest citation burst keyword. In the early stages of 2004-2023, "intravitreal triamcinolone acetonide" was the main burst keyword. Later, "anti-VEGF", "dexamethasone (DEX) implant" and "OCTA" burst. Most recently, "anti-VEGF" has still been in burst while "artificial intelligence (AI)" and "deep learning (DL)" has burst. It provides the information that there has been rapid development in anti-VEGF therapies and AI directions.

DISCUSSION

Global Trends of RVO In the current analysis, 4848 publications related to RVO were retrieved from the WoSCC. The annual publication number generally increased with slight fluctuations over time in the past 20y, which may indicate the importance of the RVO field. The United States made great contributions to publications and citations in this field. This indicates that the United States is at the core of RVO research. The United States and France were the most active countries in international cooperation. The University of California,

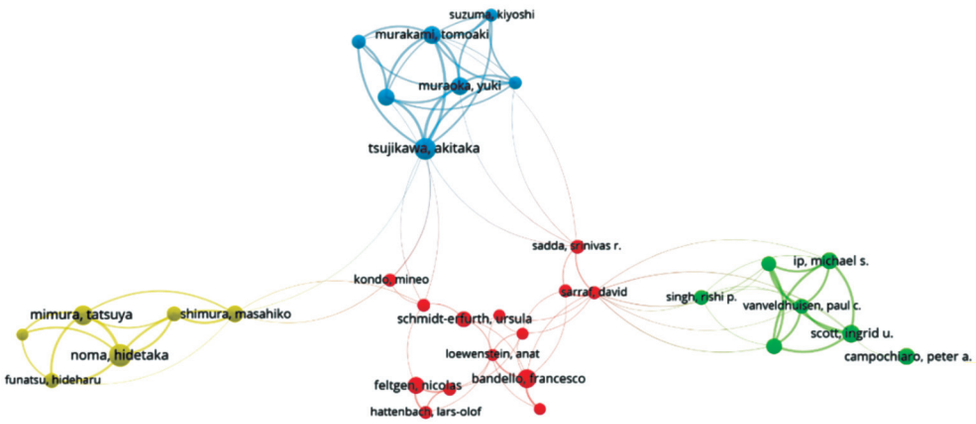

Figure 5 Distribution of the main authors of RVO studies from 2004 to 2023 The minimum number of documents for an author was set to 20. A total of 40 authors met the threshold of 17 299 authors who were involved in RVO research. RVO: Retinal vein occlusion.

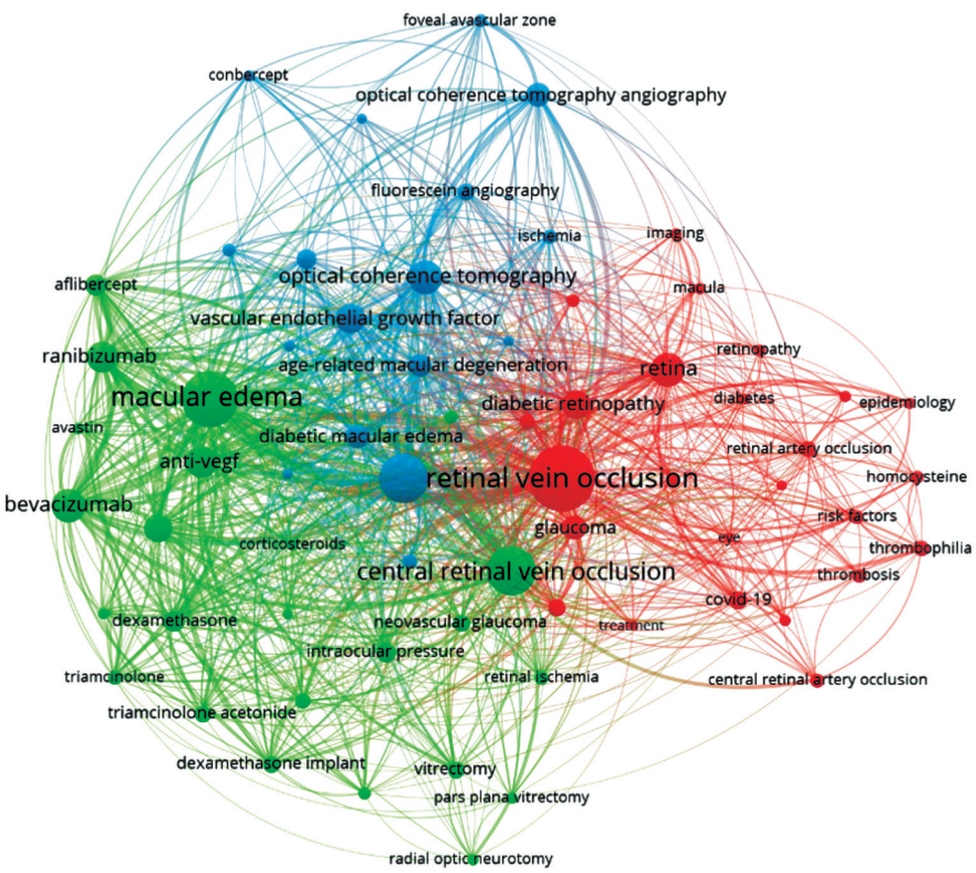

Figure 6 Co-occurrence analysis of keywords in RVO research from 2004 to 2023 The minimum number of occurrences of a keyword was set as 25. A total of 66 keywords met the threshold of 5635 keywords involved in RVO research. RVO: Retinal vein occlusion.

Los Angeles, was the most prolific organization and was quite active in international cooperation. Notably, cooperation among countries or organizations is not restricted by geographic distance. *Retina* was the most productive journal, and *Ophthalmology* was the most influential journal. Author co-citation and co-authorship analyses can provide researchers with information about their influence and contributions. Noma H from Japan was the most productive author, and Campochiaro PA from the USA was the most cited author. From these top productive authors and top cited authors, we can find their studies in this critical field and explore research frontiers.

Based on the reference co-citation analysis, the top-ranked co-cited references may reveal the research focus in high-quality publications, which can guide us to pay attention to the research trends in this field. The publication titled "The prevalence of retinal vein occlusion: pooled data from population studies from the United States, Europe, Asia, and Australia" was ranked first by Rogers S in 2010. By analysing large sample size around the world, the study provided

Table 4 Top ten most productive journals and co-cited journals from 2004 to 2023 in the RVO field

Rank	Journal	Publications (%)	Co-cited journal	Citations
1	*Retina*	358 (7.4)	*Ophthalmology*	20500
2	*Graefes Archive for Clinical and Experimental Ophthalmology*	194 (4.0)	*American Journal of Ophthalmology*	12920
3	*Investigative Ophthalmology & Visual Science*	172 (3.5)	*Retina*	10641
4	*American Journal of Ophthalmology*	154 (3.2)	*Investigative Ophthalmology & Visual Science*	9591
5	*Ophthalmology*	147 (3.0)	*Archives of Ophthalmology*	8967
6	*British Journal of Ophthalmology*	127 (2.6)	*British Journal of Ophthalmology*	7777
7	*European Journal of Ophthalmology*	123 (2.5)	*Graefes Archive for Clinical and Experimental Ophthalmology*	5104
8	*Acta Ophthalmologica*	119 (2.5)	*Eye*	3408
9	*Eye*	114 (2.4)	*Acta Ophthalmologica*	2559
10	*BMC Ophthalmology*	113 (2.3)	*New England Journal of Medicine*	2217

The percentages were calculated by dividing the number of a journal's publications by the total number of publications (*n*=4848). RVO: Retinal vein occlusion.

Table 5 Top ten most co-cited references from 2004 to 2023 in the RVO field

Rank	Co-cited reference	Title	Citations
1	Rogers S, 2010, *Ophthalmology*	The prevalence of retinal vein occlusion: pooled data from population studies from the United States, Europe, Asia, and Australia	714
2	Campochiaro PA, 2010, *Ophthalmology*	Ranibizumab for macular edema following branch retinal vein occlusion: six-month primary end point results of a phase III study	487
3	Brown DM, 2010, *Ophthalmology*	Ranibizumab for macular edema following central retinal vein occlusion: six-month primary end point results of a phase III study	464
4	Anonymous, 1984, *Am J Ophthalmol*	Argon laser photocoagulation for macular edema in branch vein occlusion	460
5	Clarkson JC, 1997, *Arch Ophthalmol*	Natural history and clinical management of central retinal vein occlusion. The Central Vein Occlusion Study Group	400
6	Haller JA, 2010, *Ophthalmology*	Randomized, sham-controlled trial of dexamethasone intravitreal implant in patients with macular edema due to retinal vein occlusion	380
7	Klein R, 2000, *Trans Am Ophthalmol Soc*	The epidemiology of retinal vein occlusion: the Beaver Dam Eye Study	341
8	Mitchell P, 1996, *Arch Ophthalmol*	Prevalence and associations of retinal vein occlusion in Australia. The Blue Mountains Eye Study	318
9	Campochiaro PA, 2011, *Ophthalmology*	Sustained benefits from ranibizumab for macular edema following central retinal vein occlusion: twelve-month outcomes of a phase III study	317
10	Brown DM, 2011, *Ophthalmology*	Sustained benefits from ranibizumab for macular edema following branch retinal vein occlusion: 12-month outcomes of a phase III study	311

RVO: Retinal vein occlusion.

Table 6 Top 15 keywords of the three main clusters

Cluster 1 (red)	Occurrences	Cluster 2 (green)	Occurrences	Cluster 3 (blue)	Occurrences
Retinal vein occlusion	887	Macular edema	644	Branch retinal vein occlusion	496
Retina	249	Central retinal vein occlusion	505	Optical coherence tomography	239
Diabetic retinopathy	171	Bevacizumab	240	Vascular endothelial growth factor	189
Glaucoma	124	Ranibizumab	204	Diabetic macular edema	127
COVID-19	74	Anti-VEGF	198	Optical coherence tomography angiography	123
Uveitis	60	Intravitreal injection	168	Age-related macular degeneration	106
Retinal artery occlusion	58	Aflibercept	101	Visual acuity	82
Thrombophilia	58	Dexamethasone	96	Fluorescein angiography	62
Risk factors	47	Intraocular pressure	88	Ischemia	48
Central retinal artery occlusion	45	Triamcinolone acetonide	67	Cystoid macular edema	45
Inflammation	42	Dexamethasone implant	66	Angiogenesis	35
Thrombosis	42	Vitrectomy	66	Foveal avascular zone	35
Homocysteine	36	Neovascular glaucoma	65	Laser photocoagulation	34
Epidemiology	32	Ozurdex	52	Intravitreal bevacizumab	29
Ophthalmology	32	Triamcinolone	46	Conbercept	27

VEGF: Vascular endothelial growth factor.

a more precise estimate of the prevalence in the general population. It also suggested the need for further research to better understand the key roles of the principal systemic and ocular factors as well as appropriate preventive and treatment strategies. From the top 10 co-cited references, we could find 7 out of the 10 were clinical trials and 3 out of 10 were observational studies. Notably, the former made great significance to RVO therapies, while the latter mainly focused

Table 7 Top 20 keywords with the strongest citation bursts

Keywords	Year	Strength	Begin	End
Triamcinolone acetonide	2004	14.48	2004	2011
Intravitreal triamcinolone	2004	6.1	2004	2008
Radial optic neurotomy	2005	12.91	2005	2011
Intraocular pressure	2005	11.21	2005	2008
Intravitreal triamcinolone acetonide	2005	9.47	2005	2009
Central retinal vein occlusion	2004	6.02	2006	2007
Intravitreal bevacizumab	2007	7.97	2007	2014
Vascular endothelial growth factor	2007	10.14	2008	2013
Macular oedema	2005	5.62	2008	2012
Intravitreal injection	2005	7.87	2009	2011
Dexamethasone implant	2013	4.76	2013	2019
Foveal avascular zone	2016	6.59	2016	2020
Optical coherence tomography angiography	2016	17.59	2018	2020
Anti-vascular endothelial growth factor	2011	6.53	2018	2023
Vessel density	2019	6.22	2019	2022
Intravitreal injections	2013	4.89	2020	2021
Macular degeneration	2017	6.01	2021	2022
Anti-VEGF treatment	2021	4.74	2021	2023
Artificial intelligence	2021	5.59	2022	2023
Deep learning	2019	5.09	2022	2023

VEGF: Vascular endothelial growth factor.

on the prevalence of RVO. These studies and subsequent ones contributed to the better understanding of RVO pathogenesis and management.

Research Frontiers of RVO Keywords analysis can capture the current hotspots and future directions in this field. The three clusters are discussed as follows.

Cluster 1 (red) is linked to the pathogenesis and risk factors for RVO. RVO is the second most common retinal vascular disorder. The pathogenesis of this disease is multifactorial, causing an obstruction of the retinal venous system. CRVO is caused by thrombosis of the central retinal vein at the lamina cribrosa level, which can lead to retinal ischemia and hypoxia. BRVO results from abnormal hemodynamic changes and venous thrombosis at sites of arteriovenous crossing. The mechanisms of BRVO pathogenesis can be characterized by the famous Virchow triad: hemodynamic changes, vascular endothelial damage, and a hypercoagulable state[7]. According to the severity of the occlusion, retinal nonperfusion and ischemia can occur and progress. Retinal ischemia can disrupt the blood-retina barrier and lead to the release of inflammatory mediators, further aggravating vascular permeability and worsening disorders[8].

The incidence of RVO is strongly correlated with increasing age. The prevalence of BRVO is greater than that of CRVO. Whether there is a sex difference remains controversial. Ponto *et al*[9] reported that the prevalence in men was 1.7 times greater than that in women, but Song *et al*[10] reported that there was no significant difference between the sexes. Systemic hypertension, atherosclerosis, hypercholesterolemia, and smoking associated with retinal artery sclerosis are common in patients with RVO[11-13]. Hypertension was the strongest risk factor for any RVO[9]. The relationship between diabetes mellitus and RVO remains controversial[14-15]. There is evidence for an association between RVO and thrombophilic factors such as anticardiolipin antibodies and hyperhomocysteinaemia[16]. A correlation between RVO and chronic kidney disease was supported[17-18]. The blood urea concentration and narrow chamber angle were also associated factors[14]. Changes in ocular pressure gradients are associated with RVO[19]. There are controversial outcomes regarding the relationship between RVO and glaucoma[10]. A Meta-analysis indicated that open-angle glaucoma could increase RVO incidence, particularly for patients with CRVO[20]. Furthermore, CRVO was related to older age and a family history of stroke, and BRVO was related to arterial hypertension and atrial fibrillation[9]. Notably, infectious and inflammatory conditions should be considered if there is any sign of intraocular inflammation[4]. Future studies are needed to investigate further risk factors, such as genetic factors of ophthalmic parameters and coagulation parameters.

Although a variety of systemic diseases have been reported to be associated with various types of RVO, there is no exact cause-and-effect relationship[15]. The exact mechanisms are still obscure. It is necessary to study the cytokines that trigger RVO itself, which could prove to be promising treatment targets[21]. The particular systemic disease may or may not be one of the risk factors for developing a specific type of RVO, so that the

common management for all RVO patients can be misleading, and a multidisciplinary and personalized approach should be sought.

Cluster 2 (green) is linked with the ocular treatments of RVO. To date, there is no safe and reliable treatment that can reverse the actual occlusion of RVO. As such, ocular treatments are mainly directed at complications of RVO, such as ME.

CRVO is usually accompanied by ME. The incidence of MEs in BRVO patients is largely heterogeneous. In one study, ME was detected in approximately 30% of BRVO eyes[13]. Another study revealed that ME occurred in 90% of major BRVO patients and 97% of macular BRVO patients[22]. Before the introduction of intravitreal therapies, focal laser photocoagulation was considered the gold standard for treating ME caused by BRVO, while it should be considered as a second-line treatment in the era of available anti-VEGF therapies[23]. The ME is related to high levels of VEGF and proinflammatory cytokines. Anti-VEGF and anti-inflammatory agents are the mainstay therapies for ME[24]. Intravitreal injection of an anti-VEGF drug is the preferred treatment for ME[25-26]. Tadayoni *et al*[27] reported that the anti-VEGF effect of ranibizumab was superior to that of laser monotherapy. Comparing ranibizumab with dexamethasone, the improvements in best-corrected visual acuity (BCVA) and central retinal thickness were comparable in patients with BRVO, but ranibizumab treatment showed greater benefit in patients with CRVO[28]. A Meta-analysis of 11 randomized controlled trials provided evidence of the superiority of anti-VEGF compared with steroid treatment for RVO-ME with regard to BCVA, OCT outcomes and safety endpoints[29]. In clinical practice, dexamethasone implantation is applied as a complementary therapy. Yap *et al*[30] reported that intravitreal dexamethasone implants provided useful rescue in cases of anti-VEGF failure for RVO-ME patients. Blanc *et al*[31] observed that dexamethasone was effective for treating CRVO and BRVO-associated ME for more than 3y, but its functional efficacy appeared to decrease over time and with repeated injections. Qiu *et al*[32] reported that both aflibercept and dexamethasone could achieve effective visual and anatomical gains in the long-term. In addition, dexamethasone implants have fewer injections but are more likely to cause increased intraocular pressure and cataracts. Despite the superior initial response of RVO to dexamethasone compared with that to anti-VEGF agents, the use of dexamethasone as an initial therapy in routine care is rare[33].

There is no clear recommendation about the type of anti-VEGF therapy and the most suitable dosing regimen to choose[24,34]. Furthermore, a systematic review of 48 real-world studies indicated that the functional and anatomical improvements achieved with anti-VEGF therapy for BRVO-ME in the real world were not as impressive as those achieved in seminal randomized controlled trials, probably due to the decrease in injections and individual differences[35]. Overall, aggressive and timely blockade of VEGF could prevent the progression of retinal nonperfusion and ischemia[1]. It has been proven that the timing of intravitreal injections and the appropriate injection number can determine long-term vision prognosis[36-37]. In addition, age correlated with the response to aflibercept treatment, and more significant improvements were detected in younger patients[26].

Cluster 3 (blue) is linked with the imaging diagnosis of RVO. The imaging diagnosis of RVO has changed tremendously, and the assessment of retinal ischemia remains crucial. Identifying the conversion from nonischemic to ischemic status is important and requires careful multimodal imaging examinations. OCT is recommended for the diagnosis and assessment of RVO-ME. In addition, FA/OCTA is recommended for identifying retinal nonperfusion[2]. With respect to limitations, FA might limit image resolution because of dye leakage in the affected retinal areas, while OCTA can achieve higher resolution and clearly show retinal vascular changes[38]. However, alterations in vascular permeability that are detectable on FA may not be present on OCTA[39].

Remarkable progress has been made in the development of ophthalmic imaging technologies. Several studies have identified spectral domain OCT predictors of visual prognosis in RVO patients with ME in which the external limiting membrane status and presence of hyperreflective foci were correlated with the baseline BCVA and anti-VEGF response, whereas changes in ellipsoid zone disruption or central subfield thickness could predict visual outcome[40-41]. Foveal eversion is recently considered a negative prognostic biomarker in RVO, associated with higher persistence of macular edema and worse visual outcome[42]. In particular, OCTA can be used to assess the superficial and deep capillary plexus as well as the choriocapillary plexus in RVO[43-44]. The OCTA biomarkers for visual outcome in RVO revealed that the area of the superficial foveal avascular zone was negatively correlated with BCVA, and superficial and deep parafoveal vascular density were positively correlated with BCVA[45]. In particular, preservation of the deep capillary plexus is crucial for better BCVA in BRVO patients[46]. Recent studies have revealed many imaging biomarkers for the diagnosis and assessment of RVO by using multiple ophthalmic imaging devices[5]. Although imaging diagnosis is under rapid development, the pathogenic mechanisms leading to the structural changes need further investigation.

In recent years, deep learning is rapidly advancing in artificial intelligence and applied to the screening, diagnosis and classification of retinal diseases. Artificial intelligence models

based on multimodal imaging have gradually matured. Numerous studies assisting in the diagnosis of RVO based on artificial intelligence are constantly emerging[47-48]. Nagasato *et al*[49] indicated the high accuracy for the detection of a nonperfusion area caused by RVO combining OCTA with deep learning. Sun *et al*[50] built an ultra-widefield image diagnostic model using the EfficientNet network to accurately classify multiple fundus disease types involving RVO. Wang *et al*[51] described 30 types of retinal diseases, including RVO, that can be detected by deep learning algorithms *via* ultra-widefield FA. Deep learning model was used to predict therapeutic response of patients with RVO using OCT images[52]. Multimodal fusion deep learning models using OCTA images were developed to predict RVO-ME recurrence[53]. There will be a trend toward multimodal imaging and deep learning models to assess the prognosis and assist clinicians in determining the treatment strategies.

By analysing citation-burst keywords, we can find the increasing focus on anti-VEGF treatments and the emergence of artificial intelligence applications. Currently, novel intravitreal drugs are under rapid development. Due to the heterogeneity of the real-world population, current evidence from clinical trials of anti-VEGF therapy is still limited. More robust treatment strategies need to be verified using large amounts of real-world clinical data. The advancements in technology allow for the utilization of multimodal imaging and artificial intelligence, which enhance the speed of diagnosis and optimize patient care. As abundant artificial intelligence research has emerged, data from population-based studies are desirable for training more accurate artificial intelligence models and making more precise assessments. The future development of RVO may be individual-based management, which will provide more detailed management including diagnosis, treatment, prevention, and prognosis assessment regarding RVO.

In our study, data from RVO research were analysed objectively and comprehensively. However, some limitations should be considered. First, the data were extracted only from the WoSCC database and might not completely reflect the research in this field. Second, due to the lack of time for newly published papers to be examined and cited, there is bias in the analysis of studies. Third, only high-frequency keywords were selected in our study, but we cannot rule out some low-frequency keywords as possible research hotspots in the future. Fourth, the quality and methodological rigor of the publications were not assessed.

In conclusion, through this bibliometric analysis, we provide a comprehensive overview of RVO research. Our study may be helpful for researchers in choosing appropriate collaboration and research directions. The trend of combining multimodal imaging with artificial intelligence models to accurately assess the prognosis of RVO has been revealed. There are still many challenges to be overcome in regards to potential pathogenic mechanisms and treatment strategies.

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