Original Article

Global trends in indocyanine green fluorescence navigation in the field of gastric cancer: bibliometrics and knowledge atlas analysis

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Background: Indocyanine green (ICG) fluorescence navigation can enhance the visualization of gastric cancer (GC) lesions, increase the lymph node detection rate, and reduce the incidence of anastomotic leakage in the treatment of GC. It thus holds considerable potential for application in GC clinical surgery and has attracted widespread research interest. The purpose of this study was to visualize the current topics and emerging trends in research regarding ICG in GC.

Methods: We searched the Web of Science Core Collection (WoSCC) for articles relevant to the use of ICG in GC. The resulting information was then analyzed from a bibliometric and knowledge graph analysis perspective using CiteSpace, Scimago Graphica, and R Studio so that the key trends and hot spots in research within this field could be identified and visualized.

Results: Ultimately, 1,385 papers from 58 countries or regions published from 1991 to 2022 were included in this study. The largest number of publications were from China, followed by Japan and the United States. High-yield institutions were concentrated in Asian countries, especially China. The top publication contributors were Shanghai Jiao Tong University. Li Y and Bang YJ ranked first among the top 10 most productive authors and top 10 most cocited authors, respectively. *World Journal of Gastroenterology* was the most productive academic journal on ICG in GC, while *Cancer Research* was the most commonly cocited journal. The keyword "indocyanine green" was among the top 5 keywords, and will likely remain a popular topic in future research. Furthermore, the emerging themes including surgery, biopsy, lymphadenectomy, dissection, and gastrectomy have attracted increasing attention.

Conclusions: Current research hotspots in this area focus on the clinical implementation of ICG in precision surgery for GC. Given the imaging tracer characteristics of ICG and its utility in GC surgery, the optimization and application of ICG-guided precision surgery techniques for GC will be a research hot spot going forward.

Keywords: Indocyanine green (ICG); gastric cancer (GC); bibliometric analysis; CiteSpace; Web of Science (WoS)

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Introduction

Although the general prevalence of gastric cancer (GC) has declined significantly over the past decades, GC remains one of the leading worldwide healthcare issues, particularly in East Asian countries (1-4), and is the third most common cause of cancer-related death globally, ranking fifth in the incidence rate among cancers (5). According to the incidence and mortality statistics of cancer in China in 2016, the incidence and mortality rate of GC ranked in the top 5 among cancers (6). Previous studies have shown that GC has relatively lower prevalence and incidence rates in younger age groups (under 45 years). However, new evidence indicates that the prevalence of this premature cancer could increase in countries that are low- or high-risk for GC (7-9).

The prognosis of GC is closely associated with the stage of cancer, with the 5-year survival rate of patients at different stages varying greatly (10). Therefore, early diagnosis and treatment of GC are crucial to reducing mortality and improving survival. Integrated operative treatment is the primary tool for managing advanced GC, and lymphadenectomy for GC is considered an important component of the prognosis, staging, and treatment of this disease (11-14). Since Kitano *et al.* (15) in Japan reported the first case of laparoscopic-assisted distal gastrectomy for the treatment of early GC (EGC) in 1994, the traditional laparoscopic radical gastrectomy technique for GC has been developed for more than 20 years, with its surgical techniques maturing, indications expanding, and postoperative complications decreasing. Due to the growing maturity of traditional laparoscopic technology, a new surgical method of reduced-orifice laparoscopic technology has gradually emerged in recent years. This technique can substantially improve postoperative aesthetic outcomes, decrease postoperative pain, and shorten hospital stay, among other advantages, and both its benefits and drawbacks have been reported in myriad publications.

Despite the availability of these therapeutic modalities for GC, urgent intraoperative issues include precise localization of gastric tumors, sentinel lymph node navigation surgery for EGC, lymphatic drainage guidance for progressive GC, and intraoperative assessment of the anastomotic blood supply. To further address these challenges, indocyanine green (ICG) fluorescence imaging has been increasingly applied in clinic in recent years (16). ICG is a special fluorescent stain, and it is relatively free of adverse effects. Additionally, ICG allows for excitation by external light in the wavelength range of 750 to 810 nm with near-infrared light emission at a wavelength of approximately 840 nm. The near-infrared fluorescence system is designed to combine fluorescence excitation and fluorescence reception development to achieve fluorescence imaging of ICG (17). The principle of different tissues absorbing ICG at variable absorption rates can be used to effectively distinguish lymphatic tissue from other tissues intraoperatively (18). The introduction of this ICG fluorescence imaging technology in minimally invasive surgery has provided further assurance of accuracy for precision surgery, which presently constitutes an area of intense research interest.

Bibliometric analysis is an efficient interdisciplinary technique involving statistical methods and visualizations for investigating patterns and trends in specific research areas (19,20). Through bibliometrics, we can easily identify the salient information in a given field by performing qualitative and quantitative analyses of the scientific literature on a topic. Moreover, we can characterize the research output and grasp relevant research trends and frontiers within the field (21,22). Bibliometrics has been applied in various fields by numerous researchers to evaluate their respective research areas (23-27).

We used CiteSpace (version 6.1.3, 64-bit) and R Studio (Bibliometrix: R-tool version 3.2.1) in this study to analyze the literature related to the application of ICG in GC and to draw scientific knowledge maps for visualization of this field. This is the first specific scientometric study conducted for knowledge mapping on ICG in GC. We aimed to elucidate the research hot spots and frontiers in this field, provide a reference for ideas of subsequent research, and aid researchers in pursuing new avenues of interest.

Methods

Data source and retrieval strategies

For this study, literature was extracted through the Web of

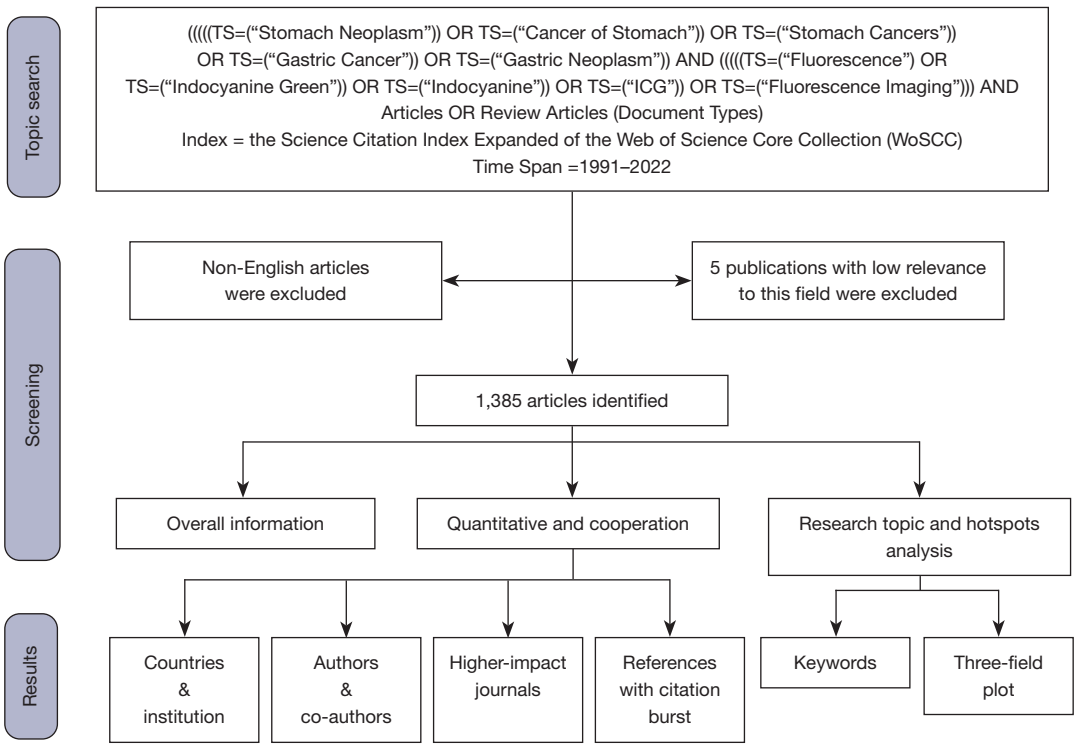

Figure 1 Study flowchart. TS, topic search; ICG, indocyanine green; WoSCC, Web of Science Core Collection.

Science (WoS), the most popular and definitive database source for scientific literature, with extensive access to key research findings from around the world. To be more specific, WoS is a multidisciplinary database containing more than 100 subjects and widely used in bibliometric studies to provide essential information on journals and other bibliometric indices.

The refined data retrieval strategy was as follows: (((((TS=("Stomach Neoplasm")) OR TS=("Cancer of Stomach")) OR TS=("Stomach Cancers")) OR TS=("Gastric Cancer")) OR TS=("Gastric Neoplasm")) AND ((((TS=("Fluorescence") OR TS=("Indocyanine Green")) OR TS=("Indocyanine")) OR TS=("ICG")) OR TS=("Fluorescence Imaging")))). The language of publications in this study was set to English. Among the various document types, only articles and reviews without duplicates were considered. The search period was set from the year 1991 to 2022. To eliminate the effects of frequently updating the database, the literature search and data collection were concluded on November 2, 2022. We excluded 5 articles with little relevance to our study. Finally, 1,385 eligible articles were obtained. The name of the exported file was "download.txt" which was then imported into CiteSpace and R Studio for quantitative evaluation. The procedure of the literature search is shown in *Figure 1*.

Analysis tools

This study used CiteSpace version 6.1.3 (64-bit) visualization software to map the scientific knowledge. CiteSpace was developed by the Chinese-American scholar Chaomei Chen as an interactive analytical program based on the fundamental assumption that "scientific knowledge is constantly changing" (28). CiteSpace can structurally and temporally analyze scientific publications to construct collaborative, co-occurrence, and cocitation networks. We additionally used Scimago Graphica, a visualization tool for analyzing and exchanging data, to discern the topographic distribution of publications on ICG in GC.

The acquired data were output to R Studio (Bibliometrix: R-tool version 3.2.1). R Studio is a relatively efficient and integrated version of the R language that is used for data analysis and processing, graphing plotting, and reporting. R Studio was utilized in this study to visualize and analyze the

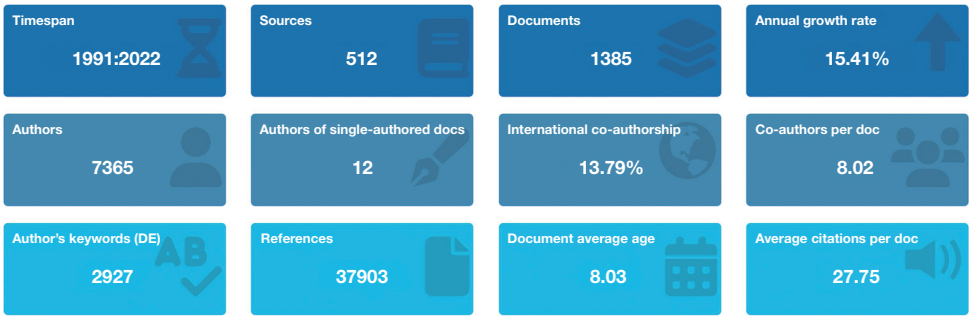

Figure 2 General information. doc, document; "DE" is a field tag. It is an abbreviation of the frequency distribution of the authors' keywords.

research topic and hotspots accordingly.

Results

General information

We retrieved 1,385 publications in WoS that met the screening criteria, including 1,309 original articles and 76 review articles. *Figure 2* shows the results obtained from importing 1,385 documents into Bibliometrix. This figure shows the general information for selected publications. Furthermore, the average age of the literature on the application of ICG in GC was as high as 8.03 years old, and the 32-year time span indicates the long history of the field. Many academics (7,365 authors) contributed to the knowledge in this field, exploring how ICG can be applied more precisely, more efficiently, and more safely in GC. ICG imaging technology has been applied in medical research since the 1950s, from its early use as a dye in cardiac surgery, ophthalmology, neurosurgery, and other fields. In recent decades, its fluorescence properties have been used in sentinel lymph node tracer navigation, tissue blood supply evaluation, lymph node tracing, and other visual surgical operations. The widespread use of ICG has shown positive therapeutic outcomes. The research on the application of ICG in GC began in 1991, showing a slight upward trend overall, with an average citation rate of 27.75% per publication and an average annual growth rate of 15.41% for publications. Overall, the volume of articles associated with the application of ICG in GC has increased year by year, from 1 article published in 1991 to 97 articles published in 2022 (as of November 2, 2022), with an average of more than 70 articles published annually in the last decade (*Figure 3*).

The activity of scientific research can be reflected by the growth pattern of the number of scientific publications over time. By analyzing the changes in the volume of literature in a specific discipline and then plotting the corresponding growth curve, we can roughly reveal the characteristics and patterns of scientific development within this discipline, which helps to ascertain the current development status of the discipline and predict its future development trend. Derek de Solla Price is considered to be the father of scientometrics. After conducting a statistical analysis of a large amount of literature, he proposed the law that the volume of scientific and technological documents increases exponentially with time (29). Based on his law, we calculated the logarithm of the cumulative publication volume and then used a linear fit to analyze the correlation between cumulative publication volume and year. We found that the cumulative publication volume grew exponentially after 2001. Therefore, we divided the research time into 2 periods with 2001 being considered the dividing point ($P<0.001$, *Figure 4*). The growth in the literature can be broadly described in 4 phases: the initial slow growth phase, the exponential growth phase, the linear growth phase, and the slow growth phase. From the graph, we found that the number of publications grew slowly between 1991 and 2001 (*Figure 5*), which may indicate that this phase was the initial exploration period of the field and that the research at that time was still in its infancy. The exponential growth in the number of publications from 2001 to 2021 suggests that the use of ICG in GC has been gradually expanding in the latter phase. In the future, we speculate that the frequency of ICG applications in GC will further increase as the sensitivity, specificity, and safety of ICG are further validated.

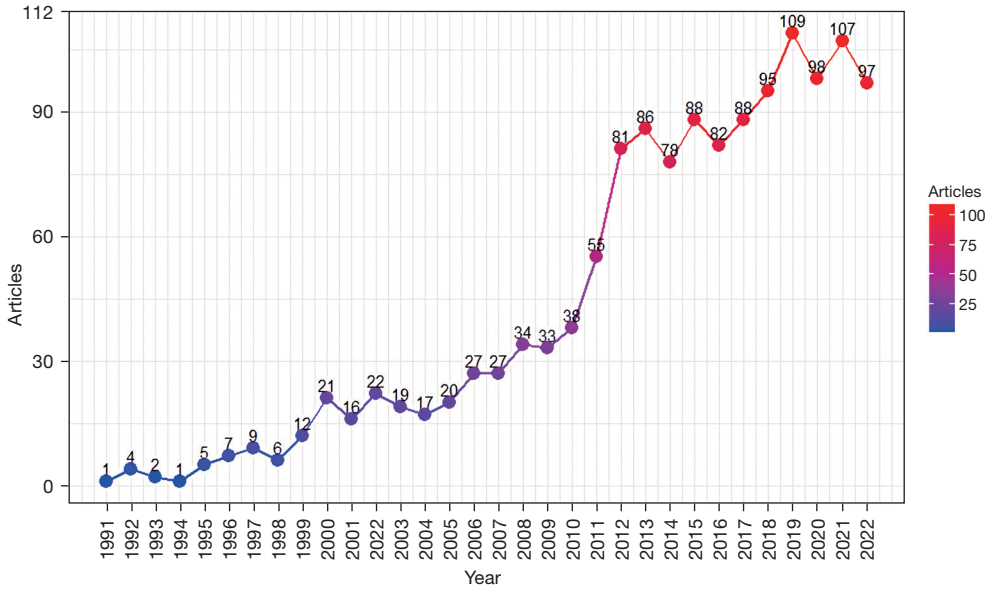

Figure 3 The overall trend of publications on ICG in gastric cancer applications from 1991 to 2022. ICG, indocyanine green.

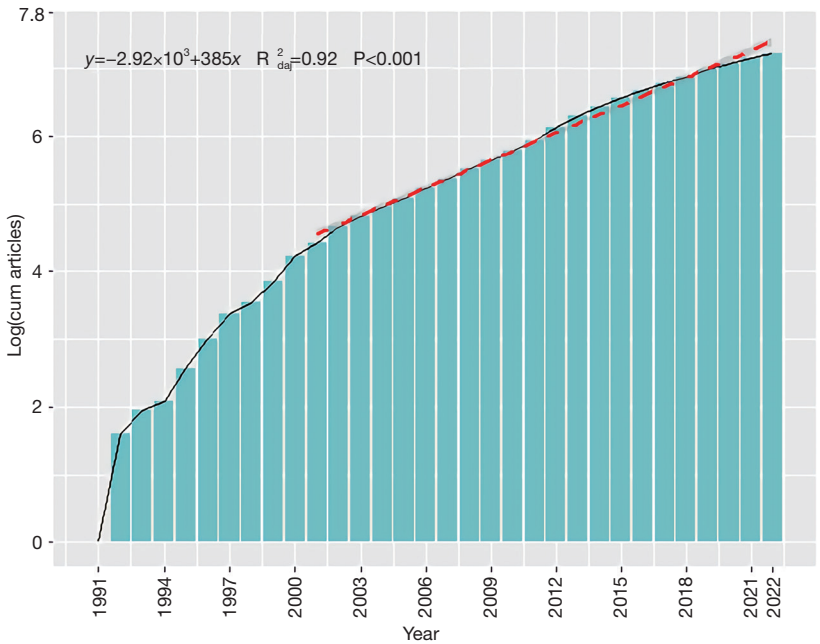

Figure 4 Trends in number of log (cumulative articles) over time. The red dashed line indicates the result of the a linear fit.

Quantitative and collaboration analyses

Country and institution analyses

The 1,385 included papers were published by 1,623 institutions in 58 countries or regions. The top 10 nations in publication number are listed in *Table 1*. We selected the institutions with the highest number of publications in the top 3 ranked countries. China leads the field in terms of the largest number of publications (645 publications; 24.14 average citations per publication; h-index 55) and also ranks first in the h-index, which is designed to measure the influence and productivity of researchers according to the frequency of their publication citation. The h-index is applied to estimate

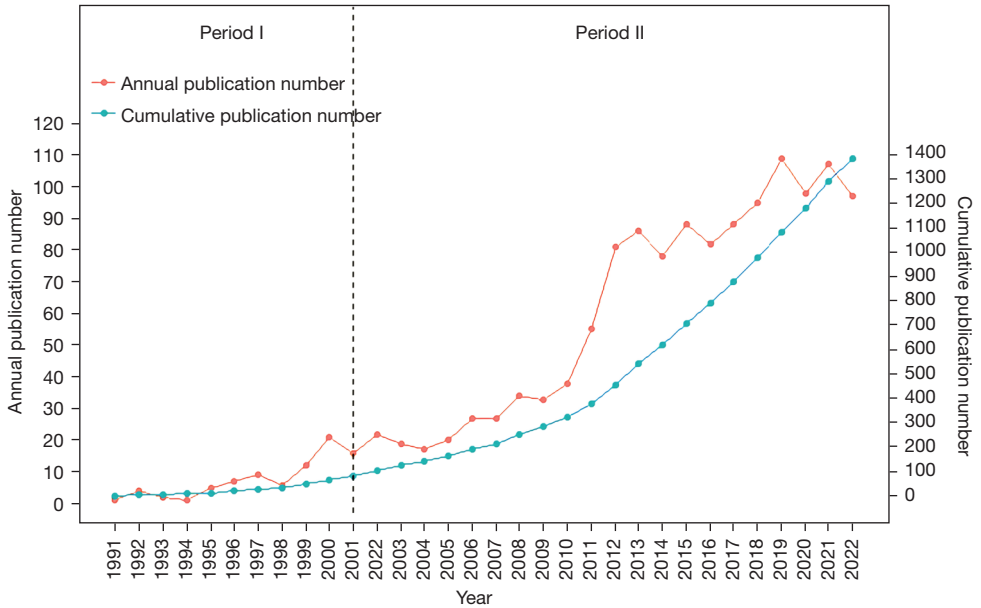

Figure 5 Cumulative number of articles and the annual number of articles over 2 time periods.

the academic influence of a country/region, journal, author, or institution (30). Japan is the country with the second most publications after China (311 publications; 34.61 average citations per publication; h-index 53), followed by the United States (151 publications, 40.01 average citations per publication, h-index 43). Apart from the United States, the countries or regions in top 4 for number of publications are from Asia, suggesting significant contributions from researchers in these regions.

Centrality is used to indicate the significance of nodes within the network. The centrality level is proportional to the importance of the nodes. The top 3 countries or regions in centrality in this study were Germany (0.41), China (0.27), and the United States (0.22). Although Germany ranked only fifth in terms of the publication quantity, it had the highest centrality, which indicates that Germany plays an important bridging role in the close cooperation with other countries or regions in this field. We used Scimago Graphica to analyze the topographic distribution of collaboration between countries or regions associated with the use of ICG in GC (*Figure 6*). Based on this analysis, we drew graphs for better visualization. In *Figure 6*, the circle size is proportional to the volume of publications, and the boldness of the lines indicates the density of collaboration among countries or regions; the redder a country's node is, the greater the total number of research papers that the country has published through collaboration with other countries. We found that China had the closest cooperative relationship with the United States. In addition, China had a wide range of collaborations with other countries or regions, including Germany, South Korea, and Japan, among others. In contrast, some developed countries, such as those in Europe, showed less collaboration with other countries.

Research institutions are oriented research forces, and the research perspectives of important research institutions often influence the academic circle in this field. In *Table 1*, the top 3 institutions in terms of the number of publications were Shanghai Jiao Tong University (51 publications), Nanjing Medical University (38 publications), and Seoul National University (34 publications). In the modern era, a variety of therapeutic cancer strategies such as photothermal therapy (PTT) have proven essential in overcoming the primary barrier of GC variability and complexity. A study from Shanghai Jiao Tong University reported on the controllable delivery and release of distinctly targeted ICG and the outstanding tumor inhibiting efficacy of PTT, creating a promising avenue for effective cancer treatment (31). Nanjing Medical University's 2021 study retrospectively collected patients with a diagnosis of GC in consecutive years who received laparoscopic radical GC surgery. The study then matched patient samples on a 1:1 basis in terms of propensity scores and finally compared the results of the 2 groups. The results demonstrated that

Table 1 Top 10 prolific countries or regions and corresponding institutions in the field of ICG in GC

Ranking	Countries or regions			Corresponding institutions				
	Country/region	Frequency	Centrality	Institution	Frequency	Centrality	Average citation	h-index
1	China	645	0.27	Shanghai Jiao Tong University	51	0.03	24.14	55
				Nanjing Medical University	38	0.02		
				Chinese Academy of Sciences	21	0.03		
2	Japan	311	0.07	Kyoto Prefectural University of Medicine	21	0.01	34.61	53
				Hamamatsu University School of Medicine	16	0.02		
				Kanazawa University	11	0.02		
3	USA	151	0.22	National Cancer Centre	20	0.07	40.01	43
				Memorial Sloan Kettering Cancer Center	7	0		
				AntiCancer Inc.	6	0.01		
4	South Korea	124	0.15	Seoul National University	34	0.05	46.34	33
5	Germany	83	0.41	Technical University of Munich	4	0	56.33	30
6	Italy	41	0.11	The University of Milan	3	0	42.45	16
7	France	23	0.09	University of Strasbourg	2	0	60.22	15
8	Poland	19	0.06	Wielkopolska Cancer Centre	2	0	29.53	9
9	The Netherlands	100	0.02	Leiden University	3	0	136.24	14
10	Brazil	16	0	Federal University of Paraná	10	0	23.82	13

ICG, indocyanine green; GC, gastric cancer.

ICG-guided laparoscopic radical gastrectomy is reliable and efficacious (32).

In terms of centrality, the National Cancer Centre (0.07) had the highest score among institutions, followed by Seoul National University (0.05), Shanghai Jiao Tong University (0.03), and the Chinese Academy of Sciences (0.03). A recent study by Seoul National University found that ICG fluorescence imaging with tissue marking dyes is helpful for visualizing the perigastric lymphatic network in advanced gastric cancer (AGC) and for tracking the precise position of ICG-stained lymph nodes. Despite this, ICG imaging is not generally preferred for selective lymph node dissection in AGC due to confined perigastric lymph node staining (33).

Furthermore, we mapped research institutional collaboration using CiteSpace. The institutional collaboration network knowledge graph consists of 158 nodes and 121 links. In *Figure 7*, the node size indicates the quantity of publications within the institution, and the node color and thickness indicate the quantity of publications at various time frames. The high-yield institutions are concentrated in Asian countries, especially China. This indicates that Asian-located institutions are an important research force in this field. Many Chinese institutions (Shanghai Jiao Tong University, Chinese Academy of Sciences, Nanjing Medical University) have established close ties with one another, indicating that China has a relatively advanced status of study within this area and has an array of research institutions with core competencies.

Author and coauthor analyses

Reviewing the literature produced by highly influential authors in a field can provide a quicker means of more comprehensively grasping the classical theory in this field. In our study, we found that a total of 7,365 authors contributed 1,385 articles to the field of ICG in GC. *Table 2* lists the leading authors by volume of publications.

Li Y had the highest volume of publications (54 papers; h-index 22), followed by Wang Y (48 papers; h-index 24). Liu Y, Zhang Y, and Wang J were next in the highest number of publications, respectively. Zhang Y had the highest h-index among those ranked top 10 in the number of publications. He is dedicated to the research of anticancer drugs, but we found that his papers have not

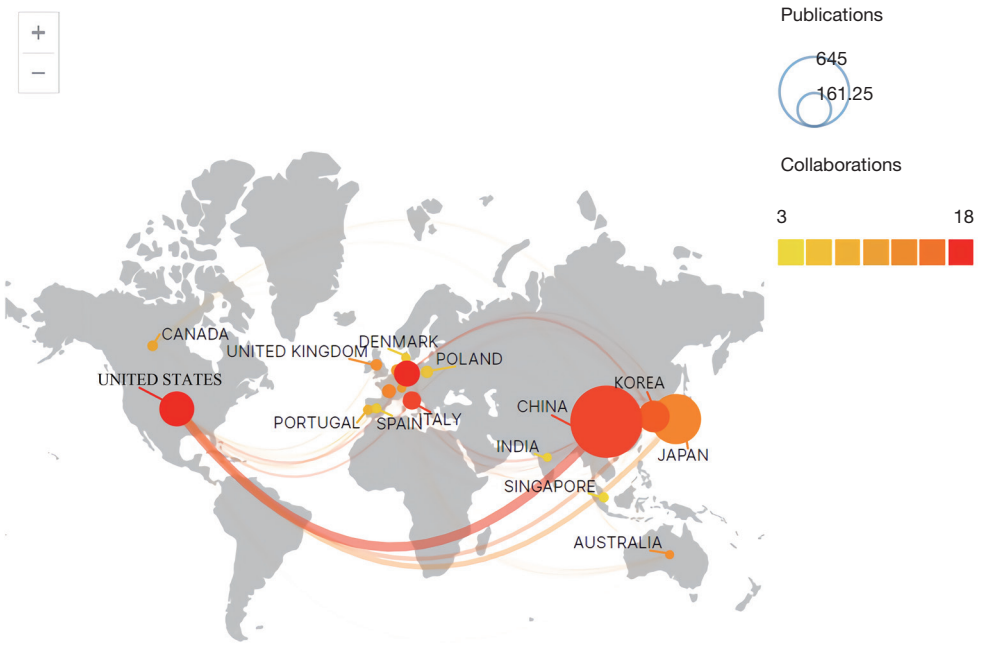

Figure 6 Geographical distribution of collaboration between countries or regions in the field of ICG in GC. ICG, indocyanine green; GC, gastric cancer.

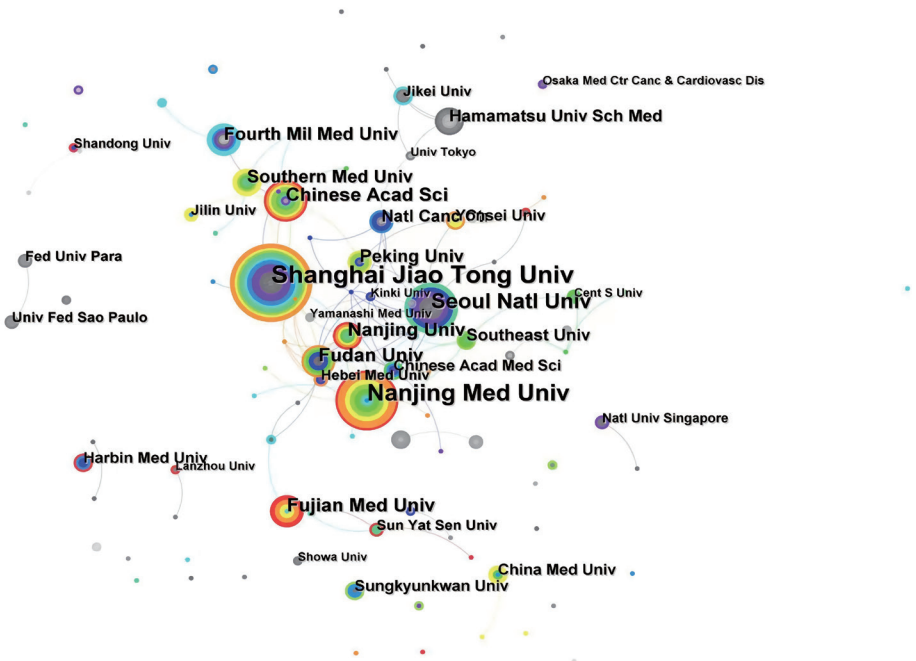

Figure 7 Knowledge map and institutional collaboration network of ICG in GC. ICG, indocyanine green; GC, gastric cancer.

Table 2 Top 10 most productive authors and top 10 most cocited authors in ICG research

Ranking	Most productive authors			Most cocited authors		
	Author	Count	h-index	Author	Count	h-index
1	Li Y	54	22	Bang YJ	185	87
2	Wang Y	48	24	Hofmann M	112	2
3	Liu Y	43	22	Jemal A	89	128
4	Zhang Y	43	31	Miyashiro I	79	41
5	Wang J	34	5	Ferlay J	70	4
6	Zhang X	34	16	Ruschoff J	66	48
7	Kim H	32	14	Kitagawa Y	64	62
8	Li Z	30	8	Tajima Y	63	18
9	Chen J	25	25	Gravalos C	62	11
10	Zhang J	25	29	Bray F	62	108

ICG, indocyanine green.

been included in WoS in recent years. His latest study described a color-coded imaging model. According to this model, the quantification of neointimal length can be achieved by implanting Gelfoam into nestin-driven green fluorescent protein (ND-GFP) nude mice. Using color-coded imaging, he also identified *Salmonella typhimurium* A1-R as potentially applicable in antiosteosarcoma angiogenesis-targeted therapy (34). Wang Y was not only the second most published author in this field, but his paper titled "Differential expression of microRNA species in human gastric cancer versus non-tumorous tissues" was the top ranked article among the top 10 cited articles (*Table 3*) (35). This paper constitutes one of the earliest reported associations of microRNAs (miRNAs) with GC. This novel finding could indicate a possible role of miRNA in the diagnosis of GC. The third most cited article titled "The clinical use of indocyanine green as a near-infrared fluorescent contrast agent for image-guided oncologic surgery" analyzed the advantages and limitations of the application of ICG in near-infrared fluorescence cancer-related surgical treatment (36).

A knowledge map of authors' collaboration, consisting of 852 nodes and 1,622 links, is shown in *Figure 8*. The node size indicates the quantity of authors' publications, and the lines and their thickness indicate the relative degree of collaboration between authors. We found that the authors of relevant ICG studies were mainly located in Asia. Chinese authors have contributed greatly to this area and have established extensive contacts with other authors in China. In *Figure 8*, a purple circle indicates an author centrality greater than 0.1. From the figure, we can discern that there are no authors with high centrality in China, indicating that China's research results are relatively independent, and thus Chinese research in this field could be strengthened via greater cooperation with other countries.

In addition, the cocitation analysis of authors allows for the identification of key authors in the in a given field. In general, commonly cited authors are considered to be more influential than less frequently cited authors, and cocited authors are likely to focus on related research areas. In this study, Bang YJ, from the Seoul National University College of Medicine, was found to be the most commonly cocited author, with a total citation frequency of 185. Over the past few years, his research has focused on the use of pembrolizumab to treat GC. Human epidermal growth factor receptor 2 (HER2) overexpression/expansion correlates to the progression of diverse solid tumor patterns. Based on the relationship between HER2 and GC, some researchers have inspected the status of GC by detecting the status of HER2. The second most cited author Hofmann M used fluorescence in situ hybridization (FISH) to determine the HER2 status in formalin-fixed, paraffin-embedded GC samples. Combined with this test technique, a GC HER2 scoring system was established to identify patients with advanced metastatic GC eligible for trastuzumab trials (37). Based on the above 2 authors' studies, we can speculate that fluorescence assay is a capable method for detecting the therapeutic effect of anticancer drugs.

Table 3 Top 10 most cited publications

Ranking	Article title	Cited frequency	
		Average annual citation frequency	Count
1	Assessment of a HER2 scoring system for gastric cancer: results from a validation study	55.73	836
2	Trastuzumab in combination with chemotherapy versus chemotherapy alone for treatment of HER2-positive advanced gastric or gastro-esophageal junction cancer (ToGA): a phase 3, open-label, randomized controlled trial	56.92	740
3	The clinical use of indocyanine green as a near-infrared fluorescent contrast agent for image-guided oncologic surgery	46.83	562
4	Circular RNA cSMARCA5 inhibits growth and metastasis in hepatocellular carcinoma	85.8	429
5	Lapatinib plus paclitaxel versus paclitaxel alone in the second-line treatment of HER2-amplified advanced gastric cancer in Asian populations: TyTAN–a randomized, phase III study	46.44	418
6	Differential expression of microRNA species in human gastric cancer versus non-tumorous tissues	29.43	412
7	Circular RNA_LARP4 inhibits cell proliferation and invasion of gastric cancer by sponging miR-424-5p and regulating LATS1	64.17	385
8	HER2 testing in gastric cancer: a practical approach	34.73	382
9	HER2 diagnostics in gastric cancer-guideline validation and development of standardized immunohistochemical testing	27.38	356
10	MET amplification identifies a small and aggressive subgroup of esophagogastric adenocarcinoma with evidence of responsiveness to crizotinib	29.58	355

HER2, human epidermal growth factor receptor 2; ToGA, Trastuzumab for Gastric Cancer; MET, mesenchymal to epithelial transition.

Higher-impact journal analysis

A total of 1,385 papers concerning the application of ICG to GC were published in 512 journals. The top 10 journals with the most publications were visualized using the R-tool bibliometrix (*Figure 9*). *Table 4* provides the essential summary profiles of the top 10 most prolific journals and cocited journals, respectively. Among leading journals with the highest number of publications, *World Journal of Gastroenterology* [43 publications; 2021 impact factor 5.374 (Q2)] ranked first, followed by *Gastric Cancer* and *Oncology Letters* (31 and 26 publications, respectively). The annual publication volume of these journals in the last decade has been concentrated around 2–4 articles. In 2018, 8 related articles were published by *Oncology Letters*, which is the highest volume of annual publications among these journals over the past 3 decades (*Figure 10*). We found that *International Journal of Oncology* was the first journal to publish in this field, but as of 2022, it only ranked fourth in terms of the number of articles published. *World Journal of Gastroenterology* began to include ICG-related articles in 1991 and have since published an ever-growing number of relevant papers. This journal ranked first among the top 5 journals for the volume of papers published. *Gastric Cancer* started late with the inclusion of ICG-related articles in 2007 but has since then moved to second place in terms of the volume of relevant articles published (*Figure 11*).

The journal impact factor is an important indicator of the value of articles (38). The impact factor in the majority of journals in this study was below 5, which indicates that the level of research in this field is not very high. Researchers need to intensify efforts to elevate the research level in this field and improve the quality of articles. Cocitation frequency determines the journal's impact and indicates if it has had a significant influence over a specific area of research. Our results indicated that *Cancer Research* ranked first among the cocited journals, indicating its absolute impact on the application of ICG in GC. Almost any cocited journal was found to be closely associated with cancer research. Moreover, all cocited journals were Q1 (e.g., *Nature* and *Science*), which indicates that the quality of

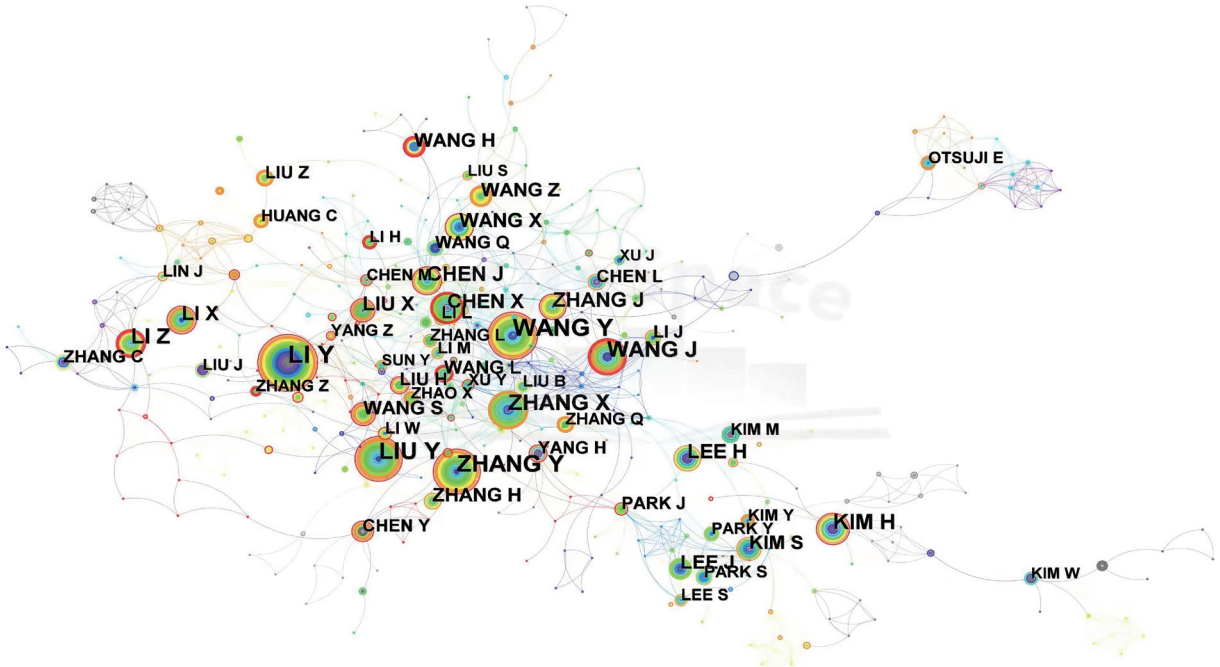

Figure 8 Knowledge map of authors' collaboration network related to ICG in GC. ICG, indocyanine green; GC, gastric cancer.

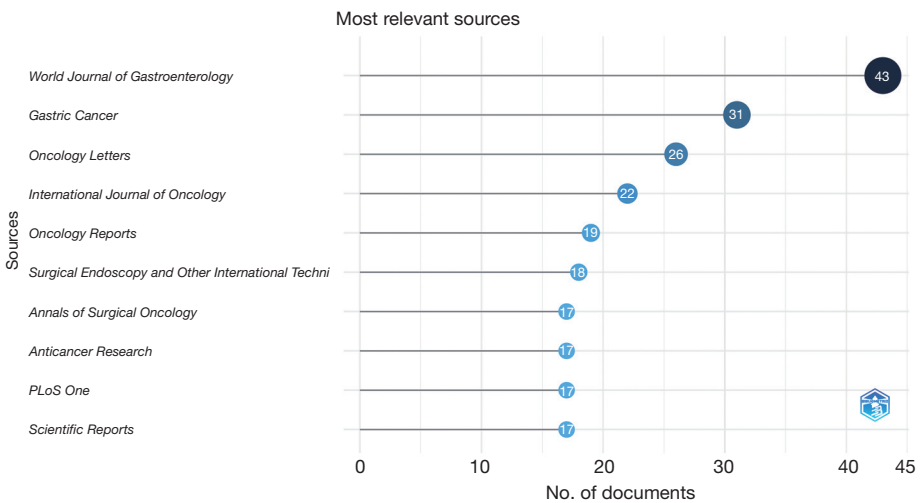

Figure 9 Top 10 journals in terms of the number of publications.

cocited articles in the field is extremely high and produced from journals with high impact.

References with a citation burst

A citation burst is a surge in citations of certain papers over a short period of time. Research trends in a given field can be predicted through analysis of reference citation bursts (39). In *Figure 12*, the red lines indicate the citation outbreak duration, denoting the development of popular topics while the blue lines represent the time intervals. The strength of the burst is proportional to the impact of the publication. In 2010, Bang YJ published the first reference to have the maximum burst intensity in *Lancet*. The samples for this study included only patients with

Table 4 Top 10 most prolific journals and cocited journals that published articles on ICG in GC

Ranking	Prolific journal				Cocited journal			
	Journal name	Output	IF	JCR	Journal name	Citation	IF	JCR
1	*World Journal of Gastroenterology*	43	5.374	Q2	*Cancer Res*	576	13.312	Q1
2	*Gastric Cancer*	31	7.701	Q1	*Int J Cancer*	440	7.316	Q1
3	*Oncology Letters*	26	3.111	Q3	*J Clin Oncol*	413	50.717	Q1
4	*International Journal of Oncology*	22	5.884	Q2	*Clin Cancer Res*	412	13.801	Q1
5	*Oncology Reports*	19	4.136	Q2	*P Natl Acad Sci USA*	395	12.779	Q1
6	*Surgical Endoscopy and Other Interventional Techniques Interventional Techniques*	18	3.453	Q2	*Brit J Cancer*	382	9.075	Q1
7	*Annals of Surgical Oncology*	17	4.339	Q1	*Lancet*	363	202.731	Q1
8	*Anticancer Research*	17	2.435	Q4	*Nature*	356	69.504	Q1
9	*PLOS One*	17	3.752	Q2	*Science*	352	63.714	Q1
10	*Scientific Reports Cancer Institute*	17	4.996	Q2	*Gastric Cancer*	330	7.701	Q1

ICG, indocyanine green; GC, gastric cancer; IF, impact factor; JCR, Journal Citation Reports.

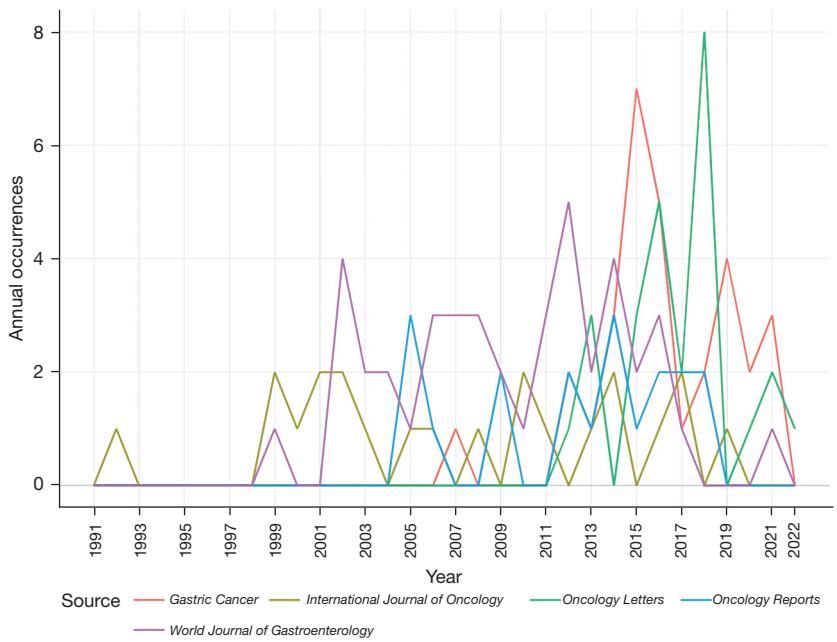

Figure 10 The trends of the top 5 journals in terms of annual publication.

tumors showing HER2 protein overexpression according to immunohistochemistry and patients with tumors showing HER2 protein-related gene amplification according to FISH. With the help of these sample of patients, he revealed that trastuzumab coupled with chemotherapy may be regarded as an emerging criterion for screening HER2-positive patients with late-stage GC (40).

Among the top 25 articles with the highest citation bursts, 6 had citation bursts ending in 2022. This is consistent with the recent emergence of ICG research. Lan *et al.* developed

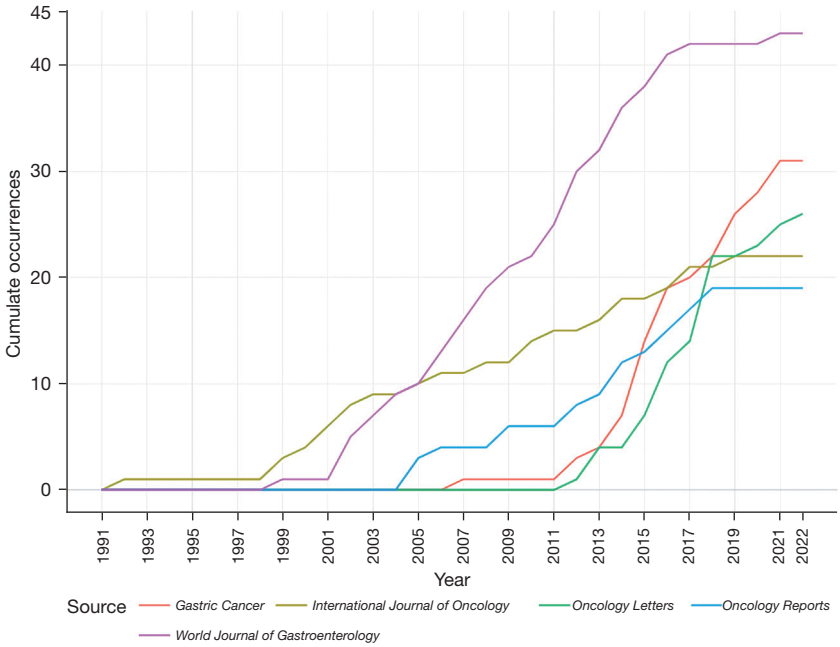

Figure 11 The trends of the top 5 journals in terms of total number of publications.

Top 25 references with the strongest citation bursts

References	Year	Strength	Begin	End	1991–2022
Parkin DM, 2005, CA-CANCER J CLIN, V55, P74, DOI 10.3322/canjclin.55.2.74, DOI	2005	7.45	**2008**	2010	
Fujimoto-ouchi K, 2007, CANCER CHEMOTH PHARM, V59, P795, DOI 10.1007/s00280-006-0337-z, DOI	2007	6.75	**2008**	2011	
Hofmann M, 2008, HISTOPATHOLOGY, V52, P797, DOI 10.1111/j.1365-2559.2008.03028.x, DOI	2008	23.65	**2010**	2013	
Marx AH, 2009, HUM PATHOL, V40, P769, DOI 10.1016/j.humpath.2008.11.014, DOI	2009	10.02	**2010**	2013	
Tajima Y, 2009, ANN SURG, V249, P58, DOI 10.1097/SLA.0b013e3181927267, DOI	2009	9.95	**2010**	2014	
Gravalos C, 2008, ANN ONCOL, V19, P1523, DOI 10.1093/annonc/mdn169, DOI	2008	9.13	**2010**	2013	
Bang YJ, 2010, LANCET, V376, P1302	2010	28.47	**2011**	2015	
Ruschoff J, 2010, VIRCHOWS ARCH, V457, P299, DOI 10.1007/s00428-010-0952-2, DOI	2010	10.47	**2011**	2015	
Barros-silva JD, 2009, BRIT J CANCER, V100, P487, DOI 10.1038/sj.bjc.6604885, DOI	2009	9.47	**2011**	2013	
Jorgensen JT, 2010, ONCOLOGY-BASEL, V78, P26, DOI 10.1159/000288295, DOI	2010	6.6	**2011**	2013	
Jemal A, 2011, CA-CANCER J CLIN, V61, P69, DOI 10.3322/caac.20107, DOI	2011	18.16	**2012**	2016	
Bang YJ, 2010, LANCET, V376, P687, DOI 10.1016/S0140-6736(10)61121-X, DOI	2010	8.82	**2012**	2014	
Grabsch H, 2010, CELL ONCOL, V32, P57, DOI 10.3233/CLO-2009-0497, DOI	2010	8.68	**2012**	2015	
Ruschoff J, 2012, MODERN PATHOL, V25, P637, DOI 10.1038/modpatho1.2011.198, DOI	2012	11.93	**2013**	2017	
Kitagawa Y, 2013, JCLIN ONCOL, V31, P3704, DOI 10.1200/CO.2013.50.3789, DOI	2013	11.78	**2014**	2018	
Torre LA, 2015, CA-CANCER J CLIN, V65, P87, DOI 10.3322/caac.21262, DOI	2015	18.18	**2017**	2019	
Chen WQ, 2016, CA-CANCER J CLIN, V66, P115, DOI 10.3322/caac.21338, DOI	2016	15.16	**2017**	2020	
Ferlay J, 2015, INT J CANCER, V136, P0, DOI 10.1002/jc.29210, DOI	2015	13.66	**2017**	2020	
Bass AJ, 2014, NATURE, V513, P202, DOI 10.1038/nature13480, DOI	2014	7.28	**2017**	2019	
Japanese GASTRCANCASSOC, 2021, GASTRIC CANCER, V24, P1, DOI 10.1007/s10120-020-01042-y, DOI	2021	19.04	**2021**	2022	
Bray F, 2018, CA-CANCER J CLIN, V68, P394, DOI 10.3322/caac.21492, DOI	2018	25.35	**2019**	2022	
Kwon IG, 2019, JAMA SURG, V154, P150, DOI 10.1001/jamasurg.2018.4267, DOI	2019	13.93	**2020**	2022	
Kim TH, 2018, J GASTRIC CANCER, V18, P161, DOI 10.5230/jgc.2018.18.e19, DOI	2018	9.22	**2020**	2022	
Lan YT, 2017, SAGE OPEN MED, V5, P0, DOI 10.1177/2050312117727444, DOI	2017	8.28	**2020**	2022	
Huh YJ, 2019, JLAPAROENDOSC ADV S, V29, P476, DOI 10.1089/1ap.2018.0263, DOI	2019	6.89	**2020**	2022	

Figure 12 Top 25 references in terms of strongest citation bursts.

Table 5 Top 20 keywords in ICG in GC research

Ranking	Keyword	Centrality	Count	Year
1	Gastric cancer	0.17	778	1991
2	Expression	0.16	255	1991
3	Carcinoma	0.12	195	1992
4	Breast cancer	0.1	149	1995
5	Indocyanine green	0.02	100	2006
6	*In situ* hybridization	0.06	97	1998
7	Cancer	0.11	95	1997
8	Gene amplification	0.03	83	1998
9	Growth	0.04	79	2000
10	Colorectal cancer	0.04	77	1996
11	Apoptosis	0.07	73	2001
12	Cell	0.05	69	1993
13	Therapy	0.05	66	2002
14	Survival	0.04	65	1997
15	Identification	0.11	63	1991
16	Amplification	0.07	62	1996
17	Gene	0.04	61	1999
18	Metastasis	0.02	61	2007
19	Adenocarcinoma	0.06	60	1996
20	Overexpression	0.02	56	1997

ICG, indocyanine green; GC, gastric cancer.

ICG combined with near-infrared imaging as a prospective approach for locating lymph in the robotic gastrectomy of GC (41). Huh *et al.*'s study demonstrates that the use of near infrared imaging with ICG-enhanced fluorescence is a feasible and effective method for evaluating blood vessel perfusion in the surgical anastomosis of GC (42). Kwon *et al.*'s findings in 2019 suggest that ICG may help to identify and visualize each lymph node draining from the primary lesion intraoperatively to perform thorough lymph node dissection (43). Rüschoff *et al.*'s paper titled "HER2 testing in gastric cancer: a practical approach" had the longest citation burst among the top 25 references. In this paper, the authors used immunohistochemistry as an initial testing method. Furthermore, given the predictive value of HER2 protein levels related to response in trastuzumab treatment studies for GC, FISH or silver *in situ* hybridization was used to reassay immunohistochemical 2+ samples (44).

Research topic and hotspots analysis

Keyword analysis

Keywords are a distillation and abstract of the article's research theme and content, and they are a manifestation of the content of the article. Identification of research hotspots in a given field can be achieved through keyword co-occurrence analysis. *Table 5* shows that in keyword frequency ranking, "gastric cancer" appeared 778 times, ranking first, followed by "expression" (n=255), "carcinoma" (n=195), "breast cancer" (n=149), and "indocyanine green" (n=100), indicating that the use of ICG in GC, particularly in detecting the expression of genes or proteins, has been a popular research topic worldwide. The top 3 keywords for centrality were "gastric cancer" (centrality 0.17), "expression" (centrality 0.16), and "carcinoma" (centrality 0.12). In terms of the chronological order of the first occurrence of keywords, "indocyanine green" is relatively recently introduced. This indicates that the use of ICG in GC is relatively cutting edge.

A keyword burst refers to keywords whose frequency surges within a short period. Through the analysis of emergent keywords, we could determine the cutting edge of research and further ascertain the development trend of future research. *Figure 13* lists the top 25 outbreak keywords, with the shortest duration being 1 year and the longest being 15 years. "*In-situ* hybridization" (burst strength 11.99) had the highest burst strength and the longest duration, indicating that it was a hot topic before 2013, receiving sustained attention. The second ranked keyword in terms of burst strength was "proliferation" (burst strength 10.53), followed by "trastuzumab" (burst strength 9.16). "Indocyanine green" was the fifth ranked in burst strength. Although it first appeared in 1991, it began to be studied in 2020 and continued to be a hot topic in 2022. Over the past 3 years, researchers have focused mainly on "migration" (burst strength 6.03; duration 2019–2022), "indocyanine green" (burst strength 8.66; duration 2020–2022), and "lymph node dissection" (burst strength 5.84; duration 2020–2022).

Moreover, R Studio was used to draw a graph of the distribution of 30 high-frequency keywords against time, as seen in *Figure 14*, in which every cell indicates the frequency of the keyword occurring within a year. These occurrence

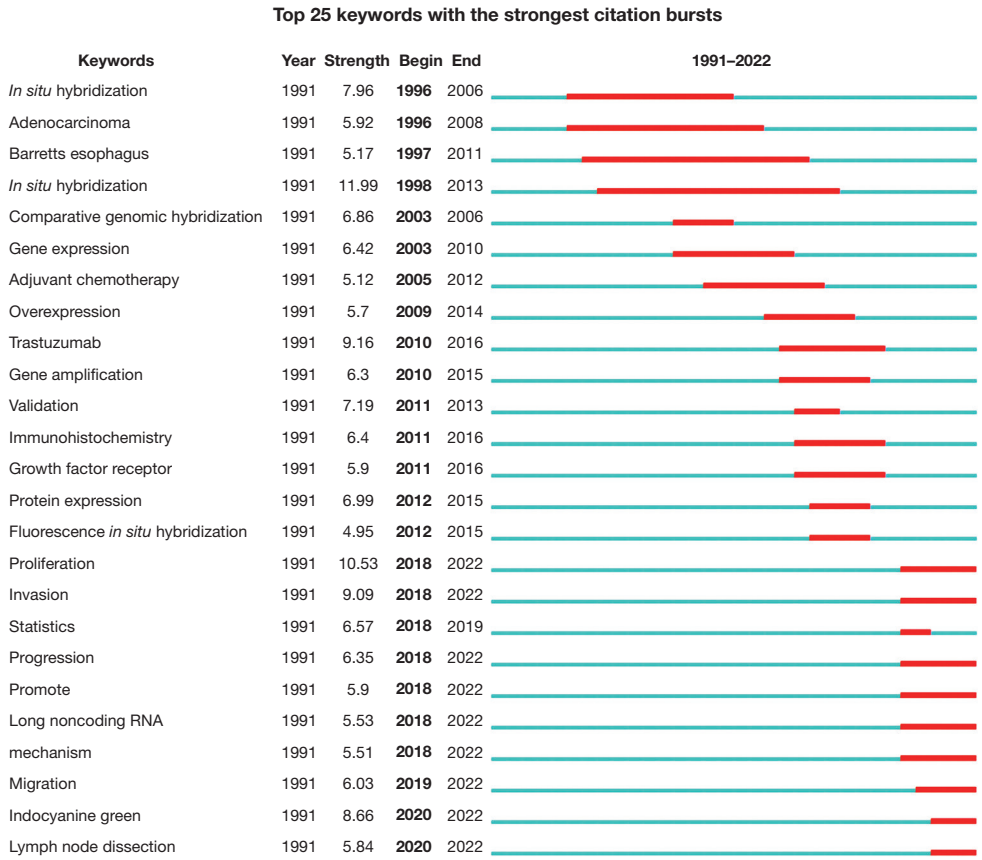

Figure 13 Top 25 keywords with the strongest citation bursts.

frequencies (0–1) were normalized to form the corresponding values. The lowest value in the black cell indicates the least frequent occurrence of the keyword in the year. The yellow cells have the largest value, corresponding to the most frequent occurrence of the keyword in the year. The frequency of "gastric cancer" and "apoptosis" is high from 2012 to 2022 (as of November 2022), while the occurrence frequency of "HER2" gradually increased from 2012 to 2015 and showed a decreasing trend from 2016 to 2022. Over the past 5 years, the frequency of "FISH" has decreased while the frequency of "ICG" has gradually increased.

Finally, the R-tool bibliometrix was used to process 250 keywords (*Figure 15*), in which the minimal clustering frequency was 5, and each clustering had a count of 5 labels. In *Figure 15*, the x-axis denotes centrality, which shows the significance of the topic while the y-axis denotes density, which shows the development degree of research on the topic. The upper right quadrant (motion theme) has high-intensity and high-centrality features, indicating that it could be a well-established and significant subject within the ICG research domain. In the motor themes, the main domains of research are "gastric cancer", "expression", "carcinoma", "breast cancer", and "cancer". Motor themes are considered to be themes that support the development and strengthening of areas of knowledge because of their centrality and density. The upper left quadrant (niche themes) represents a subject with good internal development. The cluster includes "apoptosis", "proliferation", "*in-vitro*", "activation", and "pathway". Clusters from the third quadrant (new or falling topics) were marked as less central and less dense; that is, less advanced, gradually emerging, as well as marginally significant, with "surgery", "biopsy", "lymphadenectomy", "dissection" and "gastrectomy" as major themes. The thematic keywords belonging to basic themes with weak intrinsic development are "metastasis", "ICG", "diagnosis", "fluorescence" and "*in vivo*". They cover general themes that span different research areas in the field.

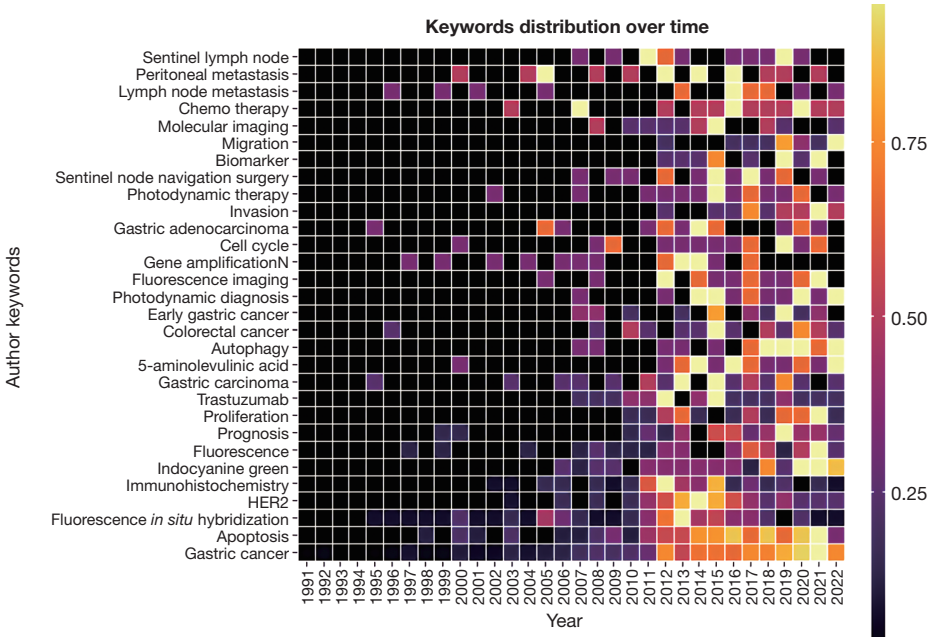

Figure 14 Distribution of the 30 most high-frequency keywords over time. HER2, human epidermal growth factor receptor 2.

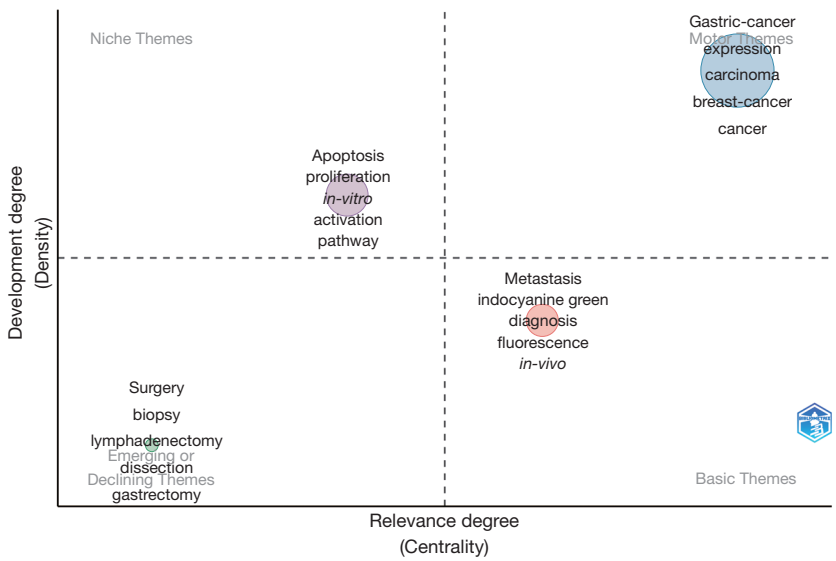

Figure 15 The keywords thematic map generated with the R-tool bibliometrix.

Three-field plot for top authors, keywords, and countries

We used a three-field diagram to plot the relationship between the top 10 authors, keywords, and countries in terms of research intensity, as shown in *Figure 16*. The height of the rectangle in the three-field diagram is based on the rate or value of the sum of the relationships generated between the components plotted in the three-field diagram. The closer the relationships between the plotted components are, the taller the rectangle appears. We found that the authors' studies, mainly in China, Japan, and Korea, focused on keywords such as "gastric cancer",

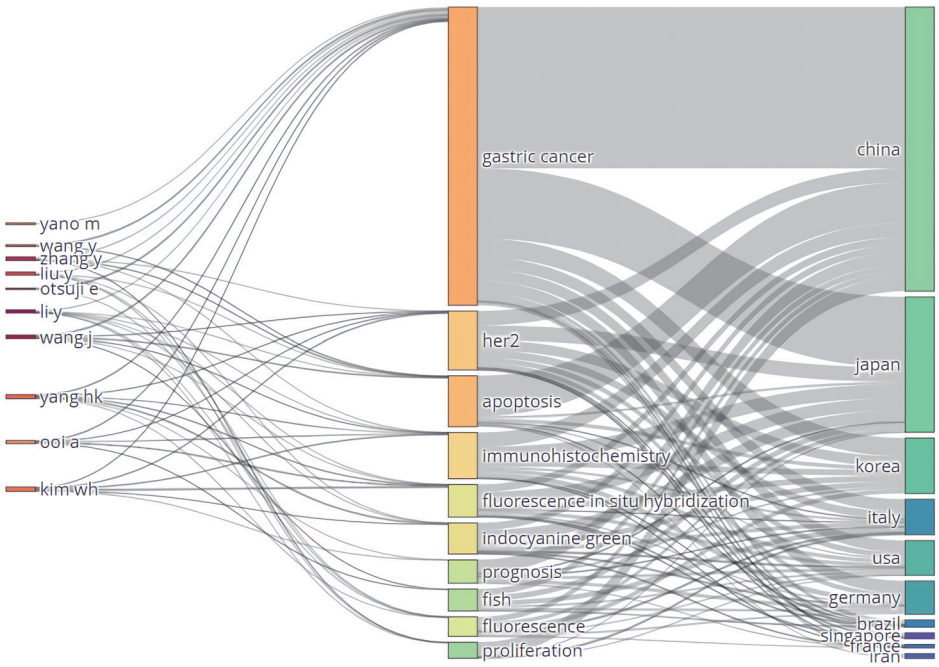

Figure 16 Relations between authors (left), keywords (middle), and countries (right) in ICG in GC research. ICG, indocyanine green; GC, gastric cancer.

"HER2", "apoptosis", "immunohistochemistry", "FISH", and "ICG", among others, The relevant articles from China covered almost all keywords, while those covered by Europe and the United States were not comprehensive in terms of quantity, indicating that China dominates the field in this regard.

Discussion

General information

This study systematically searched the WoS database for papers related to ICG in GC published between 1991 and 2022. Ultimately, we retrieved 1,385 publications in WoS that met the eligibility criteria. As can be observed from *Figure 3*, the average yearly increase in publications related to ICG in GC was 15.41%, increasing from 1 publication in 1991 to 107 publications in 2021. The active level scientific research can be reflected by the growth pattern of the number of scientific publications over time. Based on the Price law of exponential growth of scientific and technical literature over time, we found that cumulative publications grew exponentially after 2001. The research time was divided into 2 periods by with 2001 being used as the cutoff point (P value <0.001; *Figures 4,5*), including a slow growth phase [1991–2001] and an exponential growth phase [2001–2021]. This may be due to the first use of sentinel lymph node biopsies with ICG in GC surgery by Hiratsuka *et al.* in 2001 (45). The procedure had excellent reliability and the sentinel lymph node status was able to predict lymph node status quite accurately. In the same year, ICG-sulfo-OSu-labeled antihuman carcinoembryonic antigen antibody and infrared fluorescence endoscopy emerged as a technology for detecting human GC in resected specimens *in vitro*, which attracted considerable interest in the application of ICG to GC (46). These 2 successful initiatives in 2001 heralded an era of the practical use of ICG in GC. Hence, the number of articles published in this field has grown at an impressive rate since 2001, suggesting that this field is attracting extensive attention and that the clinical application of ICG in GC is gradually maturing. The detection accuracy and therapeutic efficacy of ICG have also been further confirmed in an increasing number of clinical applications, and the scope and means of ICG application have been further developed and expanded. In summary, research in this area will continue to be a research

hot spot.

To understand the spatial distribution of research contributions in this area, we analyzed and visualized the distribution across states and institutions, the outcomes of which are presented in *Table 1*. According to the spatial distribution of publication, researchers in different regions can adjust the strategic layout of their research collaboration, thus making their future collaboration efficient and their information access up-to-date, maintaining and improving their contribution position within the area. Regarding the volume of published articles, China ranked first in this area with 628 publications, followed by Japan and the United States. The h-index is a metric for determining the influence and productivity of a researcher's publications according to the frequency of the publication citation, and it is widely applied in evaluating the scholarly influence of a country/region, journal, author, or institution (30). The examination of the h-index distribution in this study produced results that basically agree with the national distribution, with China's h-index (h-index =55) ranking first, followed by Japan (h-index =53) and the United States (h-index =43). Generally, East Asia made a greater contribution in this field both in terms of quantity and quality of publications. This may be related to regional differences in the distribution of GC incidence, as East Asia was one the regions with the highest incidences of GC in 2020. In addition, aside from the United States, most of the top 5 countries/regions in terms of number of publications were in Asia, reflecting the dominance of this region in this domain. Centrality can indicate the key nodes in a network, with the level of centrality scaling with the significance of the node (47). The top 3 countries or regions in terms of centrality were Germany (0.41), China (0.27), and the United States (0.22). Although Germany ranked only fifth in publication volume, it had the highest centrality, indicating that Germany has a major cohering function in this area via a close cooperation with other countries or regions, but there remains potential for growth regarding the efficiency and quality of the products of collaboration.

Regarding institutions, *Table 1* shows that the top 3 institutions in terms of publication volume were Shanghai Jiao Tong University (51 publications), Nanjing Medical University (38 publications), and Seoul National University (34 publications). The top institutions in terms of output were mainly located in Asian countries, especially China. This indicates that Asian institutions are an influential region in this area of research (*Figure 7*). Moreover, many institutions in China are actively collaborating in research in this area and have developed close connections. On the one hand, this internal collaboration suggests that China has developed research institutions with core competencies, which can complement one another and coordinate well within the country. On the other hand, it may also limit China's cooperation in this field with the rest of the world, leaving China central less than its high number of publications might indicate.

Through access to journal source analysis, researchers can not only easily and efficiently find the right journal for their research but can also visualize the more influential journals in the field and thus have a better chance of obtaining cutting-edge information. Analysis of journals and cocited journals revealed that *World Journal of Gastroenterology* (n=43) was the journal with the highest number of ICG-related publications, followed by *Gastric Cancer* (n=31) and *Oncology Letters* (n=26), suggesting a special interest and significant contribution of these journals to articles on innovative therapies for GC. Regarding the quality of research, only 3 of the top 10 journals showed impact factors above 5 (*World Journal of Gastroenterology*, *Gastric Cancer*, and *International Journal of Oncology*), which suggests a need for an improvement in output impact. Accordingly, the number of articles in this field included in some high-impact journals was low, indicating that the research on ICG application to GC has not been fully appreciated and may become a new hot spot to be included in high-impact journals in the future. Meanwhile, *Cancer Research* (576 citations) ranked first among the cocited journals. All cocited journals including *Nature* and *Science* have Q1 Journal Citation Report (JCR) rankings. These journals are the core influencers in their respective academic fields, which reflects the importance of the application of ICG in GC in the related fields in which these core journals dominate. It also shows that journals that have made major core contributions to the field and have high impact are generally of higher quality. The number of articles in journals need to be further balanced with the quality to increase the impact of the journal. This has also inspired and motivated researchers to expand and develop innovative ways to apply ICG in GC. In general, the literature of highly influential authors in the field can help us grasp the classical theory of the field more efficiently and comprehensively. The h-index is one of the indicators to assess the productivity and quality of a given author's output (48). An examination of author contributions and cocited authors (*Table 2*) revealed that Li Y contributed 54 articles with an h-index of 32 and was the most

published author in the field. Additionally, Zhang Y, who has been dedicated to research into anticancer drugs, had the highest h-index (h-index =31) and was among the 10 most prolific authors. When cocited authors were taken into account, Bang YJ from Seoul National University School of Medicine was the most cited author with 185 cocitations, indicating that this author has a central role in pioneering research in the field. A knowledge map of author collaboration, consisting of 852 nodes and 1,622 links, is presented in *Figure 8*. We found that the authors of relevant ICG studies were mainly located in Asia. It is notable that Chinese researchers have made significant contributions in this area and have established extensive links with other researchers in China. However, cooperation with other countries should be strengthened to expand the country's influence in the world and to further increase the output of scientific research in this field.

Among the top 10 most cited papers, that of Schaafsma *et al.* analyzed the advantages and limitations of ICG in near-infrared fluorescence cancer-related surgery (36). The results showed that despite nontargeting and nonconjugation characteristics, ICG lays the basis for an extensive application of near-infrared fluorescence-guided surgery. Among 25 papers with the strongest citation bursts, 6 had a burst that ended in 2022. It is encouraging to see that research on the application of ICG in GC has led to some breakthroughs. For instance, Lan *et al.* found near-infrared fluorescence imaging of ICG to be promising approach for lymph mapping during robotic gastrectomy of GC (41). Similarly, the Kwon *et al.*'s findings in 2019 suggested that ICG may be useful for the intraoperative identification and visualization of each draining lymph node of primary lesions, which aid in performing complete and thorough lymph node dissection (43). Moreover, Huh *et al.*'s study showed that near-infrared imaging with an ICG-enhanced fluorescence technique could be a viable and efficacious means of assessing the vascular perfusion of surgical anastomoses in GC (42). The above studies have served as a crucial basis in developing this field and providing directions and support for the application of ICG in GC, simultaneously allowing clearer insight into the progress of ICG applications in GC.

Research hot spots and frontiers

As a distillation and overview of study themes and article contents, keywords reflect the main theme and research direction of a paper. Through a co-occurrence analysis of keywords in a field, researchers can extract the most research topics in a given field based on their frequency of occurrence. *Table 5* summarizes the results of the keyword analysis of our study, with "gastric cancer" appearing 788 times, ranking first, followed by "expression" (n=255), "carcinoma" (n=195), "breast cancer" (n=149), and "indocyanine green" (n=100). These keywords appear more frequently in papers discussing ICG applications in GC, and to some extent represent the hot spots of research in this area. The keyword "indocyanine green" was first mentioned in 2006 and ranked among the top 10 only after "metastasis" in the keyword frequency ranking in 2006. The recent appearance of ICG and the high frequency of its first appearance indicate that the application of ICG in GC is relatively cutting edge and has high exploration value. ICG in GC is currently used for precision imaging and accurate identification in the surgical treatment of patients with GC, and its imaging properties can also be used to explore the potential impact of gene and protein expression profiles on cancer development. "Breast cancer" is among the top 5 keywords in terms of frequency of occurrence, indicating that the application scope and prospect of ICG are relatively broad, the imaging detection technology of ICG can be widely applied to similar cancer diseases, and its research significance and value are high.

A keyword burst is where the keyword frequency spikes over a given duration. Analysis of the keywords that appear at each stage allows for the identification of how the frontiers of research in the field are advancing and further reveals trends in future research. The evolution of the keywords burst related to ICG is shown in *Figure 13*, with "*in-situ* hybridization" (burst strength 11.99) having the highest burst strength and the longest duration. Notably, "indocyanine green" ranked fifth according to burst strength, with bursts initiating in 2020 and persisting until now. This indicates that the research direction in ICG is attracting considerable recently and has good prospects. More importantly, research in the past 3 years has focused on "migration" (burst strength 6.03; duration 2019–2022), "indocyanine green" (burst strength 8.66; period: 2020–2022), and "lymph node clearance" (burst strength 5.84; duration 2020–2022). This suggests that these research topics may be research trends in the application of ICG in GC, with application modalities such as tumor migration monitoring and imaging of lymph node clearance being particularly prominent in this field. Additionally, a distribution diagram for 30 keywords with high frequency was created using R Studio (*Figure 14*). The results revealed

that the frequency of "gastric cancer" and "apoptosis" increased from 2012 to 2022 (as of November 2022) and that the frequency of ICG has gradually increased over the past 5 years.

Based on what has been stated above, the clinical application of ICG in GC is not yet mature and is still in the developmental stage. Currently, ICG is used as a tracer and imaging tool during GC surgery, with its fluoroimaging being leveraged for microinvasive and precision surgery. ICG technology was used first in Asian countries to detect anterior lymph nodes in patients with EGC during GC surgery (49). The widespread use of near-infrared and ICG in Asian countries such as China has resulted in encouraging results in the prognosis of patients of GC, but the prognosis of GC in Western populations is still poor (1,50). This discrepancy can be directly attributed to the outstanding contributions made by relevant institutions and researchers in Asian countries such as China, Japan, and South Korea in applying ICG to GC. In a study published in *JAMA Surgery*, Huang *et al.* explored the impact of ICG technology on the safety and efficacy of lymph node dissection in patients with cancer (51). The findings of this study demonstrated that ICG markedly increased lymph node clearance in patients undergoing radical surgery for D2 GC and reduced the lymph node disqualification rate but did not increase the rate of postoperative complications; this study thus provides a valuable evidence-based medical basis for the application of ICG's tracer technique in GC surgery and supports its routine use in GC treatment. The success of gastrectomy following coronary artery bypass grafting in a patient with GC reported in 2023 also evinces the role and feasibility of ICG fluorescence technology in surgery. This procedure used ICG fluorescence technology to navigate the sentinel lymph nodes and to image and identify the blood vessels during the operation to (52), overall enhancing visualization during surgery and increasing the success rate of surgery. Additionally, a recent study published in *Cancers* evaluated the effectiveness of ICG diffusion which can be used to determine the resection margins for gastrectomy surgery. This study found that ICG diffusion extent combined with near-infrared imaging can be used as a simple and easy method to define the incisional margin in gastrectomy (53). It can be seen that given the convenience and effectiveness of ICG in the application of GC treatment, ICG has gradually become a powerful tool in the treatment of GC.

However, further confirmation of the application of near-infrared and ICG technology, the gain effect, and the safety of the procedure is needed. The actual clinical value of ICG remains a matter of debate due to the current lack of confirmation from clinical studies. Additional high-quality randomized controlled tests to substantiate such benefits are urgently required (54). Although several studies have shown a markedly larger average count of lymph nodes detected for an ICG group than for a non-ICG group (55), some scholars reported the opposite result. Therefore, more clinical trial results may be needed to reduce the impact of errors caused by surgical personnel in surgical and experimental trials and to confirm the effect of ICG imaging. In addition, since imaging technology has not yet been combined with machine recognition, ICG imaging may only provide surgical guidance to the surgical staff and not a surgical machine. Lan *et al.* found there to be an absence of marked variation of lymph nodes removed in patients treated with or without the near-infrared and ICG technique for robotic gastrectomy (41). Fortunately, findings from the iGreenGO study, published in *Frontiers in Oncology*, clarify how near-infrared and ICG technology works to assist surgeons in performing lymph node dissection in AGC (56). Furthermore, a recently published study in *Cancers* systematically reviewed modern uses of ICG-enhanced fluorescence imaging (ICG-FI) and evaluated the possible approaches that could improve ICG-FI. These studies provide the basis and guidance for the application of ICG in GC surgery, promote the maturation of ICG imaging tracer technology from theory to practice, and offer solutions to adapting ICG to surgery. The clinical translation of ICG for GC application in terms of basic theory may also become a new research hot spot, which is likely to provide high-value, groundbreaking results.

Although ICG is the only near-infrared imaging agent approved by Food and Drug Administration (FDA) for clinical use, it also has several intrinsic drawbacks that limit its development (57). Stable agents with relatively longer circulation times, along with good biocompatibility and specific targeting to tumors, are prerequisites for satisfactory fluorescence imaging. Unfortunately, the instability and self-aggregation of ICG in solution lead to fluorescence quenching and a short half-time in vivo. In addition, ICG is defective in its tumor-targeting ability (58). These drawbacks led to the early termination of the JCOG0302 study due to an unacceptable false-negative rate (59). Researchers have attempted to introduce a large number of carriers to encapsulate ICG to protect ICG from nonspecific binding of plasma proteins and enhance its stability and tumor targeting. Fortunately,

an arginylglycylaspartic acid (RGD)-modified distearyl acylphosphatidyl ethanolamine-polyethylene glycol micelle (DSPE-PEG-RGD) encapsulating ICG targeting GC was designed and synthesized with significant biocompatibility and improved intratumor targeting accumulation (60). Nevertheless, improving tumor penetration and targeting ability remains a challenge.

Our bibliometric study systematically analyzed the general information, hot spots, cutting-edge research in the research of ICG applications in GC from a visual perspective. The findings offer more objective and reliable data and serve as a support reference for clinicians and scholars in understanding the basic situation of the field and selecting the appropriate research direction. ICG plays an important role in GC by virtue its imaging tracer capabilities. Specifically, ICG can be used for imaging guidance in minimally invasive procedures in GC and to assess organ-related issues, such as hematologic conditions. According to our analysis, overall, the application of ICG in GC is a current research hot spot, and the studies conducted in this field demonstrate that ICG offers many benefits in the surgical treatment of GC (61). Nonetheless, more studies are needed to support this trend, both in terms of standardizing the applied techniques and definitively demonstrating the efficacy of ICG application itself; therefore, the core ICG techniques should be validated, promoted, and further developed in the future.

Limitations

Although this bibliometric analysis has generated substantial and valuable information to enable researchers to more quickly grasp the frontiers in this field, it inevitably has some limitations. Our study investigated data exclusively from the WoS and focused on English-language papers, which might have restricted the literature included in the analysis. Moreover, the uneven quality of the collected literature data may hamper the credibility of the knowledge mapping. Finally, it is likely that the recent publications, despite their high quality, might not garner commensurate attention due to their low citation rates. Nonetheless, visual analysis of reference-based data can undoubtedly aid researchers in grasping the emerging research trends and hot spots of ICG in GC.

Conclusions

This paper presents a bibliometric analysis of articles focusing on ICG in GC published from 1991 to 2022. Therapy for AGC is already in the stage of individualized and precise treatment, and ICG has research and application potential in GC therapy. Research in this field has been increasing continuously and exponentially, with the leading countries being China, Japan, and the United States. The current study trends and cutting-edge research in this area mainly focus on the application of ICG in EGC and lymphatic drainage guidance for progressive GC, which may also constitute the future research trends in this area. The introduction of ICG in the minimally invasive gastric resection or function-preserving gastrectomy in accordance with the concept of precision surgery can effectively improve patient prognosis and reduce morbidity. In summary, ICG has great potential in the fluorescence imaging of GC, and the technique has made significant progress in recent years, providing a promising means for detecting and accurately resecting GC. Improving tumor penetration and targeting and conducting large clinical trials to validate the utility of ICG are urgently required and should be realized to ultimately revolutionize clinical treatment modalities.

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Footnote

Conflicts of Interest: All authors have completed the ICMJE uniform disclosure form (available at https://qims.amegroups.com/article/view/10.21037/qims-23-391/coif). The authors have no conflicts of interest to declare.

Ethical Statement: The authors are accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved. Due to the literature review design of the present study, neither ethics

approval nor informed consent was applicable.

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