Heliyon 10 (2024) e24407

Contents lists available at ScienceDirect

Heliyon

journal homepage: www.cell.com/heliyon

Research article

Global trends and hotspots in the field of mitochondrial dynamics and hepatocellular carcinoma: A bibliometric analysis from 2007 to 2023

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A R T I C L E I N F O

Keywords:
Mitochondrial dynamics
Fission and fusion
Hepatocellular carcinoma
Bibliometric analysis

A B S T R A C T

Background: Mitochondria are dynamic organelles, and mitochondrial dynamics are important for the maintenance of mitochondrial inheritance and function. Recently, an increasing number of studies have shown that mitochondrial dynamics play an important role in the occurrence and development of hepatocellular carcinoma (HCC). However, bibliometric analyses of mitochondrial dynamics in HCC are scarce. Therefore, we conducted a bibliometric analysis to explore the current global research status and trends in mitochondrial dynamics and HCC.
Methods: Global publications on mitochondrial dynamics and HCC published between 2007 and May 2023 were retrieved from the Web of Science Core Collection (WoSCC) database. Bibliometric analysis was performed using Bibliometrix, VOSviewer, and CiteSpace to analyze the numbers, citations, countries, institutions, authors, journals, references, and keywords.
Results: A total of 518 publications were retrieved fromthe WoSCC database. China and *The Fourth Military Medical University* were the most productive countries and institutions. *Zorzano, A* published the most literature whereas *Chen, HC* was the author with the highest number of co-citations. *Plos One* was the most popular journal, whereas *the Journal of Biological Chemistry* had the highest number of co-citations. The most frequently used keyword was "mitochondria". Further analysis of the references and keywords showed that the molecular mechanisms linking them to drug therapy targets should be the focus of future studies.
Conclusions: Research on mitochondrial dynamics in HCC has received much attention, and many studies have been published. However, research on mitochondrial dynamics and HCC has been limited by insufficient regional development imbalances and global cooperation. Nevertheless, future research on mitochondrial dynamics and HCC is promising, especially regarding the

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https://doi.org/10.1016/j.heliyon.2024.e24407
Received 12 August 2023; Received in revised form 3 January 2024; Accepted 8 January 2024
Available online 11 January 2024

molecular mechanisms of mitochondrial fission and fusion and how to link the currently known molecular mechanisms with drug therapy targets for HCC.

1. Introduction

Hepatocellular carcinoma (HCC) is one of the most common malignancies worldwide with high morbidity and mortality rates, ranking seventh in morbidity and second in mortality among malignancies worldwide [1–3]. A recent study by *Rumgay H* predicted that the disease burden of HCC will increase by more than 55 % in annual diagnoses and deaths globally by 2040 [4]. HCC poses a huge economic burden on families and society [5,6]. Therefore, the treatment of HCC has been a hot topic in medical research, and substantial progress has been made, particularly in the systemic treatment of HCC. The systemic treatment of HCC includes chemotherapy, targeted therapy, and immunotherapy, among which the combination of vascular endothelial growth factor (VEGF) inhibitors and immune checkpoint inhibitors (ICIs) has brought new hope to the treatment of advanced HCC [7–9]. Additionally, many clinical trials on ICIs are underway with the aim of achieving more breakthroughs [10,11]. However, the prognosis of patients with advanced HCC is not ideal; the 5-year overall survival rate is only 10 % [12,13], so it is necessary to explore the pathogenesis of HCC in a broader field and provide new opportunities for its treatment.

Mitochondrial dynamics is the dynamic balance between mitochondrial fission and fusion, and it plays an important role in maintaining the morphology, size, and number of mitochondria and their physiological functions [14]. In 1914, *Lewis MR* et al. first observed mitochondrial fission and fusion in cultured chicken cells [15]. Since then, an increasing number of studies have shown that mitochondrial dynamics are involved in the regulation of mitochondrial function, including mitochondrial DNA stability, apoptosis, respiratory motility, cellular stress response, and mitochondrial autophagy [16–18]. Mitochondrial fission and fusion are processes that depend on various proteins; the key proteins for mitochondrial fusion are *Opa1*, *Mfn1* and *Mfn2*, whereas the key proteins for mitochondrial fission are *Drp1* and *Fis1* [19]. Simultaneously, it has been proven that the changes of dynamic balance of mitochondrial fission and fusion are closely related to various diseases, such as Alzheimer's disease, neurodegenerative diseases, cardiovascular diseases, and tumors, including breast cancer, liver cancer, gastric cancer [20–23]. In 2016, *Huang Q* et al. found that such changes promoted tumor progression by enhancing mitochondrial fission and weakening mitochondrial fusion in patients with HCC [24]. This provided new ideas for further research on mitochondrial dynamics and HCC and made the research of mitochondria and HCC a new hotspot.

Over the past few years, several studies on mitochondrial dynamics in HCC have been published. However, to date, no bibliometric analysis has explored the current global research status and trends in this field. Bibliometric analysis uses mathematical and statistical methods to quantitatively analyze publications in a certain field over a certain period, and it has been widely used in various fields [25,26]. Here, we conducted a bibliometric analysis of global publications on mitochondrial dynamics and HCC to explore the global research status and trends and provide new ideas for further research.

2. Methods

2.1. Search criteria

We retrieved global publications on mitochondrial dynamics and HCC published from January 2007 to May 2023 from the Web of Science Core Collection (WoSCC) database, which is a global authoritative citation database that is widely used in bibliometric analyses, with daily updates. Therefore, we conducted a literature search on June 13, 2023. The retrieval strategy was as follows: TS=("hepatocarcinoma" or "hepatocellular carcinoma" or "liver cancer" or "HCC" or "hepatoma" or "hepatic cancer" or "hepatic carcinoma") AND TS=("mitochondrial fission and fusion" or "mitochondrial fusion and fission" or "mitochondrial dynamics" or "dynamic of mitochondria" or "mitochondrial dynamic"). The timespan was January 1, 2007 to May 31, 2023. The document types included

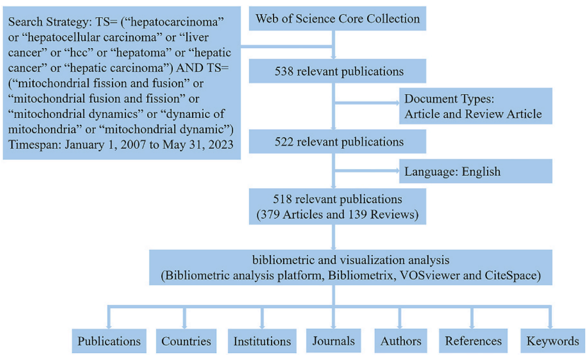

Fig. 1. The detailed retrieval process of mitochondrial dynamics and hepatocellular carcinoma in the Web of Science Core Collection database.

original and review articles. The language used was limited to English. The detailed retrieval process is illustrated in Fig. 1. Finally, 518 relevant publications were identified, including 379 original articles and 139 review articles.

2.2. Data collection and analysis

We downloaded the complete records and references in plain text format from the WoSCC database and named them download_*.txt. The following indicators were extracted and analyzed: numbers of publications, citation, country, institution, author, journal, reference, and keywords. The co-citation of authors means that the articles of two authors were cited by a third author at the same time, and the higher the frequency of co-citations, the closer the academic relationship between the two authors. An analysis of the references can quickly identify the most fundamental and important articles in a certain field. Keyword analysis can be used to quickly identify research topics in a field.

We then used the bibliometric online analysis platform (bibliometric.com), Bibliometrix (An R-tool version 4.3.0, https://www.bibliometrix.org/home/), VOSviewer (VOSviewer_1.6.18, https://www.vosviewer.com/), and CiteSpace (CiteSpace_6.2. R4 version, https://citespace.podia.com/) to perform bibliometric analysis and create network visualization maps. In the network visualization maps, the nodes represent the relevant elements, and the size of the nodes represents the frequency. The lines represent the connections, and the width of the line represents the strength of the connection. The same node colors represents different clusters. In addition, a dual-map overlay of the journals, burst detection, and timeline views of references was performed using CiteSpace. Furthermore, Journal Citation Reports (https://jcr.clarivate.com/jcr/home) was used to determine the Import Factor (IF) and Journal Citation Indicator (JCI) quartiles for 2022.

3. Results

3.1. General global trends of the publications

From January 1, 2007, to May 31, 2023, we found a total of 518 global publications on mitochondrial dynamics and HCC in the WoSCC database, including 379 original articles and 139 review articles. Fig. 2A shows the geographical distribution of the global scientific productivity of mitochondrial dynamics and HCC, which demonstrates that China and the USA published more than 100 articles, whereas other countries published fewer articles, indicating that although mitochondrial dynamics and HCC have attracted widespread attention worldwide, there is a problem of regional development imbalance. However, productivity in different countries was uneven. Fig. 2B shows the annual number of publications between 2007 and 2023. In general, the annual number of publications showed an increasing trend. On the basis of simulation curve equations ($y = 3.34x+0.32$, $R^2 = 0.75$), the number of publications on mitochondrial dynamics in HCC continue to increase.

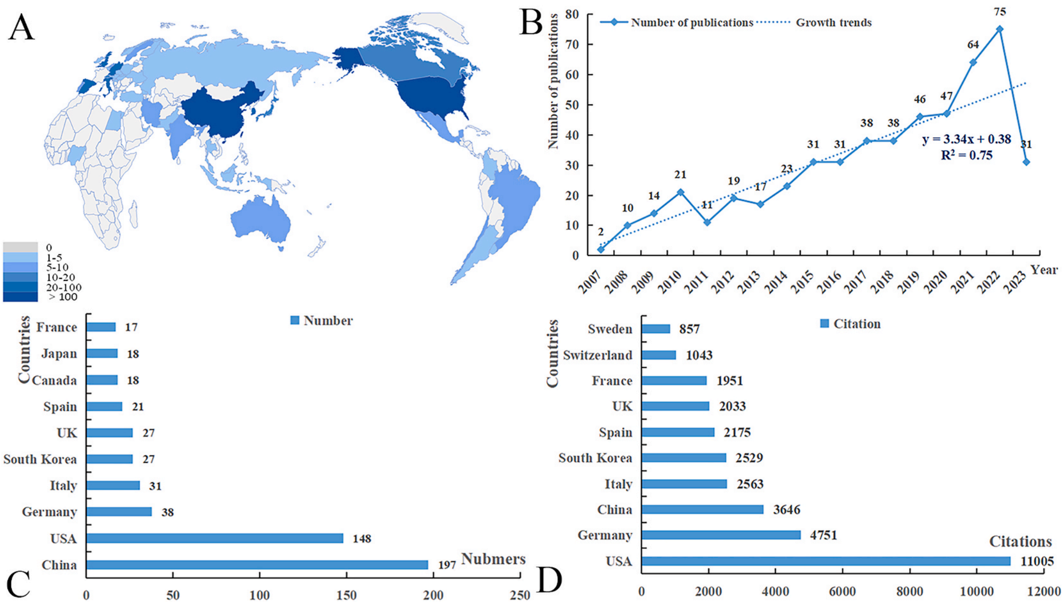

Fig. 2. The general global trends of publications of mitochondrial dynamics and hepatocellular carcinoma. (A) The geographical distribution of worldwide scientific productivity of mitochondrial dynamics and HCC. (B) The annual number of publications from 2007 to 2023. (C) The top ten countries in terms of the number of publications. (D) The top ten countries in terms of the total citations.

3.2. Analysis of countries

A total of 54 countries participated in research on mitochondrial dynamics and HCC from 2007 to 2023. As shown in Fig. 2C and D, China had the highest number of publications (197, 38.03 %), followed by the USA (148, 28.57 %), Germany (38, 7.34 %), Italy (31, 5.98 %), and South Korea (27, 5.21 %). Publications from China and the USA accounted for more than half of the total (66.60 %). The USA had the highest total citations (11,005), followed by Germany (4,751), China (3,646), Italy (2,563), and South Korea (2,529). Then, the network visualization of the co-authorship of countries was analyzed using the bibliometric online analysis platform, Bibliometrix and CiteSpace. Fig. 3A and B shows the number of publications and co-authorships between the different countries. In Fig. 3A, the darker the color, the greater the number of publications, and the pink lines represent collaboration. In Fig. 3B, different colors represent different countries; the larger the area, the greater the number of publications. These lines also represent collaboration. As shown in Fig. 3C, we generated network visualization using CiteSpace. The nodes represent countries; the larger the node, the greater the number of publications. The lines represent collaboration between different countries; the wider the line, the more frequent the collaboration. The purple ring indicates centrality, and high centrality ($\geq$0.10) indicates active cooperation. China and the USA were the most productive countries, whereas the USA, Germany, and the UK had high centrality, indicating that the USA, Germany, and the UK had active cooperation between other countries.

3.3. Analysis of institutions

A total of 1705 institutions participated in research on mitochondrial dynamics and HCC. The top 10 institutions that contributed to mitochondrial dynamics and HCC are listed in Fig. 4A and Table 1. *The Fourth Military Medical University* was the most productive institution with 20 publications, followed by *Autonomous University of Barcelona* (19), *Nanjing Medical University* (17), *University of*

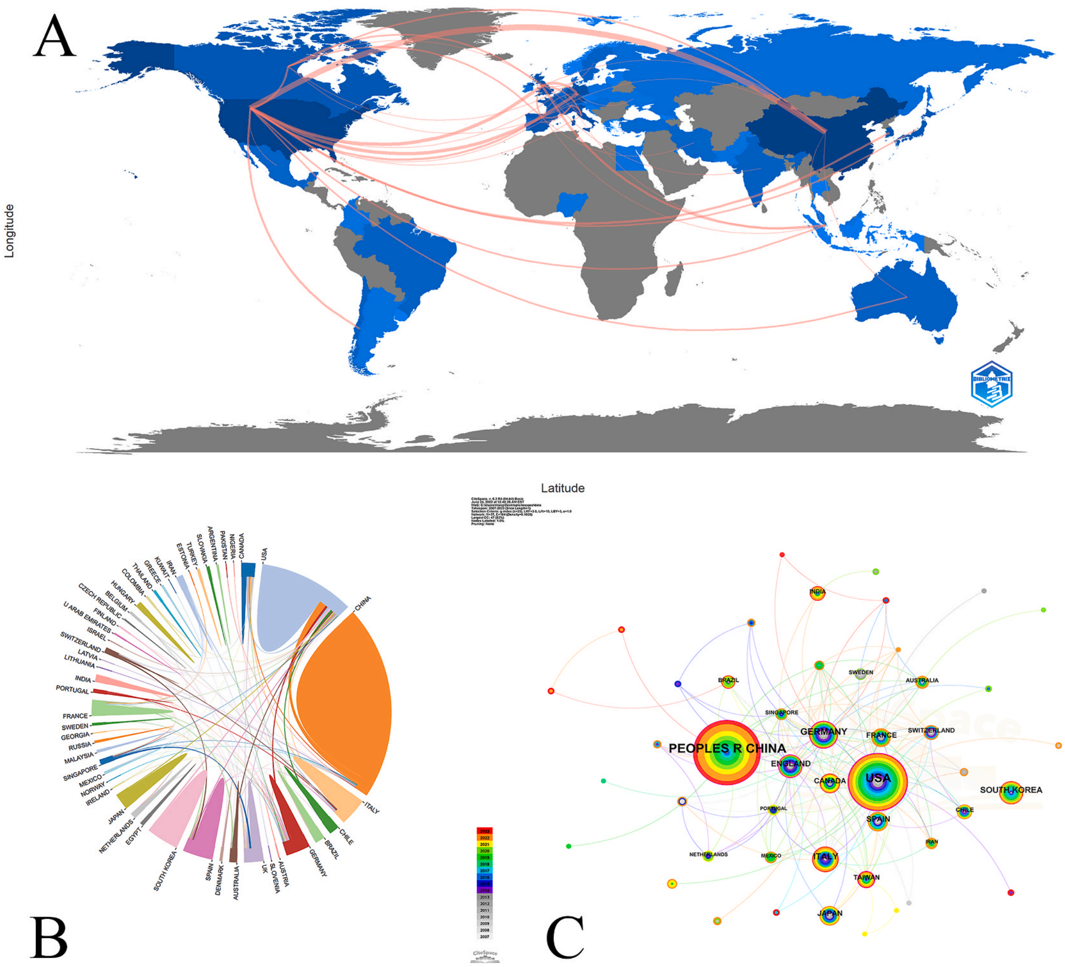

Fig. 3. The network visualization analysis of co-authorship of countries. (A) The world map of country cooperation network generated by Bibliometrix. (B) The map of country cooperation network generated by bibliometric online analysis platform. (C) The network visualization map of countries generated by CiteSpace.

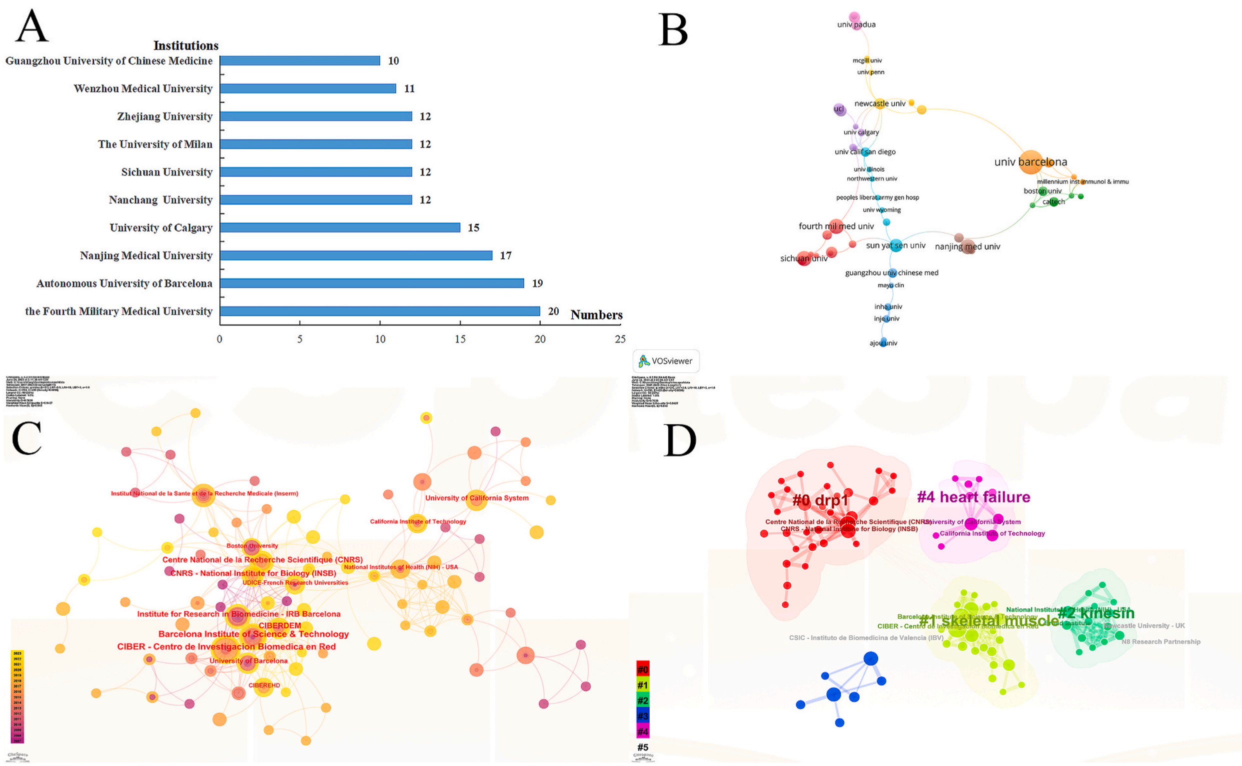

Fig. 4. The network visualization analysis of co-authorship of institutions. (A) The top institutions in terms of the number of publications. (B) The network visualization map of institutions generated by VOSviewer. (C) The co-occurrence network visualization map generated by CiteSpace. (D) The cluster visualization map of institutions generated by CiteSpace.

Table 1
The top ten institutions that contributed to mitochondrial dynamics and hepatocellular carcinoma.

Rank	Institutions	Numbers	Total citations	Citations per publication	Total number of first author	Country
1	*the Fourth Military Medical University*	20	152	7.60	5	China
2	*Autonomous University of Barcelona*	19	119	6.26	2	Spain
3	*Nanjing Medical University*	17	5	0.29	3	China
4	*University of Calgary*	15	43	2.87	3	Canada
5	*Nanchang University*	12	5	0.42	2	China
6	*Sichuan University*	12	5	0.42	1	China
7	*The University of Milan*	12	11	0.92	4	Italy
8	*Zhejiang University*	12	0	0.00	0	China
9	*Wenzhou Medical University*	11	10	0.91	2	China
10	*Guangzhou University of Chinese Medicine*	10	3	0.30	3	China

Table 2
The top ten authors and co-cited authors that contributed to mitochondrial dynamics and hepatocellular carcinoma.

Rank	Authors	Numbers	Total citations	Citations per publication	Rank	Co-cited authors	Co-citation times
1	*Zorzano, A*	13	107	8.23	1	*Chen, HC*	406
2	*Wang, Y*	9	2	0.22	2	*Twig, G*	178
3	*Palacin, M*	8	98	12.25	3	*Ishihara, N*	172
4	*Zhang, Y*	7	18	2.57	4	*Chan, DC*	150
5	*Hausenloy, DJ*	6	49	8.17	5	*Karbowski, M*	139
6	*Scorrano, L*	6	35	5.83	6	*Youle, RJ*	135
7	*Wang, L*	6	10	1.67	7	*Westermann, B*	134
8	*Westermann, B*	6	122	20.33	8	*Chen, Y*	108
9	*Zhang, X*	6	5	0.83	9	*Olichon, A*	108
10	*Chan, DC*	5	82	16.4	10	*Otera, H*	106

Calgary (15), and *Nanchang University* (12). Notably, six of the top 10 institutions were from China. Network visualizations of the institutions were also analyzed using VOSviewer and CiteSpace. As shown in Fig. 4B,61 institutions that published at least three articles and had co-authorships with others were grouped into nine clusters. However, 95 institutions reached the threshold of three articles. This indicates that there was relatively little cooperation between the institutions. Fig. 4C and D shows the co-occurrence of institutions and the cluster visualization map of the institutions. These institutions were scattered, and none hade high centrality. Cluster visualization analysis generated the following six clusters: #0 drp1; #1 skeletal muscle; #2 kinesin; #3 heart failure; and #4 and #5 with no clear topic.

3.4. Analysis of authors

A total of 3138 authors participated in research on mitochondrial dynamics and HCC. The top 10 authors contributing to mitochondrial dynamics and HCC are listed in Table 2. *Zorzano, A* published the largest number of publications (13), followed by *Wang, Y* (9), *Palacin, M* (8), *Zhang, Y* (7) and *Hausenloy, DJ* (6). The productive activities of the top 10 authors over time are shown in Fig. 5A. The visualization network of authors was also analyzed using VOSviewer; however, there was little collaboration, and no network map was generated. We then analyzed the co-citations of the authors. The top co-cited authors are listed in Table 2, and a visualization map of the authors' co-citations is shown in Fig. 5B. *Chen, HC* ranked first with 406 co-citations, followed by *Twig, G* (178) and *Ishihara, N* (172). It is worth noting that *Chan, DC* and *Westermann, B* were the top 10 authors both in terms of both number of publications and

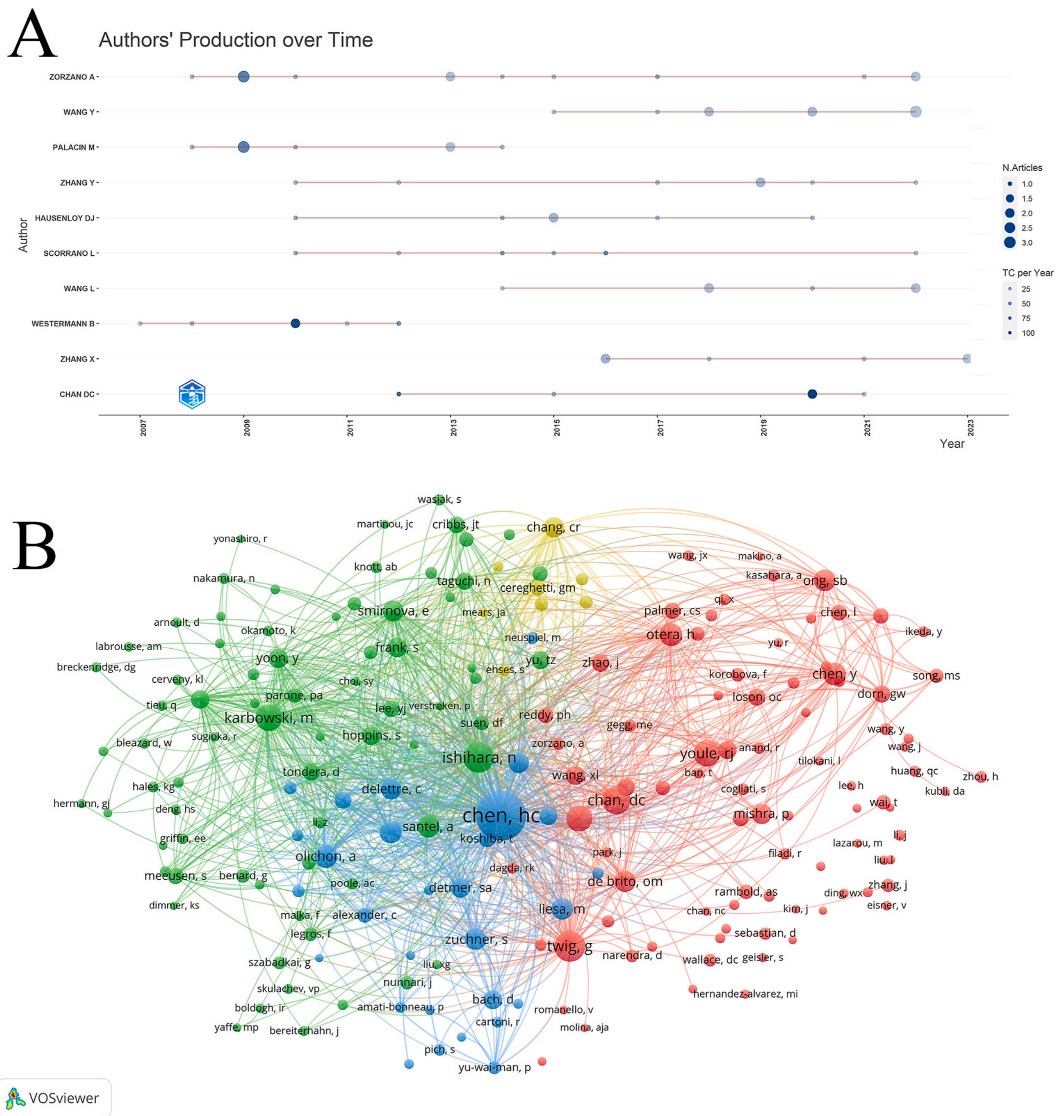

Fig. 5. The analysis of authors and co-cited authors. (A) The productive activities of the top ten authors over time. (B) The visualization map of co-citations of authors generated by VOSviewer.

number of co-citations. A total of 18,288 co-cited authors were found; when the minimum number of citations of an author was 20, 197 authors were clustered into four clusters.

3.5. Analysis of journals

A total of 288 journals participated in research on mitochondrial dynamics and HCC. The top 10 popular journals on mitochondrial dynamics and HCC are listed in Table 3. *Plos One* was the most popular journal with 18 publications, followed by *International Journal of Molecular Sciences* (17), *Biochemical and Biophysical Research Communications* (10)*, Cells* (10), and *Frontiers in Pharmacology* (7). Among these, *Cell Death & Disease* had the highest IF (2022) (9.685) and six journals were located in the JCR (2022) Q1 region. Fig. 6A shows the network visualization of journals; 46 journals were clustered into nine clusters when the minimum number of documents in a journal was three. We also analyzed journal co-citations. The top co-cited journals are listed in Table 3, *Journal of Biological Chemistry* ranked first with 1682 co-citations, followed by *Journal of Cell Biology* (1569) and *Proceedings of the National Academy of Sciences* (1,192). Fig. 6B shows the co-citations of journals; 2880 co-cited journals were found. When the minimum number of citations for a journal was 20, we grouped the 301 journals into four clusters. We generated a dual-map overlay of journals using CiteSpace, as shown in Fig. 6C. The figure shows the citation trajectory of interdisciplinary collaboration; the main citation lines are marked in orange. The studies published in Molecular, Biology and Immunology journals mainly cited studies published in the Molecular, Biology and Genetics journals.

3.6. Analysis of the references

The top 10 most cited references in this study are listed in Table 4. There were two articles cited over 1000 times, and the most cited publication was "*The role of mitochondria in apoptosis*" authored by *Jeong, SY* et al. (1574). Among them, seven were reviews and three were articles; and *Westermann, B* (Germany) and *Chan, DC* (the USA) both had two articles in the top 10 most cited references. Burst detection and timeline views of the references were performed using CiteSpace. In Fig. 7A, the timeline view map can help us understand the development of research on mitochondrial dynamics and HCC and predict future directions. The timespan is displayed at the top of the figure; all clusters are arranged vertically, with the largest cluster appearing at the top and larger circles indicating more citations or the highest frequency. Seven clusters were formed: #0 opa 1; #1 mitofusion; #2 Mfn 2; #3 mtdna; #4 HCC; #5 neurodegenerative disease; and #6 saccharomyces cerevisiae. In Fig. 7B, burst detection shows the dynamic change in references in the research on mitochondrial dynamics and HCC, and the 25 references with the strongest citation bursts are listed. The timeline is depicted as a blue line, and the duration for which a reference shows a burst is shown as a red segment in the blue timeline, indicating the beginning year, ending year, and duration of the burst. The reference with the strongest citation bursts was by *Chan, DC,* 2010 (12.48); four references continued to burst until 2022, with two references beginning to burst by 2021.

3.7. Analysis of keywords

The top 20 high-frequency keywords are listed in Table 5, and "mitochondria" was the most frequent keyword (124), followed by "mitochondrial dynamics" (123), "mitochondrial fission and fusion" (51), "mitophagy" (49) and "fission" (47). A visualization analysis of the keywords is shown in Fig. 8. As shown in Fig. 8A, 56 keywords were grouped into seven clusters when the minimum number of keyword was five. Fig. 8B shows the overlay visualization map of the keywords, which takes the score value based on the average year of the keyword for color mapping. Therefore, HCC and mitophagy are the recent hotspots in mitochondria-related research, and they may become frontiers and trends in the future. A cluster visualization map of the keywords was created, as shown in Fig. 8C. Eight clusters were generated, as follows: #0 mitochondrial biogenesis; #1 mitochondrial dynamics; #2 parkinson's disease; #3 phosphorylation; #4 mitochondrial fusion; #5 mitochondrial function; #6 sarcolipin; and #7 c elegans. Moreover, to better understand the development history and explore the future trends of this field, we used Bibliometrix to generate a visual map of trend topics based on keyword; Fig. 8D shows that HCC was the research hotspot.

Table 3
The top ten popular journals and co-cited journals that contributed to mitochondrial dynamics and hepatocellular carcinoma.

Rank	Journal (JCR category quartile in 2022)	Numbers	IF (2022)	Rank	Co-cited journals	Co-citation times
1	*Plos One* (Q2)	18	3.752	1	*Journal of Biological Chemistry*	1682
2	*International Journal of Molecular Sciences* (Q1)	17	6.208	2	*Journal of Cell Biology*	1569
3	*Biochemical and Biophysical Research Communications* (Q3)	10	3.322	3	*Proceedings of the National Academy of Sciences*	1192
4	*Cells* (Q2)	10	7.666	4	*Cell*	963
5	*Frontiers in Pharmacology* (Q1)	7	5.988	5	*Nature*	900
6	*Cell Death & Disease* (Q1)	6	9.685	6	*Science*	899
7	*Faseb Journal* (Q1)	6	5.834	7	*Embo journal*	729
8	*International Journal of Biochemistry & Cell Biology* (Q2)	6	5.652	8	*Molecular Biology of the Cell*	667
9	*Life Sciences* (Q1)	6	6.780	9	*Journal of Cell Science*	652
10	*Antioxidants & Redox Signaling* (Q1)	5	7.468	10	*Plos One*	633

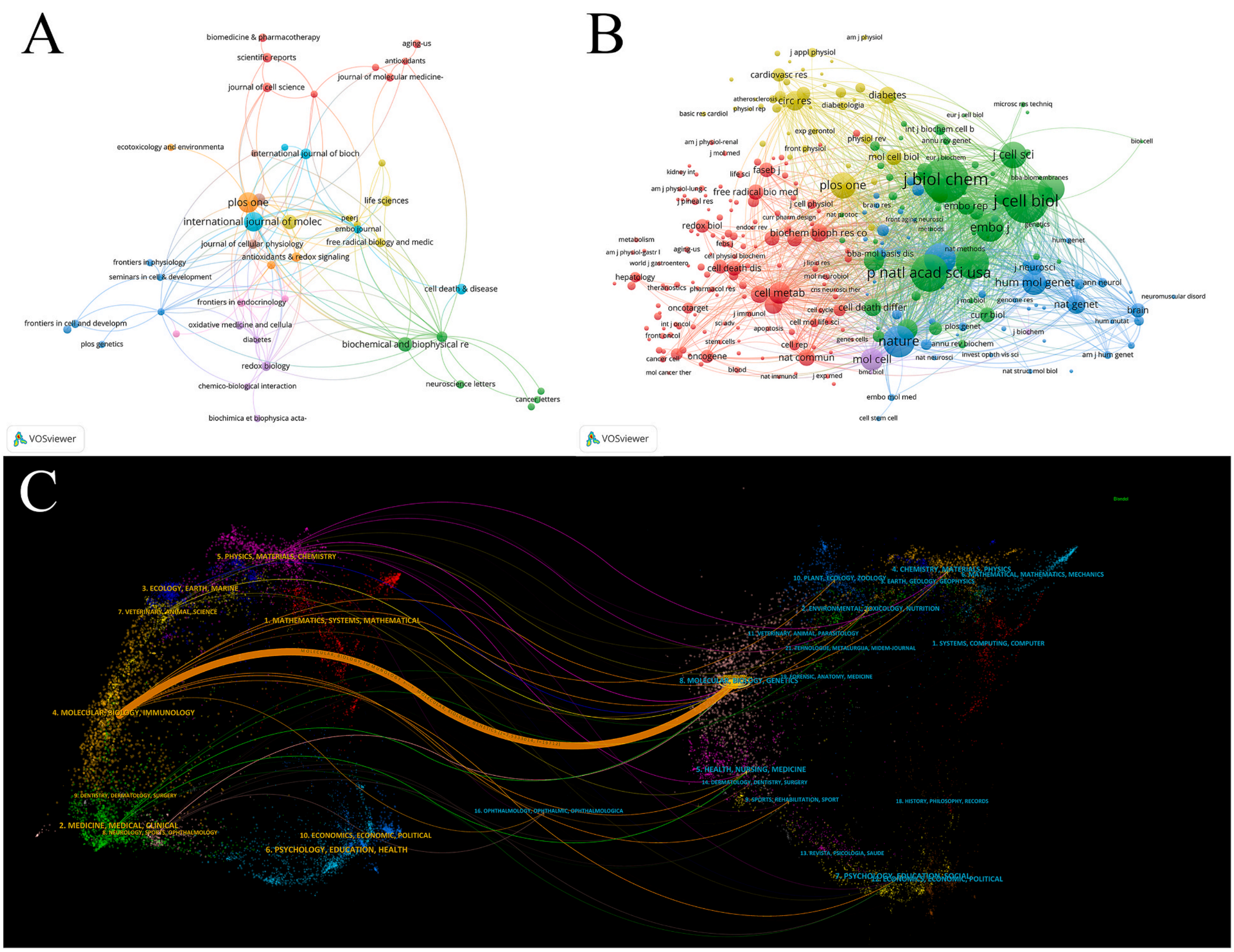

Fig. 6. The network visualization analysis of co-authorship of journals. (A) The visualization map of journals generated by VOSviewer. (B) The visualization map of co-citations of journals generated by VOSviewer. (C) A dual map overlay of journals by CiteSpace.

Table 4
The top ten most cited publications on mitochondrial dynamics and hepatocellular carcinoma.

Rank	Title (Document Type)	First author	Times	Journal	Country	Year
1	The role of mitochondria in apoptosis (Review)	*Jeong, SY*	1574	*Bmb Reports*	South Korea	2008
2	Mitochondrial fusion and fission in cell life and death (Review)	*Westermann, B*	1380	*Nature Reviews Molecular Cell Biology*	Germany	2010
3	Fusion and Fission: Interlinked Processes Critical for Mitochondrial Health (Review)	*Chan, DC*	826	*Annual Review of Genetics*	the USA	2012
4	Mitochondrial Dynamics in Mammalian Health and Disease (Review)	*Liesa, M*	691	*Physiological Reviews*	Spain	2009
5	The i-AAA protease YME1L and OMA1 cleave OPA1 to balance mitochondrial fusion and fission (Article)	*Anand, R*	489	*Journal of Cell Biology*	Germany	2014
6	Bioenergetic role of mitochondrial fusion and fission (Review)	*Westermann, B*	454	*Biochimica Et Biophysica Acta-Bioenergetics*	Germany	2012
7	Disturbed mitochondrial dynamics and neurodegenerative disorders (Review)	*Burte, F*	454	*Nature Reviews Neurology*	Italy	2015
8	The Mitochondrial Pathways of Apoptosis (Article)	*Estaquier, J*	450	*Advances in Mitochondrial Medicine*	France	2012
9	Mitochondrial Dynamics and Its Involvement in Disease (Review)	*Chan, DC*	423	*Annual Review of Pathology*	the USA	2020
10	Inhibition of mitochondrial fission prevents cell cycle progression in lung cancer (Article)	*Rehman, J*	398	*Faseb Journal*	the USA	2012

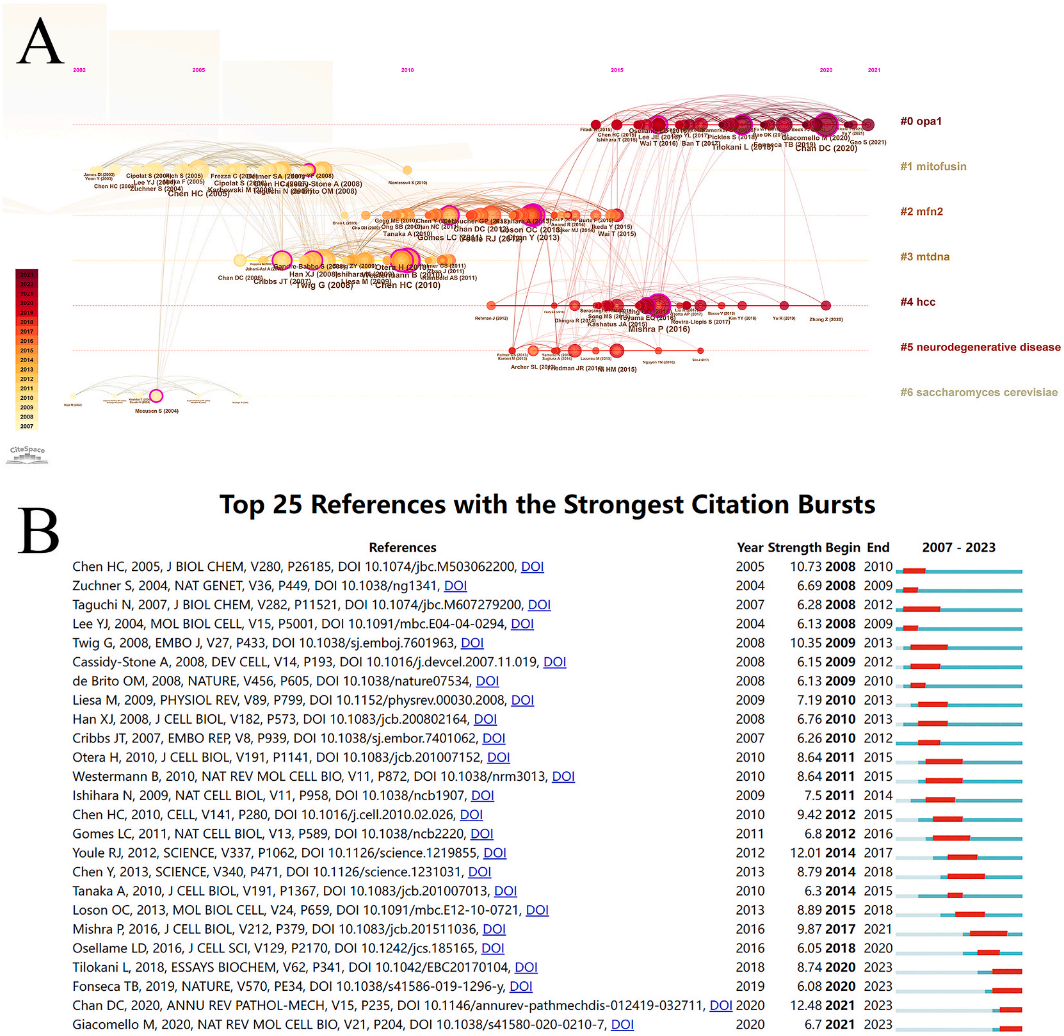

Fig. 7. The analysis of reference. (A) The timeline views map that generated by CiteSpace. (B) The burst detection of references and the top 25 references with the strongest citation bursts were listed.

Table 5
The top twenty high-frequency keywords on mitochondrial dynamics and hepatocellular carcinoma.

Rank	Keywords	Frequency	Total link strength	Rank	Keywords	Frequency	Total link strength
1	mitochondria	124	251	11	mitochondrial fission	26	73
2	mitochondrial dynamics	123	263	12	oxidative stress	26	49
3	mitochondrial fission and fusion	51	92	13	opa1	25	89
4	mitophagy	49	132	14	autophagy	22	47
5	fission	47	146	15	mitochondrial dysfunction	21	45
6	fusion	46	145	16	mitochondrial morphology	18	41
7	drp1	44	119	17	mitochondrial dna (mtdna)	17	35
8	apoptosis	41	90	18	hepatocellular carcinoma	16	31
9	mitochondrial fusion	40	90	19	insulin resistance	15	41
10	mfn2	30	85	20	skeletal muscle	15	46

4. Discussion

In this study, we analyzed global publications on mitochondrial dynamics and HCC published from January 2007 to May 2023 using bibliometric analysis. In general, the annual number of publications gradually increased, indicating that this research field has attracted widespread attention and has broad promise. Our study lists the leading countries, prominent institutions and authors, and popular journals involved in the study of mitochondrial dynamics and HCC, summarizing the current global research status and trends

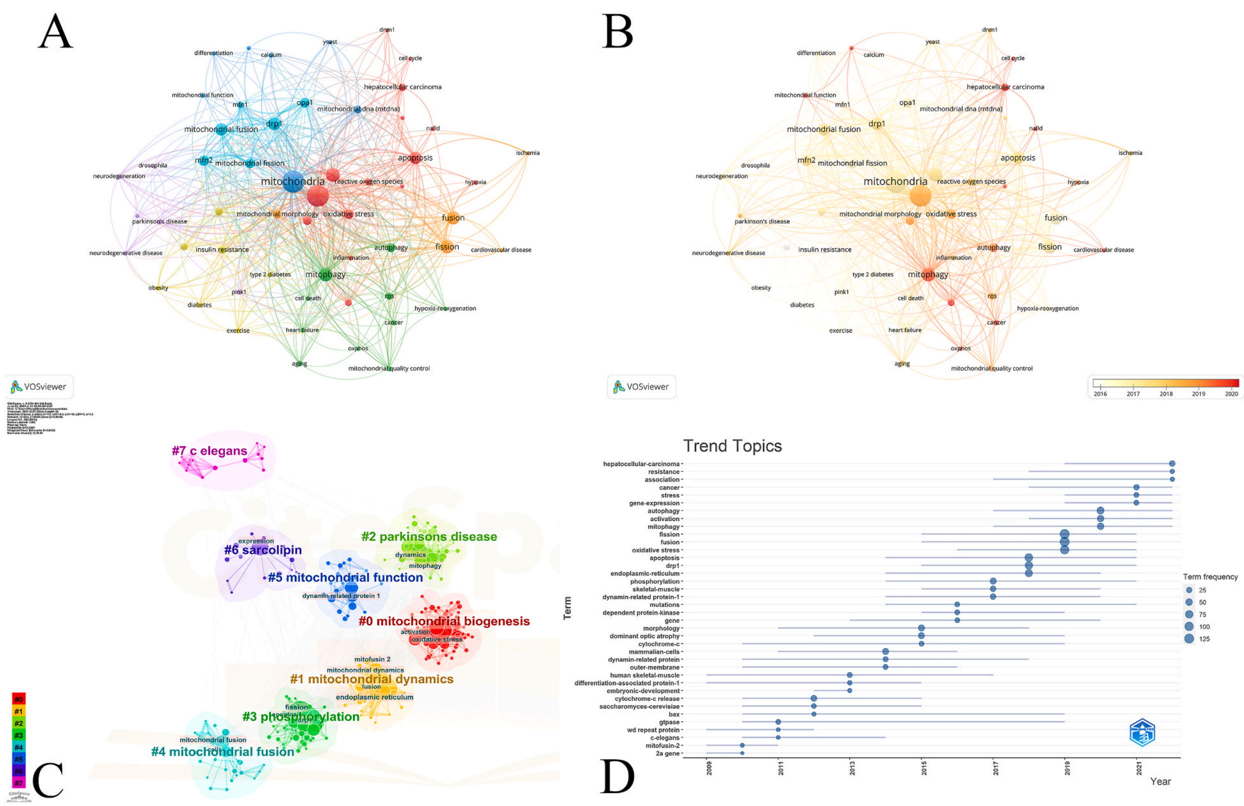

Fig. 8. The network visualization analysis of keywords. (A) The network visualization map of co-occurrence of keywords generated by VOSviewer. (B) The overlay visualization map of keywords generated by VOSviewer. (C) The cluster visualization map of keywords generated by CiteSpace. (D) A visual map of trend topics based on keywords generated by Bibliometrix.

in this field.

China has the greatest number of publications and an absolute advantage in terms of volume. This advantage is closely related to the high incidence of HCC in China, its economic development, and the increase in medical investment. However, similar to many medical research fields, the USA was the most influential country [27,28], with the highest total number of citations and three of the top 10 most cited publications. Simultaneously, European countries, such as Germany, were outstanding in this field. *Wondimagegn D* called this phenomenon of the dominance of medicine in European and American countries the colonial foundations of medical education [29]. Moreover, a visualization analysis of countries' centrality showed that the USA and China cooperated most closely and that the USA cooperated most frequently with other countries, followed by European countries, such as Germany and the UK, whereas China cooperated much less with other countries. An interesting phenomenon was revealed in the analysis of institutions: 95 institutions published more than three articles, but only 61 institutions had a cooperative relationship with each other, two of the six clusters had no clear topics in the cluster analysis of institutions and no high-centrality institutions in them. This indicates that core high-impact institutional clusters have not yet been formed.

In short, the current objective status in the research field of mitochondrial dynamics and HCC is that European and American countries dominate, developing countries such as China are actively participating, and few low- and middle-income countries are visible. At the same time, academic exchanges and cooperation between different countries, institutions, and authors have not been sufficiently extensive. What causes this gap in knowledge? We believe that these are historical and practical factors. Modern medicine originated in Western countries; earlier start and long-term accumulation made European and American countries occupy many advantages, and the rapid development of industry, science, and technology in the 20th century not only provided European and American countries with the support of technology funds but also attracted a large number of high-quality talents. Moreover, the long-standing lack of voices from low- and middle-income countries has led to academic medical exchanges occurring in only a few countries, institutions, and authors. All of these factors contributed to the aforementioned colonial foundations of medical education. While China and other developing countries are trying to catch up, this does not occur overnight. Therefore, to reduce this gap and better develop modern medicine, listening to more voices from low- and middle-income countries and applying the idea of the Olympic movement higher, faster, and lighter in medical education are considered ways to solve it [29]. Different countries and institutions can achieve a win-win situation through more extensive academic exchanges and cooperation by holding various international conferences and sending students. Developed countries can help low- and middle-income countries develop health services so that they can participate more actively in the development of global medicine. We believe that in the next 5 years, research on mitochondrial dynamics, HCC, and the entire medical field will flourish, and more medical problems will be resolved.

Co-citation analysis reflects the research direction and academic development of a certain field and draws a complete academic knowledge network. In this study, we found that *Chen, HC* was the most cited author. He has conducted in-depth research on the proteins and genes associated with mitochondrial fission and fusion. In 2015, *Chen, HC* et al. demonstrated that tissue integrity and mitochondrial physiology can be restored at the whole-organ level by retuning the balance of mitochondrial fission and fusion and that liver damage can also be reduced through the combined action of mutations in and that liver damage can also be reduced through the combined action of mutations in *Mfn* and *Mff* [30]. Another important author was *Westermann, B*, the top 10 authors in the number of publications and co-citations, whose research focused on mitochondrial morphology, genetics, aging, death, and fission and fusion [31, 32]. Through analyses by important authors, we found that the current influence of mitochondrial dynamics on HCC is mainly concentrated on genes, proteins and other mechanisms, and there are few clinical studies.

Journal analysis also showed that current research focuses on molecular mechanisms. *Journal of Biological Chemistry*, a professional academic journal that publishes the latest scientific discoveries in the fields of biochemistry and molecular biology, was the most co-cited journal. Analysis of the dual-map overlay of journals showed that current research focused primarily on molecules, biology, and genetics. These findings provide guidance for researchers to quickly and accurately understand the development of this field and show that current research hotspots in mitochondrial dynamics and HCC involve various molecular mechanisms. Although the purpose of medical research is to better serve human health and basic theoretical research is important, they should eventually be implemented in clinical research. Therefore, clinical research on mitochondrial dynamics in HCC should be the focus of future studies.

The analysis of references and keywords is the best way to reflect the research foundation, development history, research hotspots, and future trends in a certain field. The earliest high-impact article was "*The role of mitochondria in apoptosis*" published by *Jeong, SY* et al. in 2008, which summarized the proteins, their regulator of mitochondrial fusion and fission, and the role of mitochondrial fusion and fission mechanisms in apoptosis, providing theoretical support for the study of mitochondrial dynamics [33]. Subsequently, many studies have focused on the mechanisms of mitochondrial dynamics and the proteins involved in mitochondrial fusion and fission and have linked mitochondrial dynamics to various diseases [19]. Major breakthroughs have been made in the study of mitochondrial dynamics, particularly in HCC, from autosomal dominant optic atrophy and Charcot-Marie-Tooth neuropathy type 2A to cardiovascular diseases, metabolic diseases, and even cancers [34–38]. Over the past few years, the mitochondrial fusion proteins *Mfn1* and *Mfn2* have been shown to play important roles in HCC [24]. The expression of *Mfn1* protein in HCC is lower than that in neighboring non-tumor tissues, and in primary HCC, it is lower than that in distant metastatic HCC, which may be related to the fact that *Mfn1* can shift cellular metabolism from glycolysis to oxidative phosphorylation [39,40]. Moreover, loss of heterozygosity of the *Mfn2* gene is also a characteristic of HCC, and the expression of *Mfn2* protein in HCC is also reduced [41]. The expression of the *Mfn2* protein is negatively correlated with the prognosis of HCC; the lower the expression of the *Mfn2* protein in HCC, the worse the prognosis [42,43]. Moreover, *Wang W* et al. proposed that overexpression of the *Mfn2* protein in HCC can reduce cell proliferation and induce spontaneous apoptosis [44]. Regarding mitochondrial fission proteins, overexpression of the *Drp1* protein can promote cell proliferation through the crosstalk of *p53* and *nuclear factor kappa-light-chain-enhancer of activated B cells* pathways [45,46]. Although it has been proven that low expression of mitochondrial fusion proteins and overexpression of mitochondrial fission proteins are closely related to the occurrence of HCC, more molecular mechanisms need to be explored.

How do we look for the possible molecular mechanisms? We found some keywords such as "reactive oxygen species", "oxidative stress", "insulin resistance", "obesity", and "non-alcoholic fatty liver disease (NAFLD)" in keyword analysis, and they may be able to provide us with some ideas. Studies have found that oxidative stress can affect the balance between mitochondrial fusion and fission by inhibiting mitochondrial fusion, leading to mitochondrial fragmentation and loss function, and can affect the occurrence of HCC [47, 48]. Studies have also found that oxidative stress can induce the most common *p53* mutation in HCC [49]; therefore, the specific molecular mechanism by which oxidative stress induces *p53* mutations and whether oxidative stress can lead to other studies on HCC mutations are unknown. In addition, oxidative stress can affect some diseases associated with HCC. For example, oxidative stress can promote pathological polyploidization of NAFAD; oxidative stress can lead to low expression of the glucose transporter type 4, leading to insulin resistance; and obese patients have increased oxidative stress and expression of nuclear factor erythroid 2-related factor 2 (*Nrf2)* [50–52]. Bariatric surgery and reduced insulin resistance may reduce the risk of HCC, whereas NAFAD can progress to advanced liver disease or HCC [53–55]. Therefore, can new research directions be found in the intermediate mediators related to mitochondrial dynamics in HCC, such as oxidative stress? In summary, we summarize the research status of mitochondrial dynamics and HCC through bibliometric analysis and provide some possible research directions. However, more molecular mechanisms and signaling pathways need to be continuously verified, and the currently known molecular mechanisms should be combined with the drug therapy targets of HCC, which may be a research hotspot and trend in the future.

5. Limitations

Although we performed this bibliometric analysis of mitochondrial dynamics and HCC as thoroughly as possible, there were still some limitations. First, we only analyzed publications from the WoSCC database; therefore, important publications from other databases were overlooked. Second, a bibliometric analysis is a retrospective observational study and more time is required to observe a large trend; therefore, there may be some bias in the recent analysis. Lastly, we only analyzed publications in English, and some important publications in non-English languages were excluded, especially Chinese publications.

6. Conclusions

Research on mitochondrial dynamics in HCC has received much attention, and many studies have been published. China and the USA are the leading countries in this field. China had the greatest number of publications, whereas the USA had the highest total number of citations. However, regional development imbalances and global cooperation are insufficient for the research on mitochondrial dynamics and HCC, and core institutions and author collaboration communities have not yet been formed. Therefore, future research on mitochondrial dynamics and HCC is promising, especially regarding the molecular mechanism of mitochondrial fission and fusion and how to link the currently known molecular mechanisms with drug therapy targets for HCC.

Data availability statement

The data associated with our study is not deposited into a publicly available repository, but the data will be made available on request.

Additional information

No additional information is available for this paper.

CRediT authorship contribution statement

Ruiyu Wang: Writing – review & editing, Writing – original draft, Software, Methodology, Conceptualization. **Shu Huang:** Supervision, Methodology, Conceptualization. **Ping Wang:** Software, Resources, Methodology, Conceptualization. **Xiaomin Shi:** Project administration, Formal analysis. **Shiqi Li:** Supervision, Software, Resources. **Yusong Ye:** Software, Resources, Methodology. **Wei Zhang:** Supervision, Software. **Lei Shi:** Supervision, Resources. **Xian Zhou:** Writing – review & editing, Supervision, Conceptualization. **Xiaowei Tang:** Writing – review & editing, Resources, Methodology, Conceptualization.

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Acknowledgments

Sources of support**:** None.

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