



# A bibliometric analysis of testicular germ cell tumor research from 2000 to 2020

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**Background:** Thousands of papers on testicular germ cell tumor (TGCT) have been published over the past two decades. This study aimed to assess the key topics and future trends in TGCT research from a comprehensive perspective.

**Methods:** All literature defined as review and article type on TGCT published between 2000 and 2020 was identified and retrieved from the Web of Science Core Collection (WoSCC) database. Bibliometric analysis was conducted by the online analysis platform and VOSviewer (version 1.6.16). The key directions and future trends in the research field of TGCT were evaluated using Bibliographic Item Co-occurrence Matrix Builder (version 2.0) and gCLUTO software.

**Results:** Ultimately, a total of 4,550 papers between 2000 and 2020 were included in the field of TGCT. The leadership of the United States in global TGCT research with 1,549 publications during the last two decades was obvious. The Indiana University was the most productive institution with 360 publications, and it was also the institution most frequently involved in research cooperation. *Journal of Urology* published the highest number of publications on TGCT. Looijenga LHJ, Bokemeyer C, Ulbright TM, Sheinfeld J and Dieckmann KP were the top productive contributors to TGCT research. Further, five research hotspots have been identified: (I) epidemiology of TGCT; (II) TGCT-related infertility; (III) pathological classification with TGCT; (IV) management options for TGCT; and (V) Prevention of cancer metastasis in TGCT patients.

**Conclusions:** During the last two decades, the United States was a global leader, and research hotspots included epidemiology, male infertility, pathology, and therapy in the field of TGCT. Furthermore, the genetics mechanisms and cisplatin resistance will remain hotspots in future TGCT research.

**Keywords:** Testicular germ cell tumor (TGCT); bibliometric analysis; research hotspots

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## Introduction

Testicular germ cell tumor (TGCT) is the most common cancer among young adult men (1), and its incidence has been on the rise worldwide over the last two decades (2,3).

Cryptorchidism is the most common risk factor associated with TGCT, increasing the risk of cancer by nearly five times (4). Protecting reproductive function, preventing mental fatigue and anxiety, and improving the quality of life

are all crucial issues in young men with TGCT. During the last two decades, substantial advancing has been made in the field of TGCT research regarding genetic susceptibility, diagnostics, therapeutics and epidemiology (4,5). However, few scientific reports can help researchers obtain an intuitive overview in the field of TGCT research.

Bibliometric analysis, a novel comprehensive analysis method, was used to access contributions qualitatively and quantitatively in a specific field, including countries, institutions, journals, and authors. Bibliometric analysis also can predict research hotspots and future trends through data visualization (6-8). In 2013, Nason described the top 100 cited articles in urology and analyzed the key topics and advances in urology (9). However, there is no bibliometric study to evaluate hotspots and summarize progress in TGCT research field over the past 20 years.

In our study, a bibliometric analysis of TGCT was performed based on relevant literature from 2000 to 2020. Bibliometric indicators were comprehensively evaluated and visualized, including the number of annual publications, the contributions of countries, institutions, authors and journals. International cooperation and keyword co-occurrence visualization analysis were also performed. Furthermore, research hotspots and future trends in TGCT field were evaluated via the overlay map of co-occurring keywords and bi-clustering visualization analysis.

## Methods

### *Source database and retrieval strategy*

The Web of Science Core Collection (WoSCC) is one of the most authoritative and influential databases of scientific literature. In our study, all data was retrieved, filtered, and downloaded through the WoSCC database. The following search strategy was used: TS = Testicular germ cell tumor.

### *Screening criteria and data downloads*

The timespan in the present study was set from 2000 to 2020. The language type was limited as English. For publication types, only articles and reviews were included, and all other types were excluded in the study. WoSCC data including journals, titles, abstracts, keywords, author information, and cited references were downloaded in TXT format. In case of the bias caused by frequent update of the WoSCC database, data retrieval and download

were performed on the same day (January 23, 2021). Two independent authors (Chengyuan Wang and Lin Tong) finished the systematic literature search and had an agreement of 99%, showing significant consistency (10).

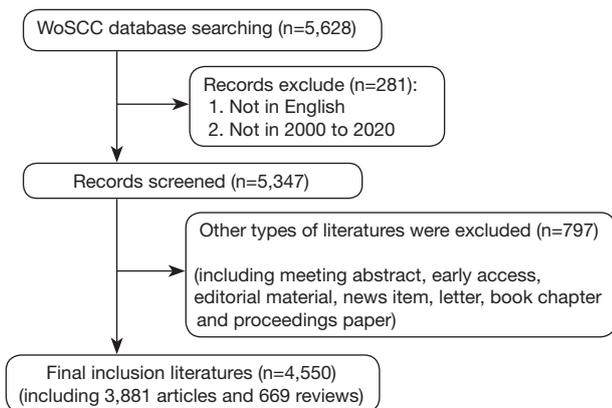
### *Statistical analysis*

In our study, a comprehensive description of various publishing characteristics is provided qualitatively and quantitatively, including countries, institutions, authors, journals, H-index and impact factors (IFs). H-index was defined as the number of papers with citation number  $\geq h$  and is considered to be an important indicator for assessing both the productivity and impact of the published work of scientists, journals, or countries (11). IFs were obtained from the latest version of Journal Citation Reports (JCR) to assess the impact of journals (12). The VOSviewer (version 1.6.15) and online platform of literature metrology analysis (<http://bibliometric.com/>) were used to perform bibliometric analysis. VOSviewer was used to visualize the networks such as institution, journal, author, co-citation, and the keywords (13). Overlay visualization maps were also conducted using VOSviewer to show the timescale of the TGCT research. The international collaboration network between countries/regions was performed using the online bibliometric analysis platform. The Microsoft Excel (version 2016) were used to evaluate the impact of countries/regions, institutions, authors, and journals. The downloaded data from the WoSCC database were imported into Bibliographic item co-occurrence matrix builder (BICOMB) to build a binary matrix of keyword-article (14). Furthermore, graphical clustering toolkit (gCLUTO) (version 1.0) software was used to perform bi-clustering visualization analysis, and to build three-dimensional mountain maps and heat maps based on the binary matrix of keyword-article (14).

## Results

### *Distribution of annual publications*

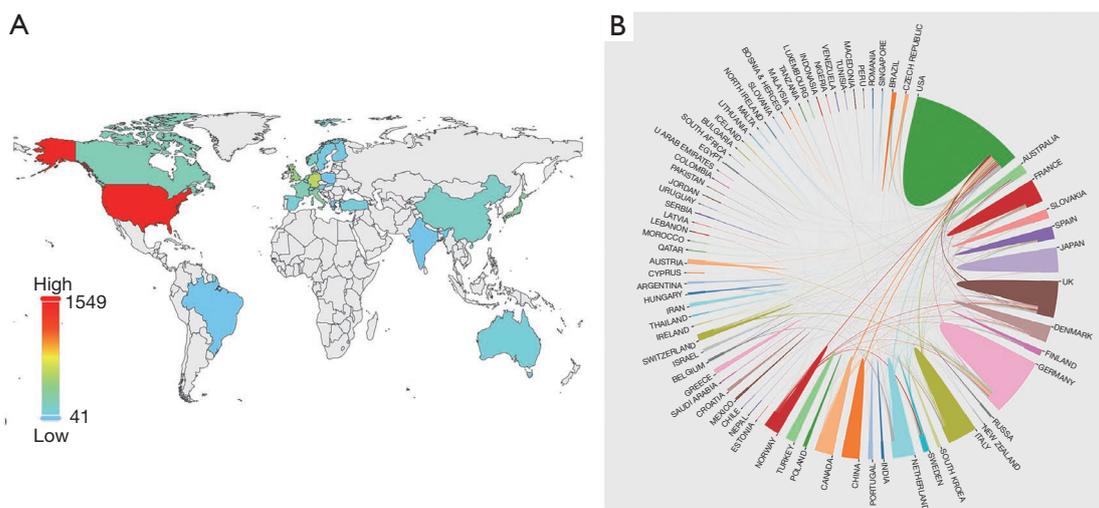
Based on the Screening criteria, a total of 4,550 papers (3,881 articles and 669 reviews) from the 20-year period were ultimately obtained (*Figure 1*). *Figure 2* showed the growth trend of annual publications in TGCT research field, from 152 in 2010 to 263 in 2020. According to the WoSCC database, the 4,550 papers were cited 122,273 times,



**Figure 1** Flowchart diagram of publications filtration. WoSCC, Web of Science Core Collection.



**Figure 2** The growth trends of the publications on TGCT from 2000 to 2020. TGCT, testicular germ cell tumor.



**Figure 3** The publications output of countries or regions on TGCT. (A) The world map of distribution of TGCT publications. (B) The cooperation network of countries or regions in the field of TGCT research. TGCT, testicular germ cell tumor.

with an average of 26.87 times in each paper.

### *Analysis of countries and institutions*

From 2000 to 2020, 86 countries or regions contributed to publications associated with TGCT. According to the WoSCC database, the top 25 most productive countries or regions are shown on the map to explore the worldwide geographic distribution in TGCT research field (*Figure 3A*). The countries or regions ranked 1–10 are presented as numbers in *Table 1*. Among them, the United States was the most productive country in the field of TGCT, with 1,549 papers published, followed by Germany (n=614),

England (n=430), Japan (n=345), Italy (n=324), Netherlands (n=298), France (n=247), Canada (n=240), Denmark (n=236) and China (n=184). As shown in *Figure 3B*, close cooperation between countries or regions was extremely popular over the past 20 years. Furthermore, the international cooperation network analysis showed that the United States was the country most actively participated in the international cooperation.

As depicted in *Table 2*, Indiana University was the most productive institution, with 360 papers published, followed by the Memorial Sloan-Kettering Cancer Center (n=247), National Cancer Institute (n=160), Institute for Cancer Research (n=156), University of Toronto (n=156),

The University of Texas MD Anderson Cancer Center (n=141), University of Pennsylvania (n=131), Comenius University (n=117), Rigshospitalet Copenhagen (n=115) and Norwegian Radium Hospital (n=113). The network

knowledge map among institutions was generated via VOSviewer, and 50 was set to the threshold as the minimum number of papers, while 500 was set to the threshold as the minimum number of citations. Ultimately, as shown in *Figure 4*, 16 out of the 3,977 institutions were identified. In addition, Indiana University cooperated with nearly every influential scientific institution in the field of TGCT during the last 20 years.

**Table 1** The top 10 most productive countries or regions in the field of TGCT research

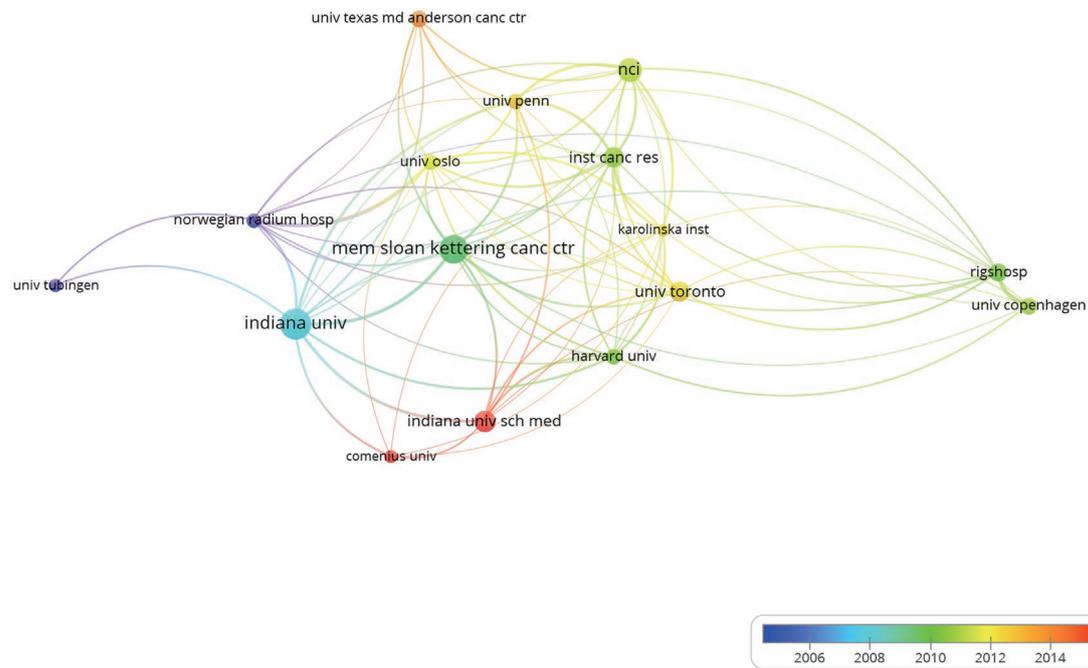
Rank	Country/region	Records	Percentage. (N/4,550), %
1	USA	1,549	34.044
2	Germany	614	13.495
3	England	430	9.451
4	Japan	345	7.582
5	Italy	324	7.121
6	The Netherlands	298	6.549
7	France	247	5.429
7	Canada	240	5.275
7	Denmark	236	5.187
10	China	184	4.044

### Analysis of journals

As shown in *Table 3*, the top 10 most productive journals, which published 926 papers, accounting for 20.35% of the total publications in the field of TGCT research. *Journal of Urology* (n=136), *Urology* (n=120), and *Journal of Clinical Oncology* (n=108) were the top three journals which had the largest number of publications in the field of TGCT research. *Journal of Clinical Oncology*, *Journal of Urology*, and *European Urology* were the top three journals which had the largest number of citations (4,026 vs. 2,327 vs. 2,190 citations, respectively). However, *Journal of Clinical Oncology*, *European Urology*, and *Annals of Oncology* had the largest number of average citations per paper (37.28 vs. 25.76

**Table 2** The top 10 most productive institutions in the field of TGCT research

Rank	Institutions	Article counts	Total number of citations	Average number of citations	Total number of first author	Total number of first author citations	Average number of first author citations
1	Indiana University	360	5,893	16.37	166	2,474	14.90
2	Memorial Sloan-Kettering Cancer Center	247	5,687	23.02	87	1,763	20.26
3	National Cancer Institute	160	2,715	16.97	75	1,328	17.71
4	Institute for Cancer Research	156	4,782	30.65	53	1,716	32.38
5	University of Toronto	156	2,289	14.67	36	470	13.06
6	The University of Texas MD Anderson Cancer Center	141	1,151	8.16	40	156	3.9
7	University of Pennsylvania	131	3,046	23.25	26	393	15.12
8	Comenius University	117	730	6.24	35	196	5.6
9	Rigshospitalet Copenhagen	115	1,961	17.05	52	974	18.73
10	Norwegian Radium Hospital	113	3,545	31.37	32	719	22.47



**Figure 4** Co-authorship overlay visualization network of institutions in the field of TGCT research. TGCT, testicular germ cell tumor.

**Table 3** The top 10 most active journals in the field of TGCT research

Rank	Journal Title	Article counts	Total number of citations	Average number of citations	IF (2019)	Quartile in category (2019)	H-index
1	<i>Journal of Urology</i>	136	2,327	17.11	5.925	Q1	30
2	<i>Urology</i>	120	943	7.86	1.924	Q3	19
3	<i>Journal of Clinical Oncology</i>	108	4,026	37.28	32.945	Q1	75
4	<i>BJU International</i>	93	786	8.45	4.806	Q1	23
5	<i>European Urology</i>	85	2,190	25.76	17.947	Q1	47
6	<i>Urologic Oncology-Seminars and Original Investigations</i>	84	453	5.39	2.882	Q2	16
7	<i>Annals of Oncology</i>	78	1,694	21.72	18.274	Q1	61
8	<i>British Journal of Cancer</i>	75	1,154	15.39	5.791	Q1	30
9	<i>Cancer</i>	74	1,292	17.46	5.742	Q1	34
10	<i>International Journal of Urology</i>	73	252	3.45	2.445	Q2	60

IF, impact factor; H-index, Hirsch index; JCR, Journal Citation Reports.

vs. 21.27 times, respectively). *Journal of Clinical Oncology*, *Annals of Oncology*, and *European Urology* had the highest IFs in the latest version of JCR (32.945 vs. 18.274 vs. 17.947, respectively). *Journal of Clinical Oncology* had the highest H-index of any journals in the field of TGCT research, with

a score of 75. Among the top 10 journals with the largest number of published papers, *Journal of Urology*, *Journal of Clinical Oncology*, *BJU International*, *European Urology*, *Annals of Oncology*, *British Journal of Cancer*, and *Cancer* were identified as Q1 based on the latest version of JCR standards

**Table 4** The top 10 high-cited papers in the field of TGCT research from 2000 to 2020

Rank	Title	Authors	Year	Journal	Total citations
1	Cisplatin in cancer therapy: Molecular mechanisms of action	Dasari, Shaloam, <i>et al.</i>	2014	<i>European Journal of Pharmacology</i>	1,696
2	Testicular dysgenesis syndrome: an increasingly common developmental disorder with environmental aspects	Skakkebaek NE, <i>et al.</i>	2001	<i>Human Reproduction</i>	1,411
3	A genetic screen implicates miRNA-372 and miRNA-373 as oncogenes in testicular germ cell tumors	Voorhoeve PM, <i>et al.</i>	2006	<i>Cell</i>	918
4	Proliferation and functional maturation of Sertoli cells, and their relevance to disorders of testis function in adulthood	Sharpe RM, <i>et al.</i>	2003	<i>Reproduction</i>	763
5	The 2016 WHO Classification of Tumours of the Urinary System and Male Genital Organs-Part A: Renal, Penile, and Testicular Tumours	Moch Holger, <i>et al.</i>	2016	<i>European Urology</i>	740
6	Molecular pathogenesis and extraovarian origin of epithelial ovarian cancer-Shifting the paradigm	Kurman Robert J. <i>et al.</i>	2011	<i>Human Pathology</i>	643
7	Testicular germ-cell tumours in a broader perspective	Oosterhuis JWS, <i>et al.</i>	2005	<i>Nature Reviews Cancer</i>	608
8	Second cancers among 40,576 testicular cancer patients: Focus on long-term survivors	Travis LB, <i>et al.</i>	2005	<i>JNCI-Journal of The National Cancer Institute</i>	545
9	Sertoli-Sertoli and Sertoli-germ cell interactions and their significance in germ cell movement in the seminiferous epithelium during spermatogenesis	Mruk DD, <i>et al.</i>	2004	<i>Endocrine Reviews</i>	533
10	Gene expression patterns in human embryonic stem cells and human pluripotent germ cell tumors	Sperger JM, <i>et al.</i>	2003	<i>Proceedings of the National Academy of Sciences of the United States of America</i>	514

(Table 3). In addition, Table 4 listed the top 10 most highly cited papers and these papers had great influence in the field of TGCT research over the last 20 years.

### *Analysis of authors*

The top 10 most productive authors in the field of TGCT research were also evaluated (Table 5). Among them, Looijenga LHJ from the Princess Máxima Center for Pediatric Oncology in Netherlands ranked first and published 130 papers over the last 20 years. Bokemeyer C from the Department of Oncology, Hematology and Bone Marrow Transplantation with Division of Pneumology, University Medical Center Hamburg-Eppendorf in Germany was the second most productive author in the field of TGCT research (n=92). Furthermore, Looijenga LHJ, Oosterhuis JW, and Bokemeyer C were the top three authors who had the highest number of citations (3,854 *vs.* 2,946 *vs.* 2,877 times, respectively). VOSviewer software was used to generate the co-authorship overlay visualization

network, and the threshold was set to 20 as the minimum number of published papers by authors. Finally, as shown in Figure 5, 33 authors who met the screening criteria were identified, of which Sheinfeld J, Motzer RJ, Bosl GJ, and Carver BS were shown to cooperate closely. VOSviewer software was also used to generate the citation overlay visualization map, and the threshold was set to 300 as the minimum number of total citations from authors. Finally, 33 authors were identified, of which Looijenga LHJ, Bokemeyer C, Ulbright TM, Sheinfeld J and Dieckmann KP were shown to make significant contributions to the field of TGCT research (Figure 5B).

### *Analysis of research hotspots*

In our study, the keywords with the highest frequency of occurrence were identified from the included publications and the top 39 most frequent keywords are shown in Table 6, with an appearance of more than 30 times. The relationship between the extracted high-frequency keywords and

**Table 5** The top 10 most productive authors in the field of TGCT research

Rank	Author	Article counts	Total number of citations	Average number of citations	First author counts	First author citation counts	Corresponding author counts	Corresponding author citation counts
1	Looijenga LHJ	130	3,854	29.65	15	671	44.73	62
2	Bokemeyer C	92	2,877	31.27	5	104	20.8	26
3	Fossa SD	85	2,509	29.52	6	189	31.5	11
4	Rajpert-De Meyts E	81	1,547	19.1	5	366	73.2	13
5	Ulbricht TM	79	1,291	16.34	15	311	20.73	29
6	Skakkebaek NE	78	2,168	27.79	5	77	15.4	6
7	Oosterhuis JW	74	2,946	39.81	7	491	70.14	6
8	McGlynn KA	72	1,407	19.54	12	452	37.67	24
9	Einhorn LH	71	1,383	19.48	6	224	37.33	17
10	Sheinfeld J	71	1,587	22.35	0	0	0	32

publications was visualized using BICOMB. gCLUTO software was utilized for visual analysis and identification of clusters. Finally, the top 39 most frequent keywords were divided into 5 different clusters according bi-clustering analysis to identify the research hotspots in the field of TGCT research (*Figure 6A*). In addition, the 3-dimensional volcano map was generated for visualization of clustering results (*Figure 6B*).

Cluster 0: Epidemiology of TGCT.

Cluster 1: TGCT-related infertility.

Cluster 2: Pathological classification with TGCT.

Cluster 3: Management options for TGCT.

Cluster 4: Prevention of cancer metastasis in TGCT patients.

VOSviewer software was used to generate an overlay visualization network of keyword co-occurrence to explore the changes of research hotspots over the last 20 years, and our results indicated that the keywords “genome-wide association” and “cisplatin resistance” began to emerge in the last seven years in the field of TGCT research (*Figure 7*).

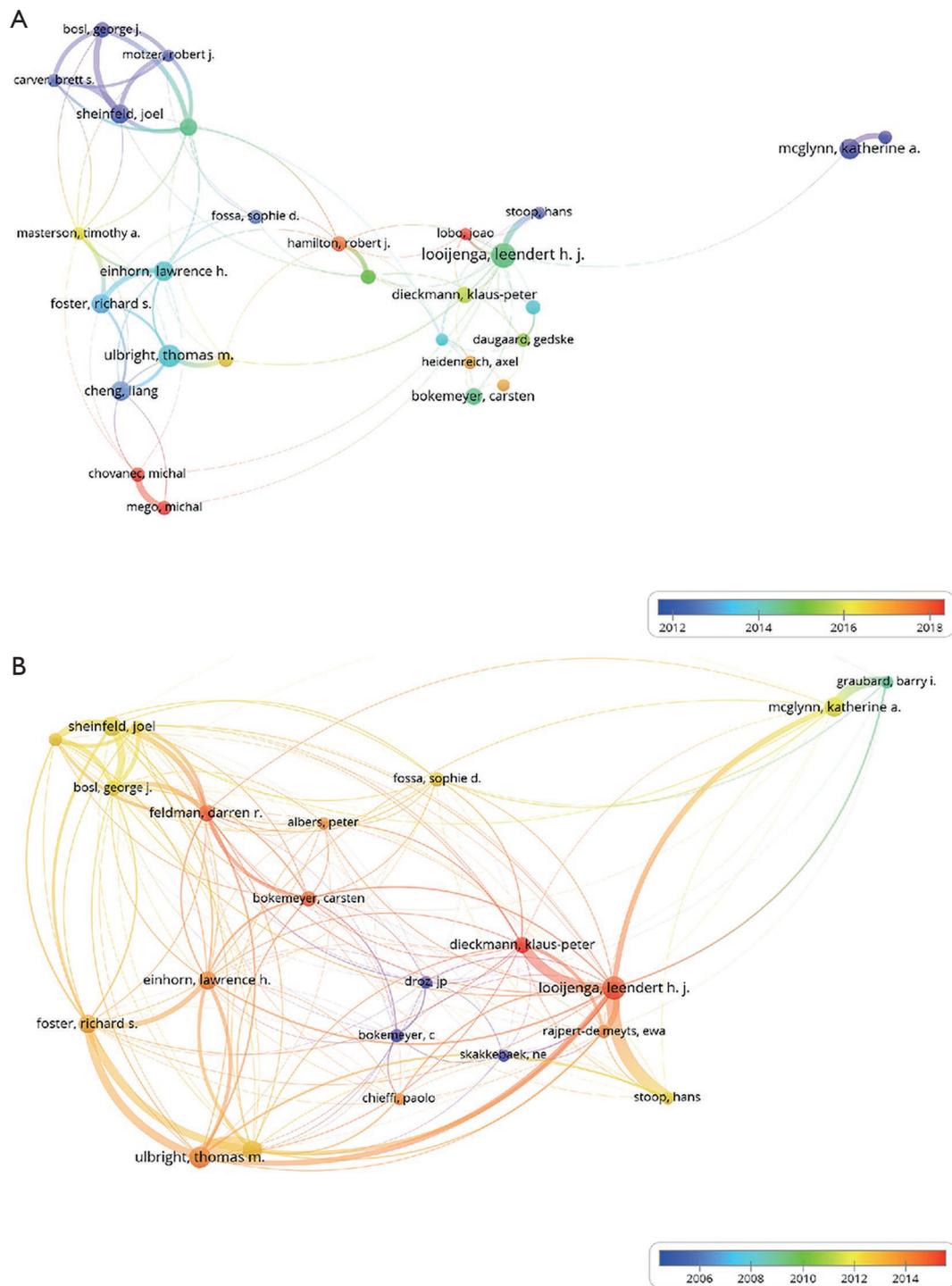
## Discussion

In recent years, bibliometric analysis has been widely used in many scientific research fields, which can help researchers with different backgrounds to understand the research progress of a certain field and visualize the knowledge structure more intuitively. In addition, many indicators obtained from bibliometric analysis will give researchers an intuitive overview such as the most productive authors,

milestone manuscripts, popular journals, research hotspots, and future trends (15-17). In the present study, we performed a comprehensive bibliometric analysis of global scientific publications in the field of TGCT research over the last 20 years.

The productivity and development of a specific field over a period of time can be reflected by the number of publications (18). A total of 4,550 publications, including 263 papers in 2020, were included in our study (*Figures 1,2*). Our results indicated that the number of publications was maintained at a substantial level over the last 20 years from 2000 to 2020, which also showed that TGCT was still a hot research field, and there may be more and more scientific problems waiting for scholars to explore in the field of TGCT research.

The number of publications is an important indicator to evaluate the scientific research level of a country or institution in a particular research field (15,18,19). Our results indicated that the United States and Germany were the 2 largest contributors in terms of the number of publications over the last 20 years (*Figure 3A, Table 1*), highlighting their dominant impact in the field of TGCT research. Meanwhile, international cooperation analysis showed that the United States participated in the cooperation most frequently from 2000 to 2020, especially with the UK and Canada (*Figure 3B*). Furthermore, Indiana University was identified as the most productive institution over the last 20 years, and had the highest collaboration performance with almost all influential scientific institutions in the field of TGCT research, including Memorial



**Figure 5** Co-authorship overlay visualization network of authors in the field of TGCT research. (A) Author co-authorship overlay visualization network. (B) Author co-citation overlay visualization network. TGCT, testicular germ cell tumor.

**Table 6** The high-frequency keywords in the field of TGCT research

Number	Keywords	Frequency	%
1	Testicular cancer	968	5.5731
2	Germ cell tumor	686	3.9496
3	Testis	463	2.6657
4	Seminoma	398	2.2914
5	Chemotherapy	285	1.6409
6	Testicular germ cell tumor	264	1.5199
7	Cancer	139	0.8003
8	Teratoma	138	0.7945
9	Cisplatin	119	0.6851
10	Immunohistochemistry	116	0.6679
11	Testis cancer	108	0.6218
12	Surveillance	99	0.5700
13	Spermatogenesis	98	0.5642
14	Apoptosis	98	0.5642
15	Germ cell	96	0.5527
16	Non-seminoma	92	0.5297
17	Retroperitoneal lymph node dissection	88	0.5066
18	Embryonal carcinoma	87	0.5009
19	Radiotherapy	73	0.4203
20	Prognosis	73	0.4203
21	Non-seminomatous germ cell tumor	71	0.4088
22	Cryptorchidism	70	0.4030
23	Germ cell cancer	65	0.3742
24	Carcinoma in situ	62	0.3570
25	Testicular tumor	55	0.3167
26	Germinoma	55	0.3167
27	Lymph node excision	54	0.3109
28	Yolk sac tumor	54	0.3109
29	Testicular neoplasm	53	0.3051
30	Fertility	52	0.2994
31	Survival	51	0.2936
32	Infertility	49	0.2821
33	Incidence	46	0.2648

**Table 6** (continued)**Table 6** (continued)

Number	Keywords	Frequency	%
34	High-dose chemotherapy	44	0.2533
35	Surgery	39	0.2245
36	Epidemiology	35	0.2015
37	P53	35	0.2015
38	Germ cell and embryonal	34	0.1958
39	Ovary	31	0.1785

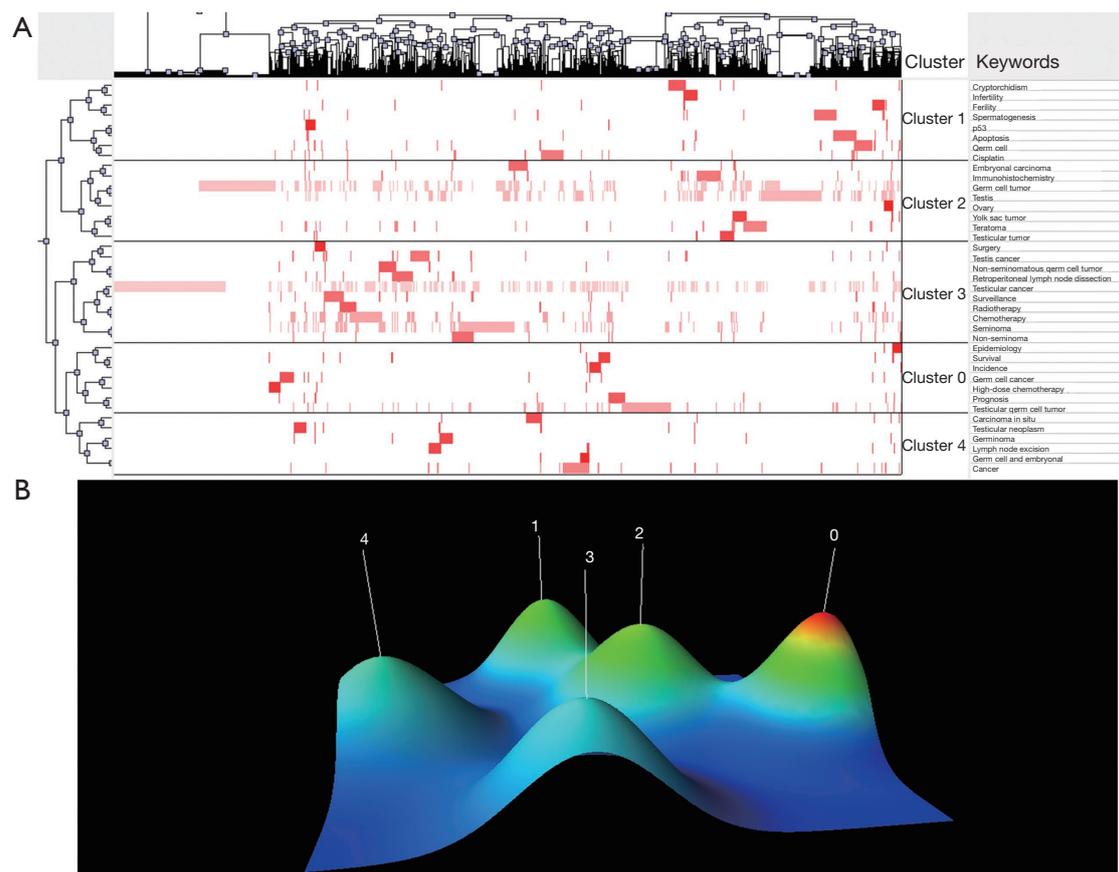
TGCT, testicular germ cell tumor.

Sloan-Kettering Cancer Center, the University of Texas MD Anderson Cancer Center, Harvard university and Norwegian Radium Hospital (*Table 2, Figure 4*). These results indicated that frequently collaborations between countries or institutions will be the future trend in the field of TGCT research.

Indicators from bibliometric analysis can provide a reliable reference for scientific researchers to manage their knowledge or submit their manuscripts (20,21). As shown in *Table 3*, the top 10 most productive journals were all included in the category of “Urology” or “Oncology”. Our results indicated that *Journal of Urology* had the largest number of TGCT research papers and *Journal of Clinical Oncology* had the largest number of total citations. Our results indicated that the largest number of cited publications was a review written by Shaloam Dasari and Paul Bernard Tchounwou from Cellomics and Toxicogenomics Research Laboratory, Jackson State University in the USA, and that “Cisplatin in cancer therapy: Molecular mechanisms of action”, was a milestone in the field of TGCT research from 2000 to 2020 (22) (*Table 4*). These highly cited papers and active journals can provide a reliable reference for researchers and TGCT had a significant role in the fields of urology and oncology.

According to the WoSCC database, Looijenga, LHJ was the most productive researcher and had the highest number of total citations in the field of TGCT research (*Table 5*). Furthermore, Looijenga LHJ, Bokemeyer C, Ulbright TM, Sheinfeld J and Dieckmann KP cooperated closely and published a considerable number of highly cited publications (*Figure 5A,B*). Thus, they can be recognized as leaders in the field of TGCT research.

Considering the heterogeneity of the TGCT research field, we divided the highly frequently keywords into 5 clusters via BICOMB and gCLUTO software (*Figure 6*).



**Figure 6** Research hotspots analysis in the field of TGCT research. (A) The visualized matrix of the highly frequent keywords base on bi-clustering analysis. (B) The volcano visualization map of the highly frequent keywords base on bi-clustering analysis in the field of TGCT research. TGCT, testicular germ cell tumor.

Cluster 0 is related to epidemiology of TGCT. In Western countries, TGCT is the most common cancer among men aged 14 to 44 (1). It is reported that Caucasians have an increase morbidity by 3–6% per year in TGCT (23). Fortunately, the disease-specific survival after 15-year was 99.3% for patients initially diagnosed with stage I seminoma (24). Cluster 1 is related to TGCT-related infertility. TGCT patients have high risks of male infertility due to the decrease of sperm concentration, the decrease of total sperm motility and the increase of morphological alterations (25,26). Because the fertility status of TGCT patients after treatment is difficult to predict, researchers consider it is necessary for extracting testicular sperm and cryopreservation of spermatozoa (27). Cluster 2 is related to pathological classification with TGCT. TGCT are mainly divided into seminoma, which resemble primordial germ cells, and non-seminoma, which are either embryonal

carcinoma or yolk sac tumor (28). Around 15% of the TGCT is a mixture of seminoma and non-seminoma (29). Cluster 3 is related to management options for TGCT. After orchidectomy, management options for early-stage TGCT include active surveillance, primary chemotherapy and retroperitoneal lymph node dissection (RPLND), are helpful to reduce the long-term morbidity (30). In addition, patients are highly curable due to excellent cisplatin sensitivity of TGCT. However, approximately 10–20% of TGCT patients with cancer metastasis cannot be cured by cisplatin-based chemotherapy (31). Cluster 4 is related to prevention of cancer metastasis in TGCT patients. RPLND has played an indispensable role in the management of male metastatic TGCT for decades. The aim of RPLND is to remove lymph nodes from the primary retroperitoneal landing site of TGCT, commonly accomplished by using a split-and-roll technique to remove tissue surrounding



diagnosis, treatment, and etiology of this condition.

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### Footnote

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*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.

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