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Bibliometric analysis of autophagy in the diagnosis and treatment of osteosarcoma: a bibliometric analysis (2007–2023)

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ABSTRACT

Osteosarcoma is the most common primary bone tumor in children and adolescents. Its pathogenesis is complex and poses difficulties in treatment. Autophagy is a cell biological process that plays a crucial role in the mechanistic study and treatment of osteosarcoma. The objective of this study is to evaluate the past research progress from 2007 to 2023 and visualize the key research directions through bibliometric methods. Relevant publications published from the start of 2007 to the end of 2023 were searched and screened in the Web of Science Core Collection. They were analyzed and visualized using CiteSpace and the Bibliometric online analysis platform in terms of country, institution, author, journal, cited references, and keywords. In total, 619 publications from 522 journals with 682 authors from 42 countries were screened. The country with the highest number of publications is China ($n = 445$, 71.890%), followed by the United States ($n = 60$, 9.693%). The research institution with the highest number of publications is Shanghai Jiao Tong University ($n = 42$, 6.785%). The author with the highest number of publications is Cai, Zhengdong ($n = 7$), while the most cited author is Mizushimma N ($n = 93$). Among many journals, AUTOPHAGY has the most citations ($n = 342$), while CANCER LETT shows the greatest centrality (Centrality = 0.05). "Autophagy" is the most cited keyword ($n = 177$), and the keyword with the largest burst intensity is "cancer cells" (Strength = 6.27), which lasted from 2011 to 2014. China is a major contributor to autophagy research in the field of osteosarcoma, followed by the United States. All publications are in high-quality journals. "Autophagy" is a hot research topic in this field.

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Autophagy; osteosarcoma; citeSpace; bibliometric; visualization

Background

Osteosarcoma is a rare but highly malignant malignancy that originates from mesenchymal tissues. The most likely site is the metaphysis, where the blood supply is adequate.[1] It usually causes symptoms such as localized pain, swelling, and limitation of movement. In severe cases, it can lead to fractures and bone destruction. Osteosarcoma occurs mainly in adolescents and may be related to bone development.[2] The specific etiology of osteosarcoma is not known, but it may be related to genetic factors, environmental factors, and lifestyle.[3] Treatment of osteosarcoma usually requires a combination of therapies, including surgical removal of the tumor, radiotherapy, and chemotherapy.[4,5] In recent years, some new therapeutic approaches such as targeted therapy and immunotherapy have also been gradually introduced into the treatment of osteosarcoma, providing more options for patients.[6]

Recent studies have demonstrated that autophagy plays a crucial role in the occurrence and development of osteosarcoma. As an important intracellular mechanism for maintaining homeostasis, autophagy can assist cells in coping with stressful situations.[7] Autophagy promotes tumor cell survival and proliferation, inhibits apoptosis, increases drug resistance, and facilitates tumor metastasis and invasive ability.[8] Autophagy can help tumor cells degrade and release some immune regulatory factors, which may suppress the body's anti-tumor immune response, allowing tumor cells to evade the surveillance and attack of the body's immune system. This phenomenon of immune evasion can lead to tumor progression and a poor prognosis for patients.[9] Researchers have found that the expression level of autophagy-related proteins is typically higher in osteosarcoma cells, which leads to increased malignancy of the tumor and aggravation of the patient's prognosis. Therefore, interfering with the autophagy process may become a strategy for the treatment of osteosarcoma. Several studies have shown that the use of specific autophagy inhibitors can effectively inhibit the proliferation of osteosarcoma cells, induce apoptosis, and improve the sensitivity of chemotherapeutic agents to tumors.[10,11]

Bibliometrics is a method for quantitatively analyzing academic literature to reveal the characteristics and patterns of disciplinary development.[12] Through bibliometric analysis, the development of a research field can be evaluated, including the trend of growth in the number of studies, research hotspots, author partnerships, and citation networks.[13] By analyzing the volume of published literature and citations, one can gain an

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understanding of the depth and academic impact of a particular study in a specific field.[14] Additionally, hotspots and cutting-edge issues in the research field can be identified through methods such as keyword analysis and topic clustering, which can provide a reference for future research directions.[15] As of now, there is no relevant bibliometric analysis for the two related fields of autophagy and osteosarcoma. The objective of this study is to evaluate the past research progress from 2007 to 2023 and the key directions in diagnostics and treatment of osteosarcoma through bibliometric methods.

Methods

Search strategy

A comprehensive literature search was conducted on the Web of Science Core Collection (accessed via https://www.webofscience.com/wos/woscc). The search strategy was set as follows: Ts (topic) = ("autophagy" and "osteosarcoma"); literature type was restricted to "Article" and "Review"; and the year of publication ranged from 2007 to 2023. Exclusion criteria (literature type): Meeting Abstract, Editorial Material, Early Access, Letter, Proceeding Paper. In total, 647 publications were retrieved. Figure 1 depicts the distribution of the included and excluded literature.

Data analysis

CiteSpace represents an extension and enhancement of VOSviewer, with a particular emphasis on the discovery of relational networks and the in-depth analysis of the evolution of knowledge domains. By generating citation network graphs, CiteSpace visualizes the citation relationships among documents, thereby uncovering the structure and evolutionary trends within research domains.[16,17] We employed this software to visualize authors, journals, co-documents, and keywords, and subsequently carried out a clustering analysis of the keywords (Parameters involved include: number of publications in the literature, number of citations, outbreaks, duration of outbreaks, centrality, and clustering categories). Additionally, we visualized and analyzed the collaboration between countries and institutions using the Bibliometric online analysis platform (https://bibliometric.com/).

Results

Visualization analysis of the number of publications and partnerships in different countries and journals

According to our search formula, from the start of 2007 to the end of 2023, there are 619 publications on autophagy in osteosarcoma. Of these, 545 are "Articles" and 74 are "Reviews". The number of publications and citations shows an upward trend year by year, and the number of publications in each period reflects the current state of research development in this field (Figure 2). From 2007 to 2020, the number of literature publications is in an increasing trend year by year, while from 2020 to 2023, the number of literature publications begins to show a decreasing trend. The literature comes from various organizations around the world (Figure 3a,b), and the top ten countries and organizations are presented in the table (Table 1). The country with the highest number of publications is China ($n = 445$, accounting for 71.890%), followed by the United States ($n = 60$, 9.693%), Italy ($n = 31$, 5.008%), Japan ($n = 27$, 4.362%), and South Korea ($n = 17$, 2.746%). China has the largest number

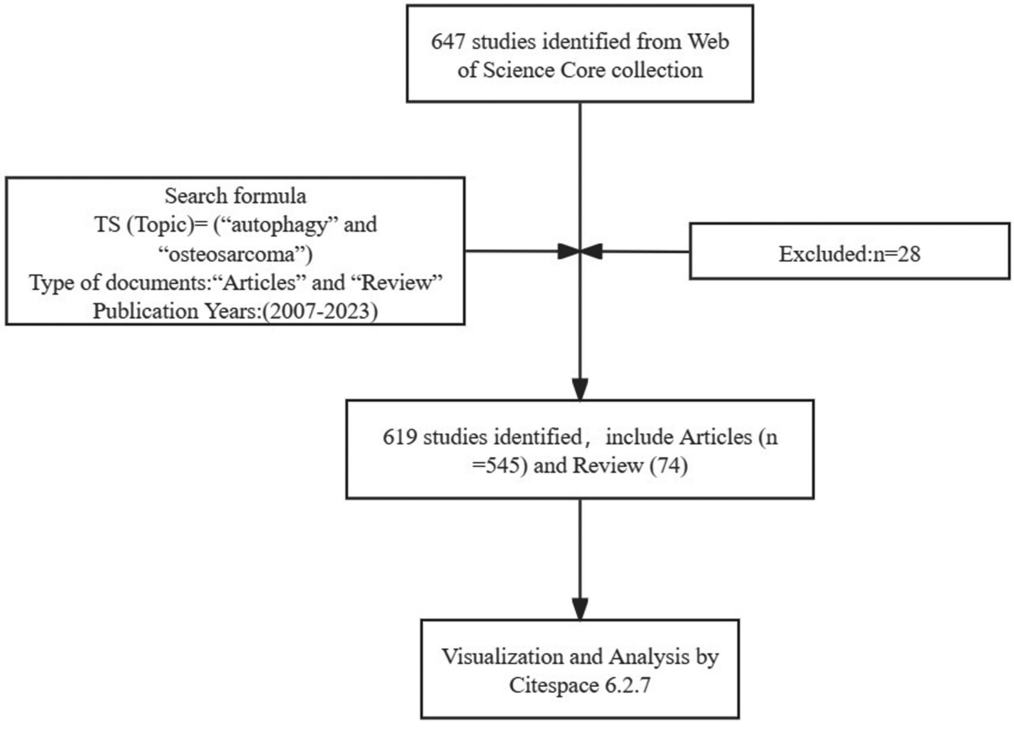


Figure 1. Publications screening flowchart.

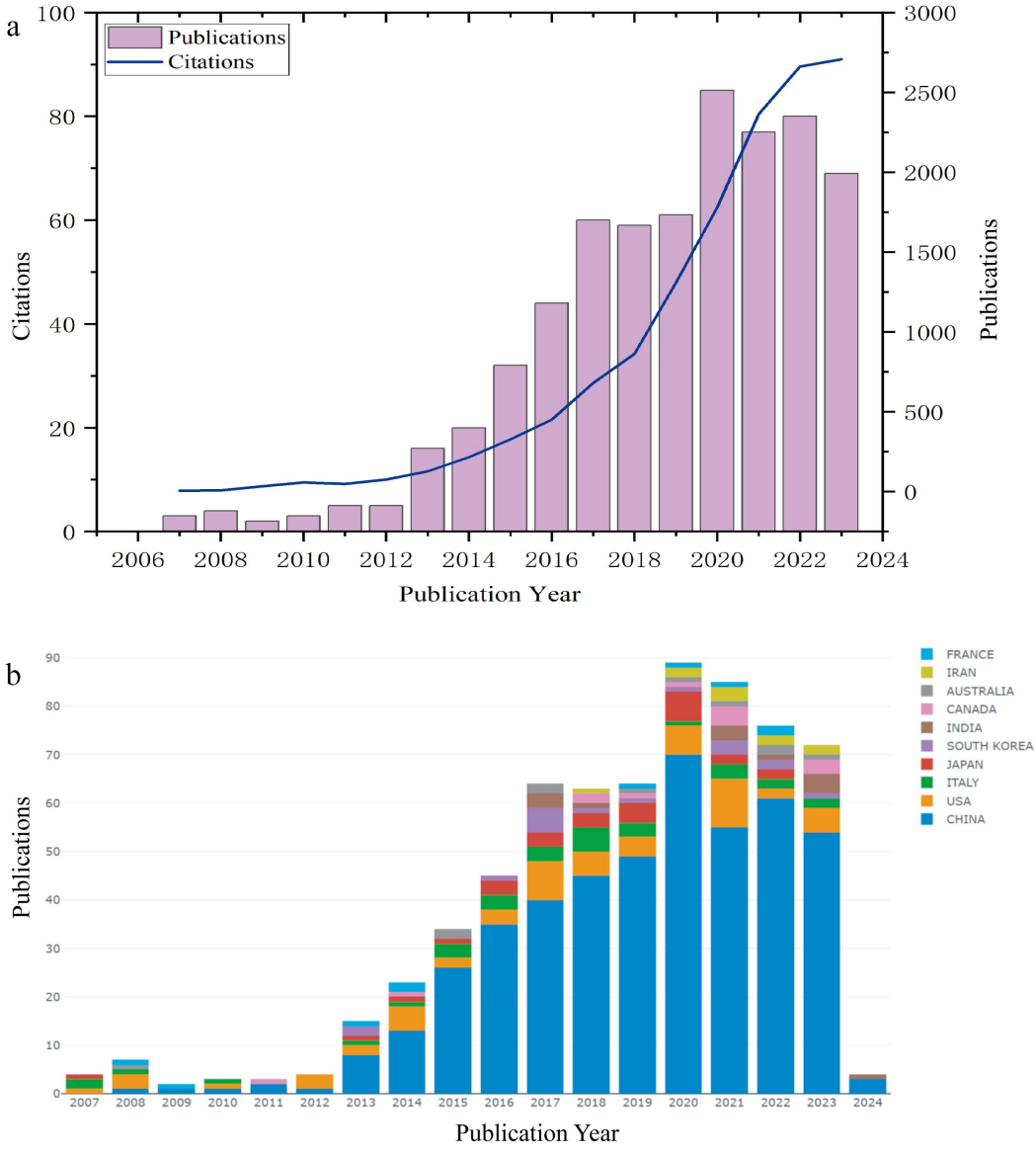


Figure 2. Number of publications in different countries at different times (a, b).

Table 1. Top ten countries and affiliations in the number of publications.

Rank	Countries	Record Count	Rank	Affiliations	Record Count
1	PEOPLES R CHINA	445 (71.890%)	1	SHANGHAI JIAO TONG UNIVERSITY	42 (6.785%)
2	USA	60 (9.693%)	2	CENTRAL SOUTH UNIVERSITY	26 (4.200%)
3	ITALY	31 (5.008%)	3	ZHEJIANG UNIVERSITY	22 (3.554%)
4	JAPAN	27 (4.362%)	4	SHANDONG UNIVERSITY	17 (2.746%)
5	SOUTH KOREA	17 (2.746%)	5	JILIN UNIVERSITY	16 (2.585%)
6	CANADA	13 (2.100%)	6	NANJING MEDICAL UNIVERSITY	16 (2.585%)
7	INDIA	13 (2.100%)	7	CHONGQING MEDICAL UNIVERSITY	15 (2.423%)
8	AUSTRALIA	11 (1.777%)	8	UNIVERSITY OF TEXAS SYSTEM	14 (2.262%)
9	FRANCE	11 (1.777%)	9	HUAZHONG UNIVERSITY OF SCIENCE TECHNOLOGY	13 (2.100%)
10	IRAN	11 (1.777%)	10	NANCHANG UNIVERSITY	13 (2.100%)

of published literature and makes the greatest contribution in this field. The research institutions with the highest number of publications are Shanghai Jiao Tong University ($n = 42$, 6.785%), followed by Central South University ($n = 26$, 4.200%), Zhejiang University ($n = 22$, 3.554%), Shandong University ($n = 22$, 3.554%), Jilin University ($n = 16$, 2.585%), and 90% of the institutions in the top ten are in China. As shown in the figure of cooperation between different countries and institutions (Figure 3c,d), there is close cooperation between China and the United States among many countries, while the cooperation between different institutions needs to be enhanced.

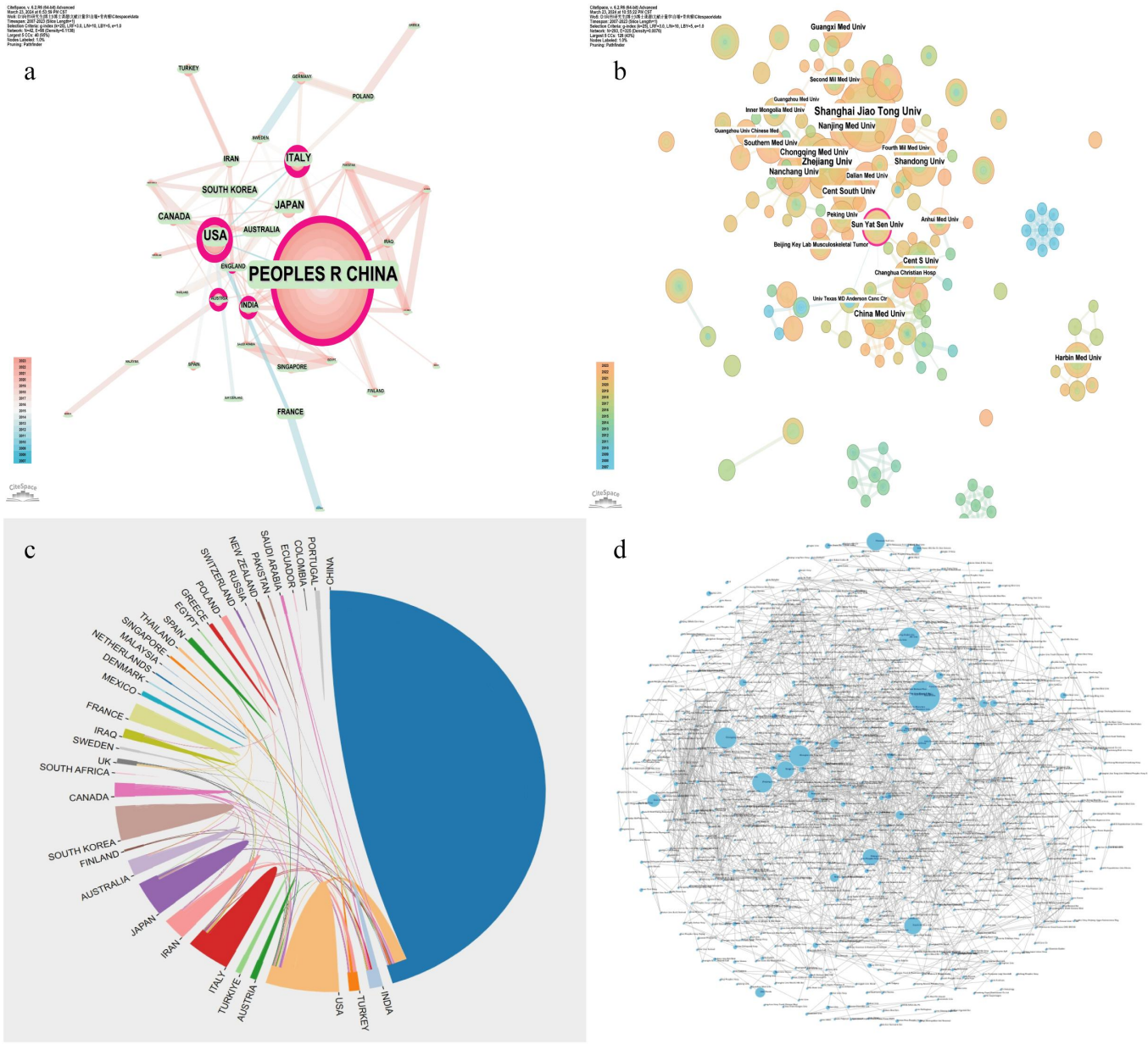


Figure 3. Visualization map of the cooperative relationships between various countries (a) and affiliations (b). Pie charts and co-occurrence plots of the number of articles issued in different countries (c, d). Nodes represent countries or institutions, with node size indicating publication volume and edges representing collaboration strength.

Visualization analysis of co-authors and highly cited authors

Table 2 presents the top ten authors in terms of the number of publications and high citations. Nine of the top ten authors with the highest literature output are from China. However, the total number of publications per author does not vary significantly. The author with the highest number of publications is Cai, Zhengdong ($n = 7$). The most cited author is Mizushimma N ($n = 93$), followed by Klionsky Dj and Levine B, both with 73 citations. The network co-occurrence graph reveals that authors do not collaborate closely enough with one another (Figure 4a), and the clusters are more numerous and dispersed. In the network co-occurrence graph of cited authors (Figure 4b), Klionsky Dj showed the highest level of collaborative centrality (0.11). This is an important metric for evaluating the importance of nodes in a network. Nodes with high centrality are represented by purple rings, and the thickness of the rings indicates the magnitude of the centrality values. The higher the centrality of a node, the greater its connecting role in the network. It appears more frequently on the shortest paths within the overall network and has greater influence and importance.

Visualization analysis of highly cited journals

We summarized all the publications in terms of Category and Index (Table 3). The Oncology category had the highest number of literature with 225 (36.349%), and Science Citation

Table 2. Top ten authors and cited authors.

Rank	Co-Author	Record Count	Rank	Cited Author	Record Count	Centrality
1	Cai, Zhengdong	7	1	Mizushimma N	93	0.09
2	Hua, Yingqi	6	2	Klionsky Dj	73	0.11
3	Wang, Gangyang	6	3	Levvine B	73	0.08
4	Liu, Wei	6	4	Li J	69	0.05
5	Zhang, Tao	5	5	Wang Y	67	0.01
6	Zuo, Dongqing	5	6	Ottaviani G	64	0.04
7	Chowdhury,Rajdeep	5	7	Huang J	61	0.09
8	Guo, Wei	5	8	Mirabbello L	59	0.02
9	Zhao, Wei	5	9	Zhang Y	58	0.03
10	Xu, Jing	5	10	Liu Y	57	0.03

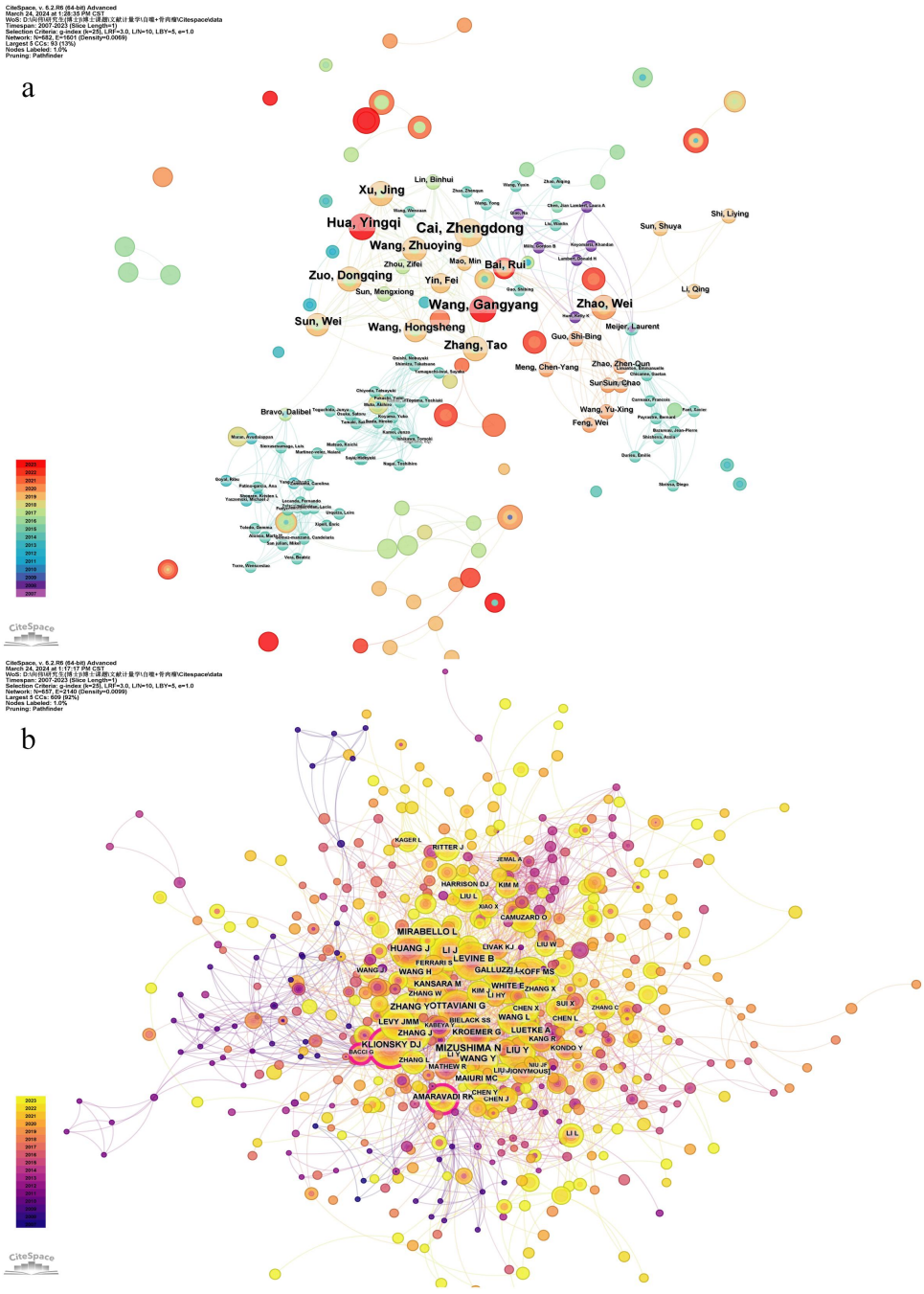


Figure 4. Visualized network co-occurrence maps for authors (a) and cited authors (b). Nodes represent authors or cited authors, node size indicates the number of author publications or cited authors, and lines indicate the strength of the partnership.

Table 3. Web of science categories and web of science Index.

Web of Science Categories	Record Count	Web of Science Index	Record Count
Oncology	225 (36.349%)	Science Citation Index Expanded (SCI-EXPANDED)	611 (98.708%)
Cell Biology	121 (19.548%)	Emerging Sources Citation Index (ESCI)	7 (1.131%)
Biochemistry Molecular Biology	90 (14.540%)	Book Citation Index – Science (BKCI-S)	5 (0.808%)
Pharmacology Pharmacy	81 (13.086%)	Index Chemicus (IC)	1 (0.162%)
Medicine Research Experimental	72 (11.632%)	Conference Proceedings Citation Index – Science (CPCI-S)	1 (0.162%)
Chemistry Multidisciplinary	26 (4.200%)	Social Sciences Citation Index (SSCI)	1 (0.162%)

Table 4. Top ten cited journals.

Cited Journal	Count	Centrality	Year	2022 JCR	IF
AUTOPHAGY	342	0.02	2007	Q1	13.3
CANCER RES	302	0.02	2007	Q1	11.2
CELL	289	0.03	2008	Q1	64.5
ONCOGENE	274	0.01	2008	Q1	8.0
J BIOL CHEM	271	0.01	2007	Q1	4.8
ONCOTARGET	266	0.01	2015	Q2	4.0
PLOS ONE	265	0.02	2012	Q2	3.7
CELL DEATH DIS	262	0.01	2013	Q2	9.0
CANCER LETT	245	0.05	2009	Q1	9.7
BIOCHEM BIOPH RES CO	228	0.04	2007	Q3	3.1

Index Expanded (SCIE) had the highest number of literature with 611 (98.708%). Table 4 lists the top ten most cited journals. AUTOPHAGY had the highest number of citations (n = 342), followed by CANCER RES (n = 302), CELL (n = 289), ONCOGENE (n = 274), and J BIOL CHEM (n = 271). Among these, CANCER LETT exhibits the greatest centrality at 0.05, representing the greatest impact of its nodes (Figure 5a). Figure 5b lists the top ten journals with the greatest intensity of outbreaks. Of these, CANCER RES has the greatest intensity of outbreaks (Strength = 18.16), which lasts for the period 2007 – 2016. This indicates that during this ten-year period, the journal was the hottest and most popular journal. The double graph overlay reveals the cross-citation relationship between the journals (Figure 6). The journals on the left are the citing journals and the journals on the right are the cited journals. These lines indicate the citation relationship between them. The graph identifies a major citation pathway, where publications in molecular/biological/genetic journals are cited mainly by publications in molecular/biological/immunology journals.

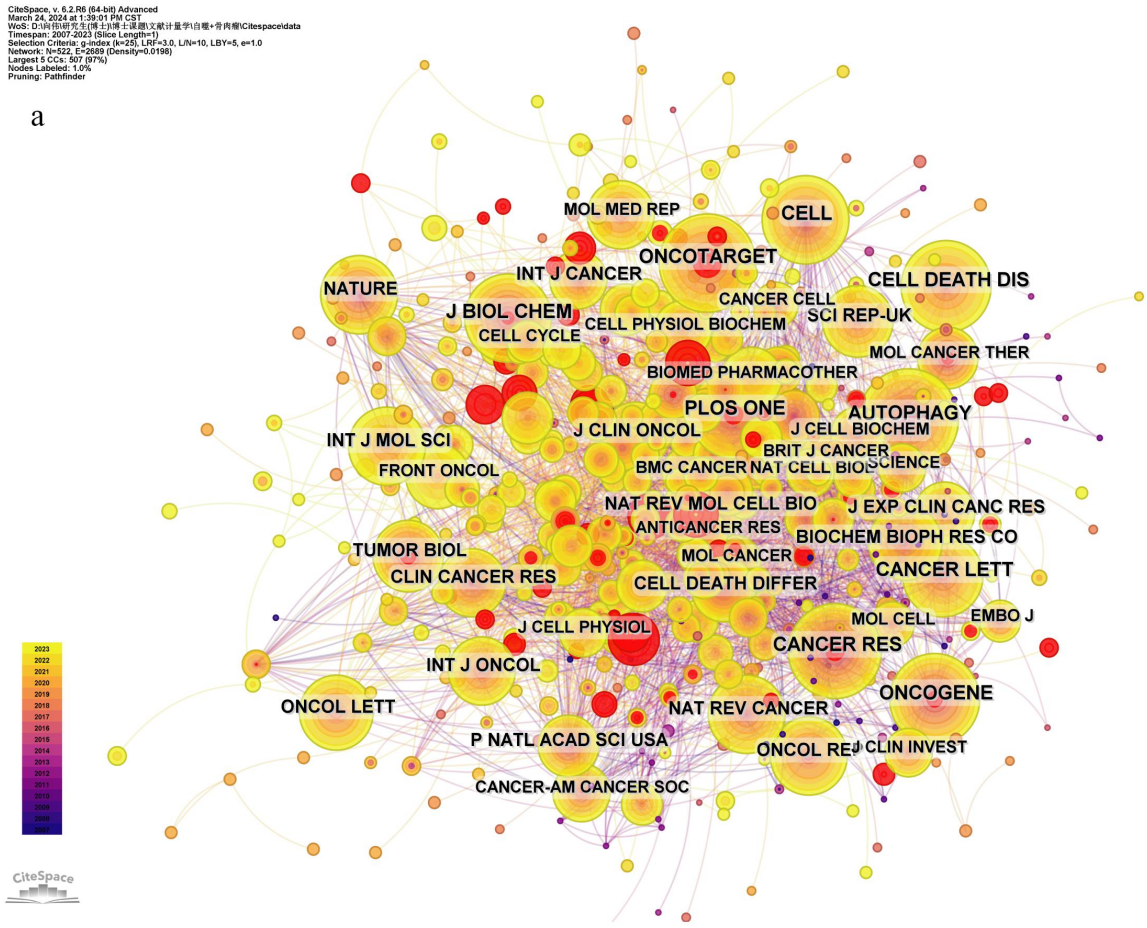
Visualization analysis of highly cited references

The top ten most cited references are shown in Table 5. Huang J et al.[18] found that HMGB1, through its role as an autophagy regulator, is a key factor in the development of chemotherapy resistance, providing a new target for improving osteosarcoma treatment. Li HY et al.[19] found that celastrol, through the ROS/JNK signaling pathway in human osteosarcoma cells, caused G2/M phase arrest and induced apoptosis and autophagy in human osteosarcoma cells. Liu K et al.[20] found that overexpression of BCL-2 reduced apatinib-induced apoptosis and autophagy. In summary, the top ten core references mainly focused on the mechanism of autophagy and therapeutic targets in osteosarcoma. The content reported in the top ten references is all related to the mechanisms of autophagy in osteosarcoma and related treatment methods, showing a high degree of relevance. We visualized the references (Figure 7a) and listed the top ten references with the highest burst intensity (Figure 7b), where the highest burst intensity was 10.99, representing the highest citation enthusiasm during the period. In each of these highly cited references, a very in-depth study of the mechanisms of autophagy as a major biological behavior for osteosarcoma cell survival was made.

Visualization and cluster analysis of highly cited keywords

Table 6 lists the top 20 keywords with the highest number of occurrences in all retrieved articles. "Autophagy" was the most frequently mentioned keyword (Figure 8a,b), with a frequency of 177. Keyword emergence detection is considered an indicator of research frontiers or emerging themes in a particular field. The keyword with the greatest bursting intensity is "cancer cells" (Strength = 6.27), which lasted from 2011 to 2014. This is followed by "death" (Strength = 6.27), which had a duration from 2011 to 2015. All other keywords had similar outbreak strengths.

We used CiteSpace to cluster the keywords and plot a Circular View (Figure 9), which was divided into 14 clusters. In the process of clustering, CiteSpace first constructs a co-citation network, in which the nodes represent the literature, the connections between the nodes represent the co-citation relationship, and the thickness of the connections reflects the intensity of the co-citation. Subsequently, a clustering algorithm (based on modularity optimization, Louvain's algorithm) is used to divide the network, whose goal is to maximize the modularity of the network, so that the connections within the clusters are tight, while the connections between the clusters are relatively sparse. Modularity is a measure of the strength of a network's clustering structure. The basic idea is to compare the difference between the actual connections present in the network and the case of random connections. Louvain's algorithm first treats each node as a separate cluster and then tries to optimize the modularity by locally



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Top 10 Cited Journals with the Strongest Citation Bursts

Cited Journals	Year	Strength	Begin	End	2007 - 2023
CANCER RES	2007	18.16	**2007**	2016	
CELL DEATH DIFFER	2007	11.6	**2007**	2016	
J BIOL CHEM	2007	9.13	**2007**	2016	
ONCOGENE	2008	11.4	**2008**	2016	
EMBO J	2008	9.51	**2008**	2014	
J CELL BIOL	2010	10.86	**2010**	2017	
MOL CELL BIOL	2011	8.41	**2011**	2016	
PLOS ONE	2012	8.42	**2015**	2017	
CANCERS	2019	10.9	**2021**	2023	
THERANOSTICS	2019	8.05	**2021**	2023	

Figure 5. Co-occurrence visualization (a) and citation bursts (b) analysis of cited journals. Nodes represent journals, node size indicates the number of journal publications, and lines indicate the strength of the partnership.

moving nodes. It operates at two levels: first, at the node level, where it calculates the change in modularity after each node is moved to a neighboring cluster, and second, at the cluster level, where the clusters of nodes found in the first step that can increase the modularity are merged to form new clusters. This process is iterated until the modularity is no longer increasing. Each cluster is given a unique identification number and is presented as a different colored or shaped region in the graph by means of visualization.The cluster with the highest occurrence was “reactive oxygen”.

Subsequently, Landscape and Time zone plots (Figure 10a,b) were created for the clusters to visualize the changes over time by combining the cluster categories with time. The time zone and clustering analysis of keywords can help us quickly locate the research hotspots and cutting-edge research directions in a certain time period and can also predict the research evolution trends.

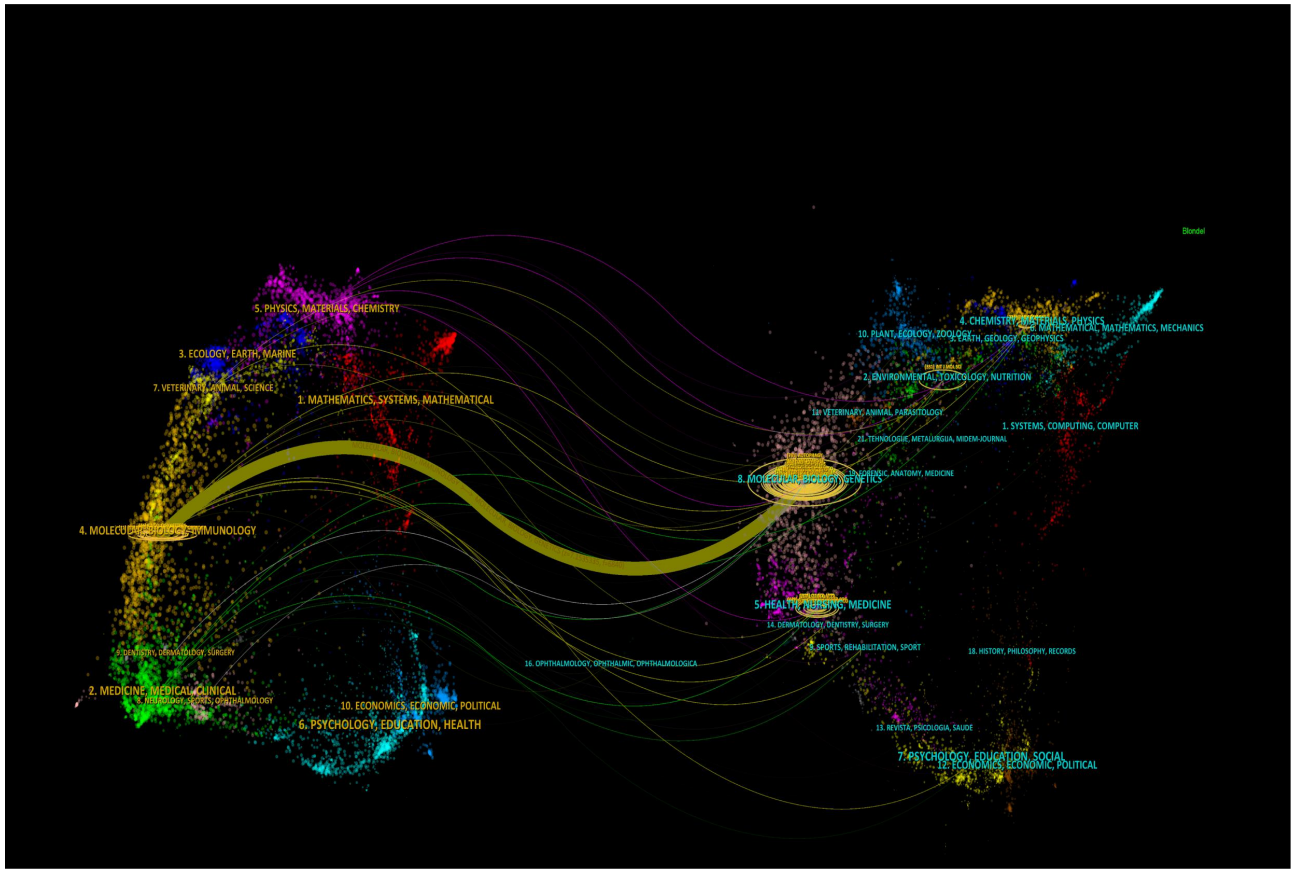
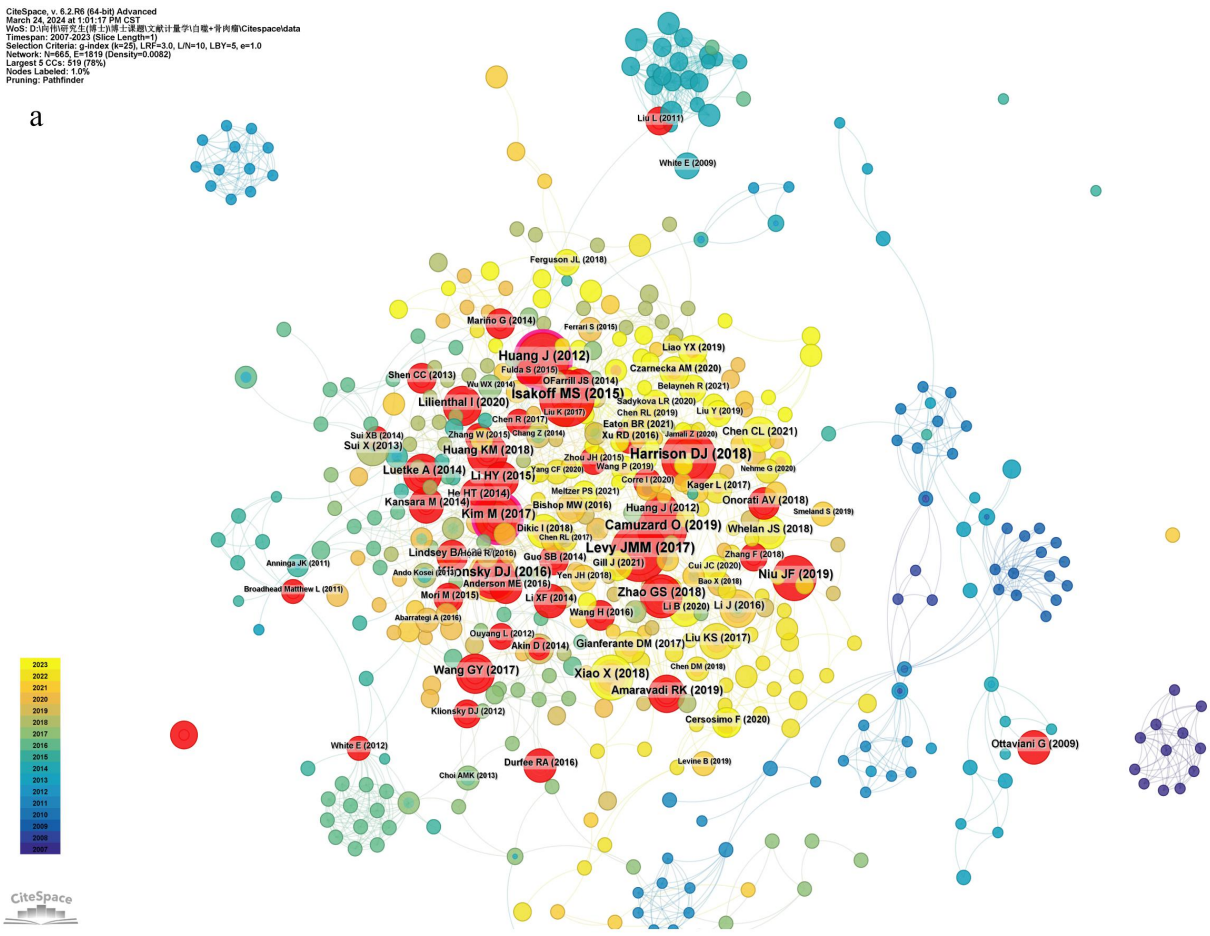


Figure 6. The dual-map overlay of journals on the autophagy studies in osteosarcoma. Dual-map distinguishes the disciplines of citation links by color, allowing a clear view of where the citations come from and where they go. Lower-colored bars indicate years with relatively stable publication venues, while higher-colored bars indicate a more diverse distribution of publications.

Table 5. The top ten cited references.

Publications	Author	Citations	Journal	2022JCR	IF
Curcumin-loaded γ-cyclodextrin liposomal nanoparticles as delivery vehicles for osteosarcoma(DOI10 .1016/j.nano.2011.07.011)	Santosh S Dhule	245	NANOMEDICINE-NANOTECHNOLOGY BIOLOGY AND MEDICINE	Q2	5.4
HMGB1 Promotes Drug Resistance in Osteosarcoma(DOI10 .1158/0008-5472.CAN-11-2001)	Jun Huang	224	CANCER RESEARCH	Q1	11.2
Celastrol induces apoptosis and autophagy via the ROS/JNK signaling pathway in human osteosarcoma cells: an in vitro and in vivo study(DOI10 .1038/cddis.2014.543)	H-Y Li	213	CELL DEATH & DISEASE	Q1	9.0
Apatinib promotes autophagy and apoptosis through VEGFR2/STAT3/BCL-2 signaling in osteosarcoma(DOI10 .1038/cddis.2017.422)	Kuisheng Liu	187	CELL DEATH & DISEASE	Q1	9.0
Molecular mechanisms of chemoresistance in osteosarcoma(DOI10 .3892/ol.2014.1935)	Hongtao He	189	ONCOLOGY LETTERS	Q3	2.9
A novel ATG4B antagonist inhibits autophagy and has a negative impact on osteosarcoma tumors(DOI10 .4161/auto.32229)	Debra Akin	163	AUTOPHAGY	Q1	13.3
Erianin induces G2/M-phase arrest, apoptosis, and autophagy via the ROS/JNK signaling pathway in human osteosarcoma cells in vitro and in vivo(DOI10 .1038/cddis.2016.138)	H Wang	144	CELL DEATH & DISEASE	Q1	9.0
HSP90AA1-mediated autophagy promotes drug resistance in osteosarcoma (DOI10 .1186/s13046-018-0880-6)	Xin Xiao	135	JOURNAL OF EXPERIMENTAL & CLINICAL CANCER RESEARCH	Q1	11.3
Initial testing (stage 1) of the mTOR inhibitor rapamycin by the pediatric preclinical testing program(DOI10 .1002/pbc.21296)	Peter J Houghton	132	PEDIATRIC BLOOD & CANCER	Q2	3.2
Autophagy and doxorubicin resistance in cancer(DOI10 .1097/CAD.0000000000000572)	Chao Chen	123	ANTI-CANCER DRUGS	Q3	2.3



b

Top 10 References with the Strongest Citation Bursts

References	Year	Strength	Begin	End	2007 - 2023
Ottaviani G, 2009, CANCER TREAT RES, V152, P3, DOI 10.1007/978-1-4419-0284-9, 1, DOI	2009	6	2013	2014	
Huang J, 2012, CANCER RES, V72, P230, DOI 10.1158/0008-5472.CAN-11-2001, DOI	2012	10.99	2014	2017	
Isakoff MS, 2015, J CLIN ONCOL, V33, P3029, DOI 10.1200/JCO.2014.59.4895, DOI	2015	7.67	2016	2020	
Luetke A, 2014, CANCER TREAT REV, V40, P523, DOI 10.1016/j.ctrv.2013.11.006, DOI	2014	5.17	2016	2019	
Li HY, 2015, CELL DEATH DIS, V6, P0, DOI 10.1038/cddis.2014.543, DOI	2015	4.8	2016	2019	
Klionsky DJ, 2016, AUTOPHAGY, V12, P1, DOI 10.1080/15548627.2015.1100356, DOI	2016	5.82	2017	2020	
Levy JMM, 2017, NAT REV CANCER, V17, P528, DOI 10.1038/nrc.2017.53, DOI	2017	5.81	2019	2023	
Camuzard O, 2019, J BONE ONCOL, V16, P0, DOI 10.1016/j.jbo.2019.100235, DOI	2019	5.4	2020	2023	
Niu JF, 2019, FRONT ONCOL, V9, P0, DOI 10.3389/fonc.2019.01232, DOI	2019	7.12	2021	2023	
Lilienthal I, 2020, INT J MOL SCI, V21, P0, DOI 10.3390/ijms21186885, DOI	2020	5.12	2021	2023	

Figure 7. Visualisation of cited references (a) and top ten references with strong citation bursts (b).

Discussion

As of the end of 2023, no bibliometric studies have been published in this field. Thus, we conducted a bibliometric analysis and visualized a network map of publications related to autophagy in osteosarcoma research from 2007 to 2023. The number of publications across countries and journals increased annually, reaching a peak in 2020. Subsequent visualization of authors and cited authors, cited journals, cited references, and keywords, identified cited journals, cited references, and keywords with a high intensity of outbreaks, thereby providing a foundation for future research directions within this field.

Autophagy plays a significant role in many fields, and numerous bibliometric analyses have been reported, such as in diabetic cardiomyopathy,[21] cardiovascular disease,[22] and atherosclerosis.[23] However, there are no relevant reports in the field of osteosarcoma. The research hotspot of osteosarcoma is mainly centered around the study of its mechanism and treatment. There are several bibliometric analyses of the

Table 6. The top 20 keywords.

Rank	Key words	Record Count	Rank	Key words	Record Count
1	autophagy	177	11	in vitro	66
2	apoptosis	168	12	proliferation	60
3	cancer	145	13	osteosarcoma cells	49
4	expression	114	14	osteosarcoma	48
5	cancer cells	88	15	chemotherapy	47
6	activation	83	16	metastasis	44
7	death	81	17	survival	41
8	growth	80	18	breast cancer	39
9	inhibition	72	19	invasion	39
10	pathway	70	20	cells	37

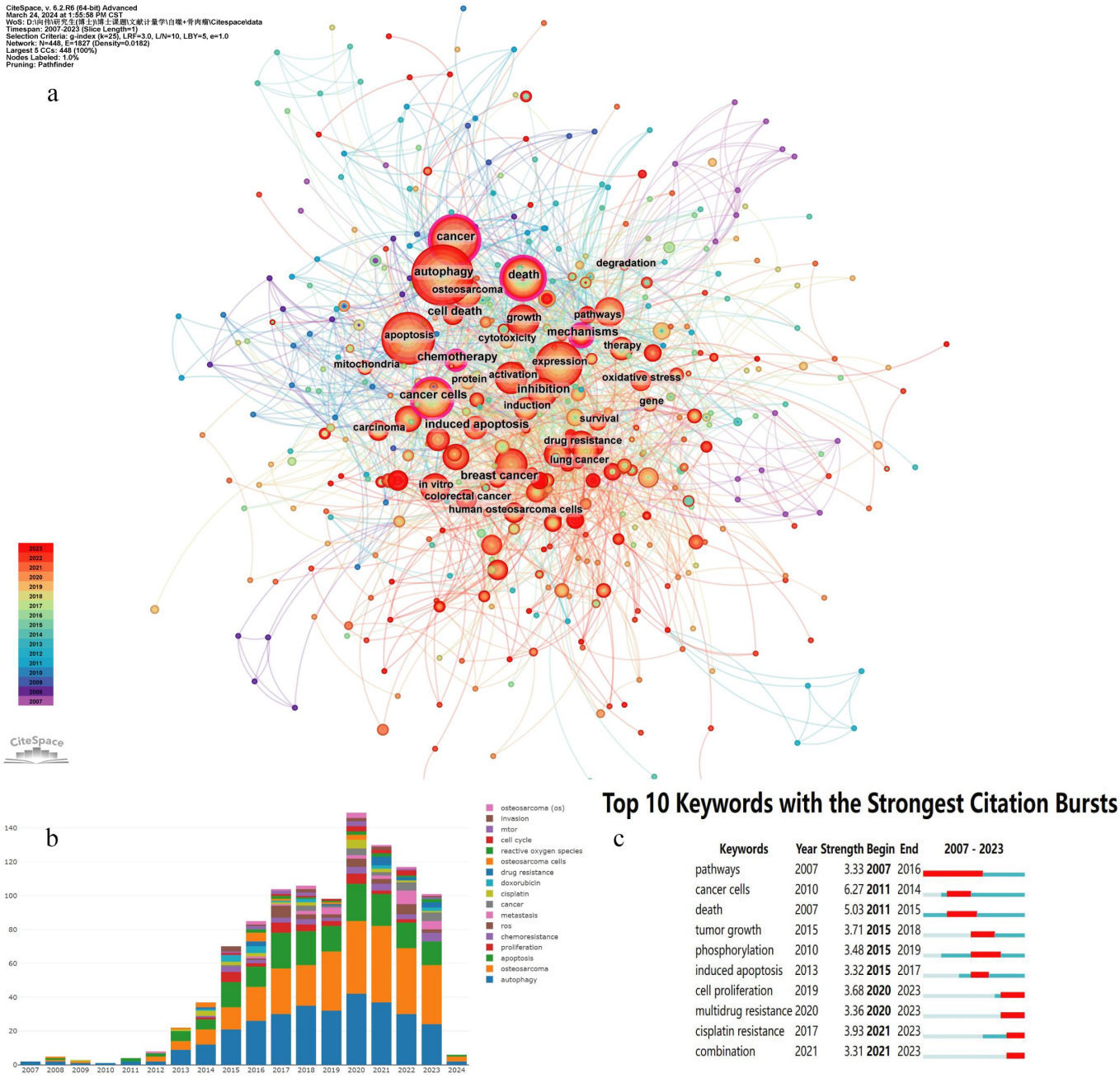


Figure 8. Keyword visualization for the study of osteosarcoma (a, b) and top ten keywords with strong citation bursts (c).

research trend of its treatment.[12,13,24] China and the United States have made the greatest contributions to this field. The research institution with the highest number of publications is from a university in China: Shanghai Jiao Tong University (n = 42, 6.785%). Ninety percent of the top ten institutions are from Chinese universities, which may be related to China's

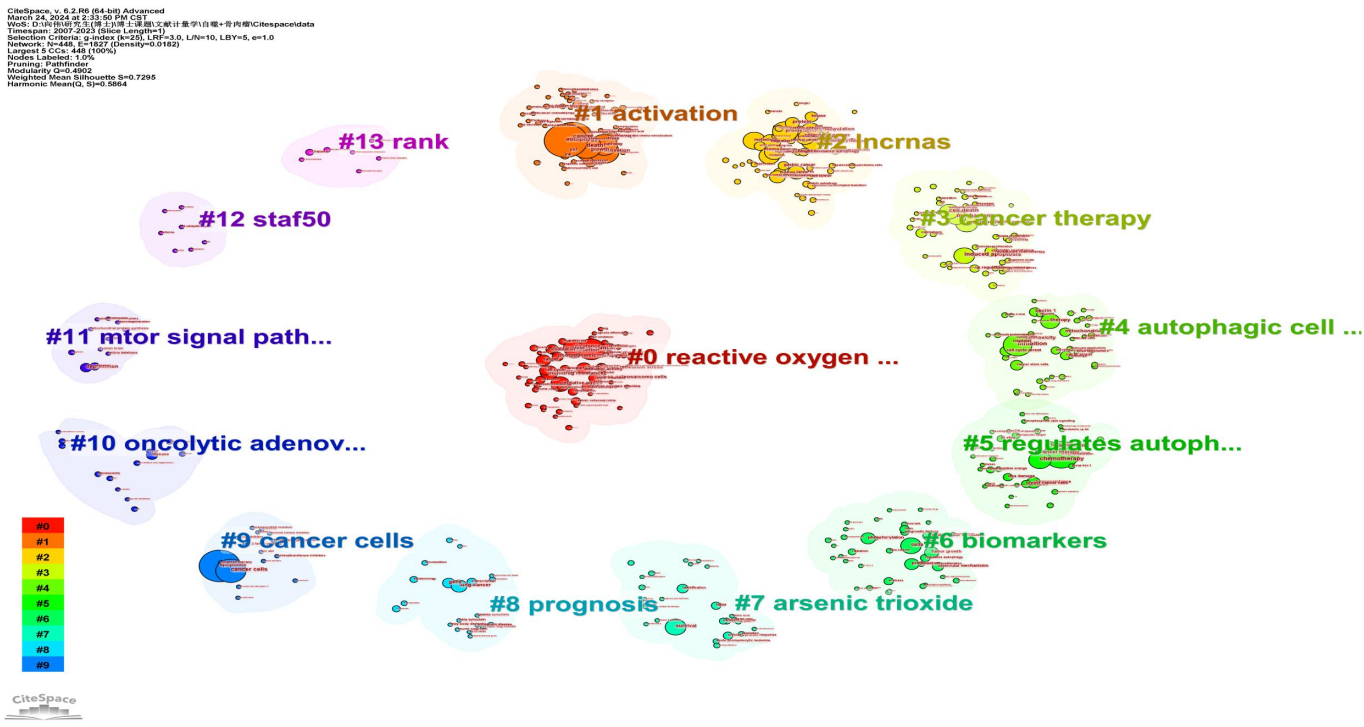


Figure 9. Cluster analysis plot of keywords for the study of osteosarcoma. Similar keywords are clustered together and labels are generated for each cluster, which are usually based on the commonality of the keywords in the cluster.

large population base and high prevalence of osteosarcoma. While the cooperative relationship between countries and institutions needs to be continuously strengthened to promote exchanges. Currently, only the United States and China have close cooperation and exchanges, and cooperation between institutions is limited to cooperation between domestic universities.

Cai, Zhengdong, as a leader in the field, has made significant contributions to the study of osteosarcoma by finding that abrogation of NDRG1 expression sensitized OS cells to CA-4 through inhibition of autophagosome-lysosome fusion. These results provide clues for the development of a more effective cancer treatment strategy through the combination of CA-4 and clinically available autophagy inhibitors.[25] Mizushimma N, who has the highest number of citations in the literature among many authors, has laid the theoretical foundation for the study of autophagy in various diseases,[26] providing researchers with ideas and entry points for their studies. As the study of autophagy on osteosarcoma is becoming more mature, therapeutic modalities related to targeting autophagy have also been gradually reported. Meng, CY et al.[27] reported that exosomes secreted by chemotherapy-resistant osteosarcoma cells promote drug resistance through miR-331-3p and autophagy. Pan, Z et al.[28] screened a candidate compound for osteosarcoma treatment, ebastine (an H1-histamine receptor antagonist), which was found to have antitumor activity in osteosarcoma and promote autophagy through activation of the IPMK-dependent AMPK/ULK1 signaling pathway. Most of the many highly cited references deal with the mechanisms by which autophagy plays a role in osteosarcoma, and very many signaling pathways are involved, such as the ROS/JNK signaling pathway,[19] the VEGFR2/STAT3/BCL-2 signaling pathway,[20] the PI3K/Akt/mTOR signaling pathway[29,30] and the AMPK/ULK1 signaling pathway.[28] The application of autophagy to the treatment of osteosarcoma is also one of the research hotspots. Debra Akin et al.[31] found that ATG4B is a suitable anti-autophagy target and promising therapeutic target for the treatment of osteosarcoma. Xin Xiao et al.[29] found that the inhibition of HSP90AA1 reduces the protection of autophagy in response to chemotherapy in osteosarcoma cells.

Co-occurrence and emergence analysis of keywords can identify current research hotspots and predict future research directions. Meanwhile, clustering analysis of keywords can help us quickly locate the research hotspots and categories at a certain stage. Undoubtedly, “autophagy” is the most popular keyword. Moreover, “pathway” and “cancer cells” have a higher burst intensity. “Death” has also been emphasized by researchers. These popular keywords are closely related to the pathological mechanism of osteosarcoma. Recent studies have found that diallyl trisulfide (DATS) inhibits osteosarcoma cell growth, migration, and epithelial-mesenchymal transition (EMT), but induces apoptosis and autophagy, which are mediated by the inactivation of the EGFR/PI3K/AKT/mTOR signaling pathway.[32] The future research direction will surely be similar to the direction of osteosarcoma treatment, which utilizes autophagy-related mechanisms to exert its autophagic effects to inhibit cancer cell growth or remove cancer cells.

The limitation of this study is that we only chose the Web of Science Core Collection and did not include other databases. This may lead to missing many important

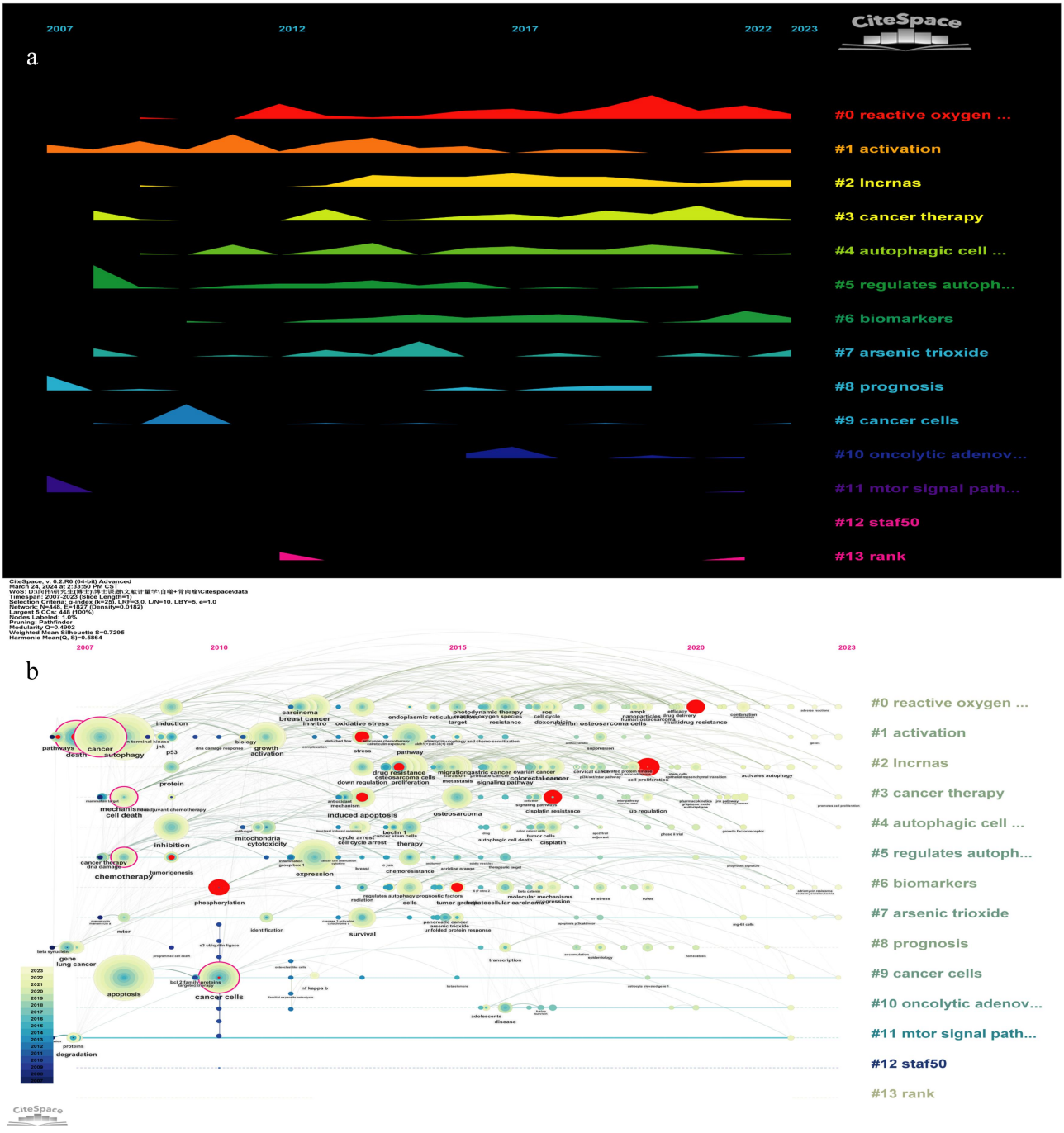


Figure 10. Map of keyword landscape (a) and time zones (b). In landscape graphs, nodes represent keywords, the size of the nodes is usually proportional to the frequency of keyword occurrence, and the color indicates the classification. In a time zones graph, the keywords for each time period are fixed to the year in which they first appear, and the same keywords appearing in subsequent years add up to the frequency of the first appearance, thus forming a kind of hotspot distribution graph over the time series.

research results. However, this database is the most commonly used database in bibliometric analysis. It not only provides comprehensive information but also is the most authoritative database. CiteSpace and the Bibliometric online analysis platform were used to analyze the data in this study. Currently, bibliometric analysis software is not functionally complete enough and needs to be analyzed in combination with different software, which may cause bias in the results.

Conclusions

This study analyzes and evaluates the progress of autophagy in osteosarcoma from 2007 to 2023 by bibliometric methods, and predicts the key directions of diagnosis and treatment of osteosarcoma, which will continue to be a hot topic of research in this field. Countries, institutions, and journals need to strengthen their cooperation to explore new directions for osteosarcoma research.

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Authors' contributions

Min Zhu wrote the manuscript. Min Zhu,Wei Xiang and Zhoujun Zhu contributed equally to this work and share first authorship. Min Zhu,Wei Xiang and Zhoujun Zhu analyzed the data and drew pictures. Bingjie Nie, Xinyue Zhen and Chen Chen helped analyzed the data and drew pictures. Tianhai Wang reviewed and revised the manuscript. All authors have agreed to publish this final version.

Data availability statement

The data that support the findings of this study are available from the corresponding author.

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