

Research progress on meibomian gland dysfunction from 2011 to 2020: a bibliometric and visualized analysis

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Research

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Abstract

Background

To explore the research areas, hotspots, and progress of meibomian gland dysfunction through bibliometrics.

Methods

Related publications were retrieved from the Web of Science Core Collection from 2011 to 2020. VOSviewer1.6.16, Citespace.5.7.R2, and GraphPad Prism 8 were used to visualize the distribution of countries, research institutions, journals, authors, keywords, and annual publication numbers in this field.

Results

A total number of 716 relevant publications were retrieved. The United States and Keio University ranked the first among the countries and organizations with the most publications. *Cornea*, *Investigative Ophthalmology & Visual Science*, and *Ocular Surface* were the top three journals with the highest publication counts and citations. The authors who contributed to this topic mainly formed three clusters which manifested the research areas, and the extracted keywords mainly formed four clusters which manifested the hotspots were explored.

Conclusions

The research areas and hotspots of meibomian gland dysfunction were as follow: (1) Pathogenesis or potential etiology of meibomian gland dysfunction; (2) Diagnosis of meibomian gland dysfunction; (3) Therapy of meibomian gland dysfunction and the International Workshop`s dedication to it; (4) Epidemiology of meibomian gland dysfunction.

1. Introduction

The meibomian glands, located in parallel rows on the upper and lower eyelids, play a vital role in ocular surface health. The meibum secreted by the meibomian gland comprises the lipid layer of the tear film, which prevents tear evaporation and protects the ocular surface[1]. Meibomian gland dysfunction (MGD) is a diffuse, chronic disorder of the meibomian glands that is characterized by quantitative/qualitative changes in glandular secretion and/or terminal duct obstruction[2]. The International Workshop on MGD, launched by the Tear Film and Ocular Surface Society in 2011[3], aimed to raise concerns about MGD and accelerate its study.

Bibliometrics, also called bibliometric analysis, is a scientific process that analyzes large amounts of literature using statistical methods to reveal the development of specified fields[4]. VOSviewer, exploited by van Eck and Waltman of Leiden University, is a visualization tool for constructing bibliometric networks[5]. Similarly, Citespace, developed by Chaomei Chen, is a Java application for visualizing patterns in scientific literature[6]. Both VOSviewer and Citespace are scientific mapping tools that directly provide visualizes of specified terms and their links.

The growing interest in MGD research has resulted in hundreds of publications in recent decades. Considering the substantial number of publications related to MGD, it is difficult to identify the progress and trends in MGD studies. Thus, applying scientific methods to quantitatively and qualitatively assess these publications will be helpful for potential cooperation, further research, and potential publications related to MGD. However, bibliometric studies in the field of MGD are lacking. Therefore, this study performed bibliometric analysis and utilized visualization tools to comprehensively and objectively evaluate MGD studies to reveal the research areas, hotspots, and progress in this field in recent decades.

2. Results

2.1 Tendency of worldwide publications in MGD research

Based on the retrieval model, 716 articles related to MGD published between 2011 and 2020 were retrieved. The distributions of annual articles and the stable growth trends are shown in Fig. 1a. The numbers of annual publications consistently and significantly increased in the past 10 years, from 39 in 2011 to 107 in 2020. Among them, the top 10 most cited publications are listed in Table 1. A total of 54 countries and 891 organizations were involved in MGD research globally. The top 10 countries and organizations with the highest numbers of publications are listed in Tables 2 and 3. Furthermore, to explore the latent connections among them, network maps with nodes and lines were sketched using Citespace. In this study, the nodes represented the analysis components, with their sizes proportional to the weight of the items. The line thickness and length between nodes were proportional to the strength of the relationship between the analysis components. In addition, each term had a corresponding centrality value, in which the terms with the highest values had the core positions in the network and were circled in purple in the figure. As shown in Fig. 1b, the United States of America (USA) ranked first among countries (217 documents, 0.33 centrality), followed by China (106 documents, 0.09 centrality) and Japan (80 documents, 0.07 centrality). Among institutions, Keio University (Tokyo, Japan) contributed the most publications and displayed high centrality in MGD research from 2011 to 2020 (Fig. 1c).

Figure 1 Tendencies in worldwide publications on MGD research, 2011–2020. (a) Annual numbers of publications on MGD research over the past decade. (b) A network map of countries in MGD research (countries with at least 25 related publications are labeled). (c) A network map of organizations in MGD research (organizations with at least 15 related publications are labeled). Every node represents a country or an organization, with the nodes representing the number of publications. Countries or institutions with high centrality are circled in purple.

Table 1

The top 10 MGD research publications with the most citation frequency over the past decade.

Rank	Title	Citations
1	The International Workshop on Meibomian Gland Dysfunction: Report of the Subcommittee on Anatomy, Physiology, and Pathophysiology of the Meibomian Gland.	417
2	The International Workshop on Meibomian Gland Dysfunction: Executive Summary.	393
3	The International Workshop on Meibomian Gland Dysfunction: Report of the Definition and Classification Subcommittee.	339
4	The International Workshop on Meibomian Gland Dysfunction: Report of the Diagnosis Subcommittee.	324
5	The International Workshop on Meibomian Gland Dysfunction: Report of the Subcommittee on Management and Treatment of Meibomian Gland Dysfunction.	275
6	The International Workshop on Meibomian Gland Dysfunction: Report of the Subcommittee on the Epidemiology of, and Associated Risk Factors for, MGD.	248
7	Distribution of Aqueous-Deficient and Evaporative Dry Eye in a Clinic-Based Patient Cohort: A Retrospective Study.	218
8	The International Workshop on Meibomian Gland Dysfunction: Report of the Subcommittee on Tear Film Lipids and Lipid-Protein Interactions in Health and Disease.	173
9	New Perspectives on Dry Eye Definition and Diagnosis: A Consensus Report by the Asia Dry Eye Society.	165
10	The Pathophysiology, Diagnosis, and Treatment of Dry Eye Disease.	141

Table 2
Top 10 leading countries in meibomian gland dysfunction (MGD) research from 2011 to 2020.

Rank	Country	Count	Centrality
1	USA	217	0.33
2	China	106	0.09
3	Japan	80	0.07
4	South Korea	64	0.07
5	Germany	49	0.27
6	Australia	46	0.02
7	Turkey	43	0.03
8	England	40	0.05
9	Italy	30	0.12
10	Spain	25	0.11

Table 3
Top 10 leading organizations in meibomian gland dysfunction (MGD) research from 2011 to 2020.

Rank	Organization	Count	Centrality
1	Keio University (Japan)	32	0.16
2	Yonsei University (Korea)	25	0.10
3	University of Louisville (USA)	25	0.08
4	Itoh Clinic (Japan)	22	0.08
5	University of Auckland (New Zealand)	20	0.02
6	Harvard University (USA)	20	0.05
7	Harvard Medical School (USA)	19	0.10
8	Fudan University (China)	18	0.06
9	Kyoto Prefectural University of Medicine (Japan)	17	0.19
10	Ohio State University (USA)	15	0.07

2.2 Journal analysis and highly cited publications

The retrieved publications on MGD were identified in 142 journals. Among them, *Cornea* had the highest number of publications on this topic (93, 12.99%), followed by *Investigative Ophthalmology & Visual Science* (68, 9.50%) and *Ocular Surface* (51, 7.12%). The top 10 journals and their impact factors are listed in Table 4.

Table 4
Top 10 main journals in meibomian gland dysfunction (MGD) research from 2011 to 2020.

Rank	Journal	Count	Count%*	Citation*	Impact Factor
1	Cornea	93	12.99%	1806	2.651
2	Investigative Ophthalmology & Visual Science	68	9.50%	3429	4.799
3	Ocular Surface	51	7.12%	1168	5.033
4	Contact Lens & Anterior Eye	36	5.03%	388	3.077
5	Current Eye Research	30	4.19%	402	2.424
6	Eye Contact Lens-Science and Clinical Practice	27	3.77%	250	2.018
7	Optometry and Vision Science	21	2.93%	488	1.973
8	Experimental Eye Research	21	2.93%	253	3.467
9	British Journal of Ophthalmology	20	2.79%	419	4.638
10	BMC Ophthalmology	19	2.65%	135	2.209

* Count% = Count/ N, count means the number of publications in each journal, N means the total number of the retrieved publications. Values presented in the citation column refer to the citation number of journals.

2.3 Author analysis

Authorship analysis revealed that 2,559 authors had contributed to MGD research. The top 10 authors are listed in Table 5. VOSviewer was used to visualize the connections between the authors, which showed three clusters of different colors (Fig. 2). The sizes of the nodes corresponded to the number of publications, while the lines between them represent the closeness of the authors. Authors in the same cluster were considered to have a closer connection and cooperation with each other. According to the relevant literature of the leading authors, the research areas of them were as follows.

Cluster 1 included Arita R, Tsubota K, Seo KY, and Kim TI, who mainly focused on MGD pathogenesis or etiology[7–9], treatments[10–12], and morphological evaluation and diagnosis[13, 14].

Cluster 2 included Craig JP, Tong L, Nichols KK, Sullivan DA, and Wang MTM, who mainly focused on the study of indicators related to MGD[15, 16]; potential drugs that may influence meibomian gland epithelial

cell function[17, 18]; and MGD epidemiology[19, 20], pathogenesis[21], assessment[22], and treatment[23].

Cluster 3 included Borchman D, Foulks GN, and Yappert MC, who mainly focused on the composition, structure, and function of meibum in MGD and the analysis of tear film stability[24–26], changes in meibum composition as measured by nuclear magnetic resonance (NMR) spectroscopy[27], and MGD treatment[28, 29].

Table 5
Top 10 leading authors in meibomian gland dysfunction (MGD) research from 2011 to 2020.

Rank	Author	Count	Citation*	Cluster
1	Arita R	27	907	1(red)
2	Tsubota K	23	1168	1(red)
3	Borchman D	22	634	3(blue)
4	Craig JP	21	726	2(green)
5	Tong L	19	504	2(green)
6	Seo KY	18	422	1(red)
7	Nichols KK	17	1351	2(green)
8	Kim TI	16	197	1(red)
9	Sullivan DA	15	1082	2(green)
10	Wang MTM	15	164	2(green)

*Values of citation column here refer to the citation number of authors.

Figure 2 Co-authorship network map of authors in MGD research, 2011–2020. Among 2,559 total authors, 21 met the criteria of more than 10 related publications. Among these, three clusters (cluster 1: red, cluster 2: green, cluster 3: blue) were observed, in which authors with closer connections and cooperation were placed in the same cluster.

2.4 Analysis of keywords co-occurrence

A total of 2,263 keywords related to MGD were retrieved. VOSviewer was used to visualize the keywords appearing with the highest frequencies. The keyword co-occurrence map comprised four different clusters shown in different colors (Fig. 3). Keywords in the same color were assigned to the same cluster, with the different clusters indicating research hotspots. The clusters were as follows: Cluster 1 (red), Cluster 2 (green), Cluster 3 (blue), and Cluster 4 (yellow). Ten representative keywords and their occurrences in each cluster are shown in Table 6.

Table 6
Representative keywords in each cluster in keywords co-occurrence analysis.

Cluster1 (red)	Cluster2 (green)	Cluster3 (blue)	Cluster4 (yellow)
meibomian gland dysfunction (491)	tear film (182)	international workshop (313)	prevalence (122)
dry eye disease (467)	meibography (79)	dysfunction report (47)	population (45)
ocular surface (145)	lipid layer thickness (53)	therapy(37)	epidemiology (44)
inflammation (25)	evaporation(41)	meibomian gland expression (46)	signs (38)
gene-expression (23)	tear film stability (13)	azithromycin (29)	risk-factors (36)
keratoconjunctivitis sicca(22)	dry eye symptoms (23)	intense pulsed light (23)	ocular surface disease (35)
contact-lens wear(15)	fluorescein (13)	rosacea (20)	quality-of-life (17)
fatty-acids(15)	aqueous-deficient (11)	doxycycline (13)	glaucoma (14)
sjogrens-syndrome(14)	keratography (10)	topical azithromycin (12)	questionnaire (10)
tear osmolarity(14)	reliability (10)	cytokines (10)	impact (10)

3. Discussion

This is the first study to report the bibliometric analysis and visualized results of research on MGD. The results of the present study provided a general view of the research progress and trends related to MGD over the last decade.

3.1 Worldwide tendencies in MGD research.

As shown in Fig. 1a, the numbers of publications in MGD research showed progressive and continuous increases from 2011 to 2020, indicating increasing concerns and interests in this area. Among the top 10 most cited publications, seven were related to international workshops on MGD. In the last decade, many countries and institutions increasingly focused on MGD. Among the intricate country network map, the USA showed the highest number of publications and centrality, suggesting that this country is the international collaborative center for MGD research. In the organization analysis, Keio University had the highest number of publications, which reflected its contribution to MGD research. Of the top 10 organizations shown in Table 3, the top three were Keio University (Japan), Yonsei University (Korea), and the University of Louisville (USA). Determining the contributing countries and organizations may help researchers find appropriate collaborations for further study and accelerate the study of MGD. In addition,

the journal analysis, which identified the top 10 journals, plays a role in illustrating the importance of a journal and helping ophthalmologists and researchers in MGD research to choose appropriate journals.

The results showed that thousands of scientists were dedicated to MGD research globally; among these 2,559 authors, VOSviewer revealed 21 with 10 or more publications. Authors with the same or similar research directions and subjects were classified into the same groups. Three main clusters and research areas were observed. Determining the leading authors and their research areas in MGD is important for researchers and ophthalmologists to find further cooperative studies.

3.2 Research hotspots.

Keywords, which were simple words, played an important role in identifying the most vital information from publications, as assessed based on the frequencies of the keywords. Both keywords and their occurrences reflect research hotspots. The keyword co-occurrence analysis identified four clusters and research hotspots, as discussed below.

Cluster 1 represented the pathogenesis or potential etiology of MGD based on the keywords “inflammation,” “gene expression,” “contact lens wear,” “fatty acids,” “Sjogren’s syndrome,” “tear osmolarity,” “versus-host-disease” and “androgen deficiency”. Consistent with previous studies, the keywords extracted in cluster 1 were the potential etiologies of MGD, including (1) inflammation/bacteria [8, 9, 30], in which increased levels of phospholipase A2, which is needed for the synthesis of inflammatory mediators, were observed in patients with MGD. Some inflammatory cytokines may cause keratinization of the meibomian gland opening. In addition, the number of commensal bacterial species increased and lipases produced by bacteria could dissolve the lipid secreted by the meibomian gland. (2) Desiccating stress, defined as an external stress and characterized by dry conditions, including “contact lens wear,” “Sjogren’s syndrome,” and “versus-host-disease,” which may influence the differentiation and renewal of meibocytes and lead to MGD[31]. (3) Hyperkeratinization[32]: many factors, including inflammatory cytokines and androgen deficiency, can cause the keratinization of ducts and lead to the obstruction of the meibomian gland. Accompanied by duct hyperkeratinization, inspissated lipid secretions can develop, and ultimately the meibomian glands drop out. (4) Variations in meibum composition/increased meibum viscosity[24, 33]: the proper composition and ratio of meibum ensure its normal flow. Changes in meibum composition alter meibum viscosity and tear osmolarity, leading to meibum accumulation and tear film instability. (5) Others: dyslipidemia[1], *Demodex* infestation, and oxidative stress[34] are also involved in MGD. Thus, the keywords in Cluster 1 mainly reflected the different causes of MGD.

Cluster 2 represented MGD diagnosis. The keywords “meibography,” “lipid layer thickness,” “tear film stability,” and “dry eye symptoms” were extracted. There remains no single gold standard diagnosis for MGD. Moreover, it is difficult to distinguish patients with MGD from those with dry eye disease (DED) based on symptoms, as the conditions share similar symptoms such as eye irritation and other ocular surface discomforts[35]. Therefore, careful slit-lamp examination and comprehensive clinical tests are required. While abnormal lid morphology and obstructed meibomian orifices can be evaluated directly in

ophthalmologist examinations, new diagnostic tools such as meibography[36], in vivo confocal microscopy (IVCM)[37], and optical coherence tomography (OCT)[38] have been widely used to assess meibomian glands.

Cluster 3 represented MGD therapy and the International Workshop's dedication to MGD. Patients with MGD are treated according to the symptoms and their severity. For patients with mild symptoms, publicity related to MGD was meaningful for symptom relief. However, a corresponding treatment is required for patients with more severe clinical symptoms. Regarding the potential etiology of MGD, the corresponding treatment measures are as follows (1) Basic treatments: basic treatments such as eyelid warming, massage, and hygiene are essential. (2) Antibiotics and anti-inflammatory agents[28]: Evidence showed that both antibiotics and anti-inflammatories effectively relieve symptoms in patients with MGD. (3) Lubricants/ artificial tears: Since MGD is the most common cause of evaporative dry eye disease, treatments used for dry eye, including lubricants and artificial tears, are also suitable for MGD. (4) Autologous serum-based eyedrops[39]: Recent studies have suggested that autologous serum-based eye drops may be effective in severe conditions or those accompanied by corneal epithelial damage. However, the safety, accessibility, and cost of these eyedrops require further investigation. (5) Intense pulsed light (IPL) therapy[40, 41]: Recent studies have demonstrated the role of IPL in decreasing telangiectatic blood vessels, *Demodex*, and antiinflammation. (6) Nutritional supplementation, such as essential fatty acid supplementation[42], vitamin D3 analog ointment[32], diquafosol instillation[43], and intraductal meibomian gland probing[44] have also been proposed. The keywords contained in cluster 3 are also related to the MGD International Workshop, which was held in 2011 and attended by many ophthalmic professors, covering almost all areas of MGD. At that time, many scientists made remarks on topics ranging from basic research to clinical concerns, such as MGD physiology, anatomy, pathophysiology, epidemiology, definition, diagnosis, classification, and treatment, which promoted the development of research on this disease. This is consistent with the growth trend of MGD-related studies in the years after 2011.

Cluster 4 revealed MGD epidemiology, with extracted keywords including "prevalence," "epidemiology," "population" and "risk factors." The growing concern regarding MGD has also emphasized its prevalence. A recent study reported an MGD prevalence of 35.8%[45]. Furthermore, according to Craig et al[19], the symptoms of MGD occurred earlier within the natural history of disorder progression, even in patients in their 20s, indicating the broad negative effects of MGD. In addition, East Asian ethnicities were more liable to develop MGD[46], which likely explained our observation of the USA and Keio University in Japan as the country and research institution with the highest levels of contributions to the field, respectively. A recent cross-sectional study[20] reported risk factors for MGD including East Asian ethnicity, age, thyroid disease, oral contraceptive therapy, and migraine headaches. In general, MGD has a high prevalence and is prone to affect the population with these risk factors.

4. Conclusions

This is the first study to apply scientific methods to evaluate MGD progress and trends in the last decade and identify research hotspots. These research hotspots included the MGD pathogenesis or potential etiology, diagnosis, epidemiology, and therapy, as well as the International Workshop's dedication to MGD. In addition, this study raised the possibility for researchers and ophthalmologists to find further cooperation.

5. Methods

5.1 Data collection and retrieval strategy

All data were collected from the Web of Science Core Collection (WoSCC) using the retrieval strategy: (1) TS (Themes)= "meibomian gland dysfunction"; (2) Time horizon: "from 2011 to 2020"; (3) Document type: "article". A total of 716 publications meeting the criteria with "full record and cited references" were downloaded and saved as "plain text" for the following visualized analysis.

5.2 Visualized analysis

The visualized analysis in this study applied GraphPad Prism 8, VOSviewer1.6.16, and Citespace.5.7.R2 as described previously[47]. GraphPad Prism is a drawing tool widely used in scientific research. The free applications VOSviewer (www.vosviewer.com) and Citespace (<https://sourceforge.net/>) were used for the visualization analysis of publications, institutions, countries, journals, authors, and keyword co-occurrence in sequence. On the basis of visual analysis, further literature retrieval of partial clustering results was carried out to clarify the research fields and hotspots.

Abbreviations

MGD	Meibomian gland dysfunction
USA	the United States of America
NMR	Nuclear magnetic resonance
DED	Dry eye disease
IVCM	In vivo confocal microscopy
OCT	Optical coherence tomography
IPL	Intense pulsed light

Declarations

Ethics approval and consent to participate: Not applicable.

Consent for publication: Not applicable.

Availability of data and materials: The datasets analysed during the current study are available from the corresponding author on reasonable request.

Competing interests: The authors declare that they have no competing interests.

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Authors' contributions: Qian Liu performed the experiments including analyzing the data, preparing tables and figures, reviewing related documents, and authoring drafts. Fangkun Zhao conceived the experiments, contributed analysis tools and reviewed drafts. Jun Kong supervised this project, reviewed drafts and revised this paper. All authors read and approved the final manuscript.

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Figures

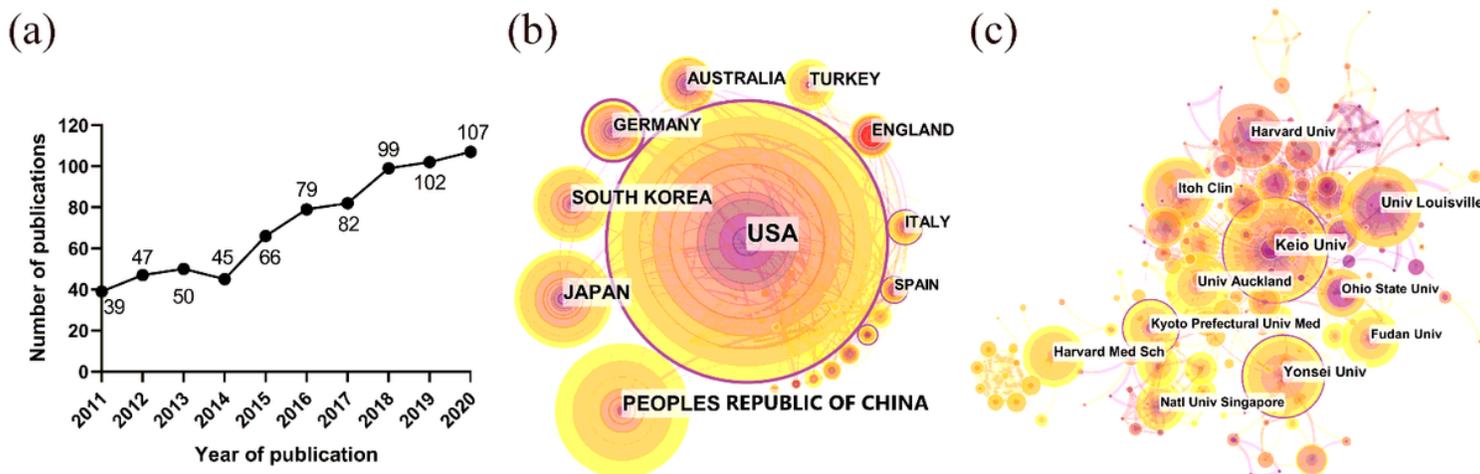


Figure 1

Tendencies in worldwide publications on MGD research, 2011–2020. (a) Annual numbers of publications on MGD research over the past decade. (b) A network map of countries in MGD research (countries with at least 25 related publications are labeled). (c) A network map of organizations in MGD research (organizations with at least 15 related publications are labeled). Every node represents a country or an organization, with the nodes representing the number of publications. Countries or institutions with high centrality are circled in purple.

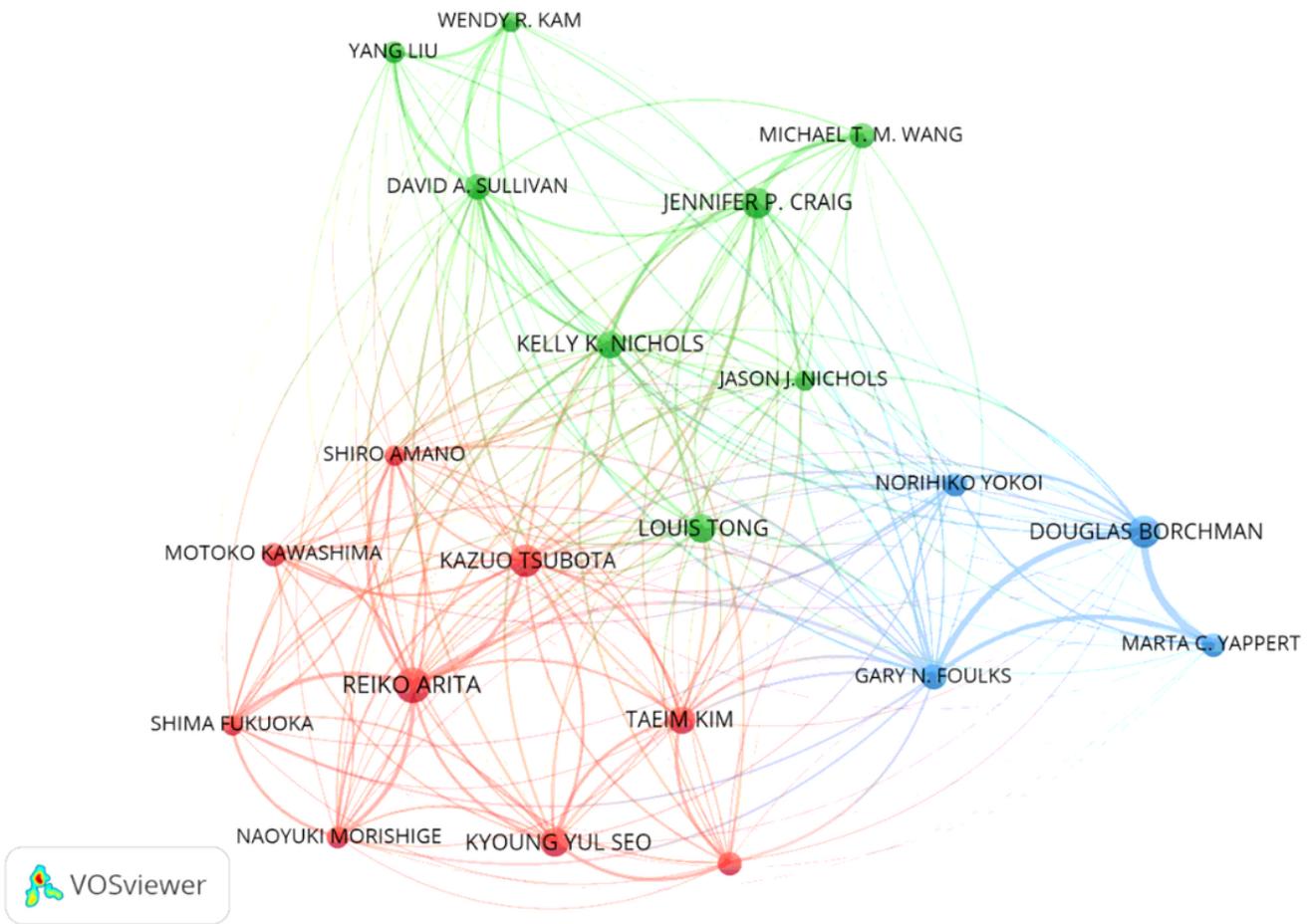


Figure 2

Co-authorship network map of authors in MGD research, 2011–2020. Among 2,559 total authors, 21 met the criteria of more than 10 related publications. Among these, three clusters (cluster 1: red, cluster 2: green, cluster 3: blue) were observed, in which authors with closer connections and cooperation were placed in the same cluster.

