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Research trends in CAR-T cell therapy

A comprehensive bibliometric analysis highlighting cardiovascular toxicity and clinical implications

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Abstract

Background: Chimeric antigen receptor T cell (CAR-T) therapy is an innovation in oncology, which provides targeted treatment alternatives for certain tumors. CAR-T therapy has been associated to adverse cardiovascular consequences despite its potential for therapeutic benefit. As research in this field expands rapidly, a bibliometric study is needed to map the current state of knowledge and highlight emerging areas of interest to guide future studies and optimize patient outcomes.

Methods: A comprehensive bibliometric analysis was conducted using the Web of Science Core Collection and PubMed to examine the literature on CAR-T cell therapy and its cardiovascular implications.

Results: The annual number of publications on CAR-T therapy and cardiovascular symptoms has steadily increased, experiencing a significant surge starting in 2018. The USA, China, and Germany emerged as the leading contributors. Key journals included Frontiers in Immunology and Blood, while highly cited journals were Lancet Oncology and the Journal of Clinical Oncology. Keyword analysis identified multiple myeloma, immunotherapy, and cytokine release syndrome as major research themes. The clustered map highlighted interconnected research areas, with a significant focus on multiple myeloma, combination therapy, cardiovascular magnetic resonance assessment, and novel therapeutic approaches.

Conclusion: This bibliometric analysis provided a detailed overview of the research landscape on CAR-T cell therapy and its cardiovascular implications, identifying trends and gaps in knowledge. Recent research trends highlighted bispecific antibodies, CAR-T cell therapy, cardiovascular events, lymphoma, management, and outcomes as emerging focus areas. These keywords underscore the developing field of cardiac events, management, and outcomes in patients undergoing CAR-T cell therapy.

Abbreviations: BCMA = B-cell maturation antigen, CAR-T = chimeric antigen receptor T cell, CRS = cytokine release syndrome, FDA = Food and Drug Administration, ICANS = immune effector cell-associated neurotoxicity syndrome, ICI = immune checkpoint inhibitor, MRI = magnetic resonance imaging.

Keywords: bibliometric analysis, cardiotoxicity, cardiovascular implications, CAR-T cell therapy, immunotherapy, multiple myeloma, research trend

1. Introduction

Chimeric antigen receptor T cell (CAR-T) treatment is one of the most recent developments in oncology, providing patients with some cancer types, especially hematologic malignancies, with promising therapeutic choices.[1,2] This treatment offers a targeted approach to eradicate cancerous cells by genetically altering a patient's T cells to express a receptor exclusive to cancer cells.[3] Since its approval by the FDA, CAR-T therapy has garnered significant attention, resulting in a substantial body of research dedicated to understanding its mechanisms, efficacy, and safety.[4]

Despite its therapeutic potential, CAR-T therapy is not without risks. The treatment has been associated with various adverse

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effects, among which cardiovascular symptoms are of particular concern.[5] These symptoms can range from mild arrhythmias to severe cardiotoxicity, which can significantly impact patient outcomes and quality of life.[6,7] Understanding the prevalence, underlying mechanisms, and management strategies for these cardiovascular effects is crucial for optimizing CAR-T therapy and ensuring patient safety.[8]

Given the fast growth of research in this area, a bibliometric analysis can offer useful insights into the current state of knowledge, research trends, and new areas of interest. Bibliometric studies look at the numbers in academic literature, such as the number of publications, citations, and collaboration networks, to pinpoint important studies, leading authors, and main research topics.[9–13] By utilizing bibliometric tools, we can map out the current state of research on CAR-T cell treatment and its cardiovascular consequences, identify knowledge gaps, and identify areas that need additional research. Our analysis also examines the distribution of studies addressing these cardiac implications, thereby highlighting the need for enhanced cardiovascular monitoring and risk stratification in patients undergoing CAR-T treatment.

This study aims to perform a comprehensive bibliometric analysis of the literature on CAR-T cell therapy and cardiovascular complications. We will examine trends in publication volume, citation patterns, and collaborative efforts within this domain. Additionally, we will identify the most influential articles, authors, and institutions contributing to this field.

2. Methods

2.1. Data collection and search strategies

On June 15, 2024, the Web of Science Core Collection and PubMed were used as the primary databases for researching published articles. The Web of Science Core Collection database is notable for its extensive coverage, encompassing over 12,000 reputable journals.[14–16] A search strategy with multiple terms was created, as detailed in Table S1, Supplemental Digital Content, https://links.lww.com/MD/O815, to enhance the search's efficiency. Initially, 881 items were retrieved. The selection was then refined to 808 pertinent papers by excluding conference papers, letters, editorials, book chapters, pre-publication papers, duplicates, and studies not aligned with the objectives. Figure 1 illustrates the study selection and methodology.

2.2. Data analysis

All relevant documents were converted into Microsoft Excel 2019 and plain text formats for analysis with VOSviewer, and CiteSpace. VOS viewer is a powerful instrument for scientometric network analysis. It aids in clarifying the connections in the academic literature by visualization and creation of maps based on network data. With the use of co-citation, co-occurrence, citation, and bibliographic coupling relationships, the software creates network diagrams illustrating a variety of academic entities, including publications, journals, authors, research institutions, nations, and keywords.

VOSviewer provides 3 types of visualization maps: network, overlay, and density visualizations, each serving a specific analytical purpose.[17,18] Its foundational concept is co-occurrence clustering, which shows the relatedness of items within the network. This approach identifies correlations of different strengths and directions, enabling the recognition of distinct groups within the data. Although primarily used for bibliometric analyses, VOSviewer can also create various web data maps. Its standout feature is its ability to produce high-quality visual graphics, making it particularly useful for large-scale academic and scientific visual analyses.[19,20]

CiteSpace is a Java-based tool for citation visualization analysis. With the use of advanced data mining, thorough information analysis, and comprehensive knowledge maps, this tool displays the dynamics, distribution patterns, and structure of scientific knowledge. CiteSpace assists in understanding the evolving context of scientific research by providing a visual representation of citation networks, emphasizing important spots and emerging areas.[21,22]

3. Results

3.1. The annual growth trend of publications

Figure 2 illustrates the annual publication and temporal revolution of research, distinguishing between 2 series: the number of publications each year (Series 1) and the cumulative number of publications (Series 2), commencing in 1991.

From 1991 to 2018, the number of publications remained relatively low and stable. However, there was a noticeable increase from 2018 onwards. By 2021, the annual number of publications exceeded 100, indicating a significant rise in research activity.

The cumulative count remained relatively low until 2020 when it began to increase more substantially. This trend

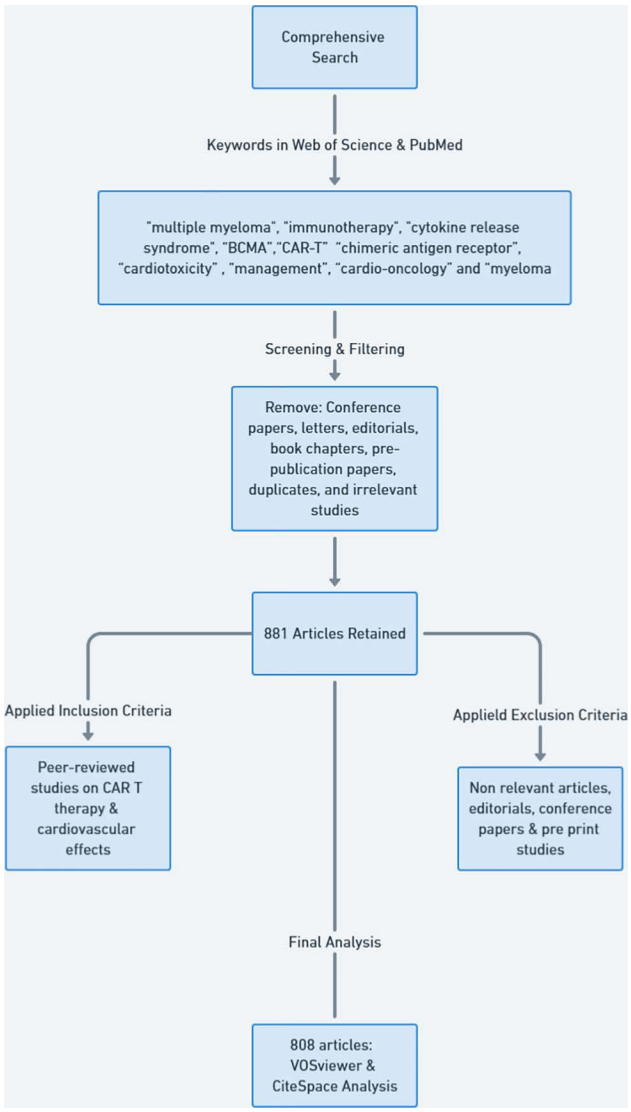

Figure 1. Study selection and methodology flow diagram.

accelerated significantly from 2020 onwards, reflecting the cumulative effect of the growing annual publications.

3.2. Countries and institutions

Several papers involving multiple countries have been coauthored in recent years. The USA (n = 372) has emerged as the top contributor regarding the number of publications, followed by China (n = 124) and Germany (n = 62) (Table 1). As shown in Figure 3, the USA also had the highest centrality (0.62), followed by China (0.47) and Germany (0.30). An elevated degree of centrality signifies the importance of these nations' studies and their crucial function in this domain. Regarding the institutions, Xuzhou Medical University led with the highest number of publications (n = 245) followed by the University of Pennsylvania (n = 217). Memorial Sloan Kettering Cancer Center ranked third (n = 214) (Table 2).

3.3. Journals and co-cited journals

The publications were dispersed throughout a total of 266 scholarly journals. The top 10 leading journals in the field were as follows: Frontiers in Immunology (n = 35), Blood (n = 24), Haematologica (n = 22), British Journal of Haematology (n = 22), Blood Advances (n = 20), Journal of Hematology & Oncology (n = 20), Blood Cancer Journal (n = 18), Clinical Lymphoma, Myeloma & Leukemia (n = 16), International Journal of Molecular Sciences (n = 15), and The New England Journal of Medicine (n = 14) (Fig. 4 and Table 3).

The journal with the highest number of citations was Lancet Oncology (n = 1397), followed by Journal of Clinical Oncology (n = 612) and Journal of the National Cancer Institute (n = 498). Other highly cited journals included Cancer Immunology Research (n = 441), Biology of Blood and Marrow Transplantation (n = 126), JACC: Cardio Oncology (n = 120), International Journal of Molecular Sciences (n = 90), Journal of the American College of Cardiology (n = 81), European Journal of Cancer (n = 80), and Biomed Research International (n = 66) (Table 3).

A total of 1313 co-cited journals were identified. The journal with the highest number of co-citations was New England Journal of Medicine (n = 350), followed by Blood (n = 223) and Journal of the American College of Cardiology (n = 175). Other highly co-cited journals included Journal of Clinical Oncology (n = 170), Circulation (n = 131), Blood and Marrow Transplantation (n = 106), JACC: Cardio Oncology (n = 97), Lancet (n = 84), Journal for Immunotherapy of Cancer (n = 76), Lancet Oncology (n = 68) (Fig. 5 and Table 3).

The analysis identified the top 10 journals that were the most central and influential in the field. The journal with the highest centrality score of 0.27 was the Annals of Internal Medicine. The second most central journal was Alimentary Pharmacology & Therapeutics with a score of 0.26. Other prominent journals included Cancer: A Journal for Clinicians and British Journal of Cancer, both with a centrality score of 0.15 (Fig. 6 and Table 3).

Citation dynamics are demonstrated via the dual-map overlay, which shows journal relationships. Citing journals are on the left, and cited journals are on the right. Three primary citation paths (2 in green and 1 in yellow) are shown in Figure 7, which highlights this illustration. The overlay demonstrated the high citation rate of research articles from Health/Nursing/Medicine journals by publications in the Medicine/Medical/Clinical field. Moreover, both Molecular/Biology/Immunology and Medicine/Medical/Clinical publications regularly mentioned research published in Molecular/Biology/Genetics articles.

3.4. Authors and co-cited authors

A total of 4560 authors contributed to the publication of these articles. As shown in Table 4, each of the top 10 authors has published at least 13 documents. Saad Z. Usmani and Sham Mailankody were the most active authors, each with 17 publications, followed by Sundar Jagannath with 16 publications. Other leading authors include Adam D. Cohen and Hermann Einsele (each with 15 publications), Jiang Cao, Niels W. C. J. van de Donk, and Nina Shah (each with 14 publications), and Zhenyu Li and Kailin Xu (each with 13 publications) (Fig. 8).

Authors who are cited in 1 or more follow-up papers are known as co-cited authors. The top 10 co-cited writers were all co-cited more than 30 times (Table 4). The most frequently co-cited author was D.W. Lee (78 co-citations), followed by Sattva.S. Neelapu (66 co-citations) and S.L. Maude (63 co-citations). Other co-cited authors included S. Ganatra (62 co-citations), S.J. Schuster (49 co-citations), R.M. Alvi (44 co-citations), S.A. Rosenberg (37 co-citations), B. Lefebvre

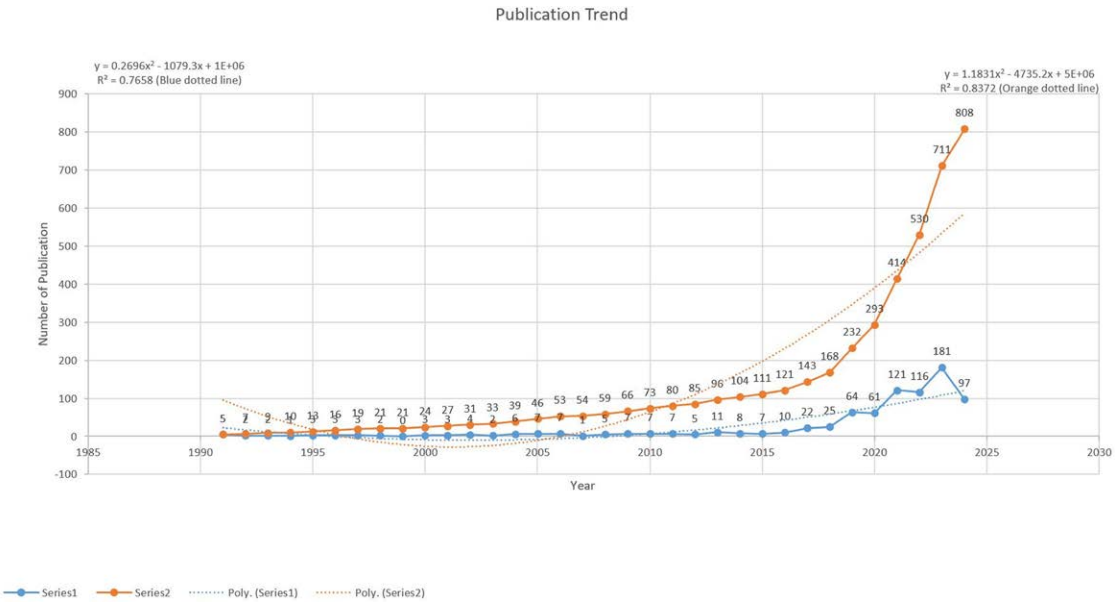

Figure 2. Trends in publication output frequency about the CAR-T cell research and cardiac implications. CAR-T = chimeric antigen receptor T cell.

(35 co-citations), F.L. Locke (35 co-citations), and J.N. Brudno (33 co-citations) (Fig. 9).

3.5. Keyword analysis and hotspots

The keywords of an article can indicate its main focus and direction. Therefore, examining these keywords can provide an understanding of the key research areas and their respective trajectories within the field. A total of 1171 keywords were identified. The top keywords are presented in Figure 10. The keyword "multiple myeloma" was found to be the most frequently used (n = 189), followed by "immunotherapy" (n = 99) and "cytokine release syndrome (CRS)" (n = 50). Other keywords included "BCMA" (n = 46), "CAR-T" (n = 45), "chimeric antigen receptor" (n = 44), "cardiotoxicity" (n = 34), "management" (n = 27), "cardio-oncology" (n = 25), and "myeloma" (n = 24).

The clustered map reveals several key research areas and trends within the field. The clusters are identified by specific keywords or phrases, each representing a focal point in the research. In this study, the largest cluster, labeled "#0 multiple myeloma," was characterized by a dense network of connections, indicating a high volume of related research. Another significant cluster was "#1 combination therapy," which showed substantial activity in studies exploring therapeutic combinations. Cluster "#2 CAR T-cell therapy" highlighted an important area of research focused on this specific cancer treatment approach. Cluster "#3 cardiovascular magnetic resonance assessment" reflected studies centered around the use of cardiovascular magnetic resonance imaging (MRI). Cluster "#4 cardiac function" encompassed research on cardiac health and its assessment. The cluster "#5 sustained complete responses" pointed to research on achieving and maintaining complete responses in treatment. Clusters "#6 novel" and "#7 novel molecular target" represented areas focused on new and emerging therapies and targets (Fig. 11).

Table 1

Top 10 countries in the field of CAR-T cell therapy and cardiovascular implications.

Number	Country	Number of publications	Centrality
1	USA	372	0.62
2	China	124	0.47
3	Germany	62	0.30
4	France	39	0.08
5	Italy	35	0.10
6	Spain	34	0.11
7	Belgium	23	0.07
8	Netherland	22	0.01
9	Japan	21	0.06
10	Canada	20	0.06

CAR-T = chimeric antigen receptor T cell.

4. Discussion

In recent years, remarkable advancements have been made in immune-based cancer therapies, offering the promising future of long-term remission and even potential cures for cancer patients.[23,24] One such innovative approach, CAR-T based cell adoptive immunotherapy, is rapidly gaining traction as a personalized and targeted immunotherapeutic option in the ongoing battle against various types of tumors.[25,26] However, the COVID-19 pandemic has significantly impacted cancer care. Besides the bidirectional relation between chronic inflammation and malignancies,[27,28] delays in diagnosis and treatment can also have a detrimental effect on patient outcomes and may defer CAT-T cell therapy in patients likely to benefit from curative treatments.[29] Even while CAR-T cell therapy has made advances, it can still have serious side effects, including immune effector cell-associated neurotoxicity syndrome (ICANS) and CRS, which can be fatal.[30,31]

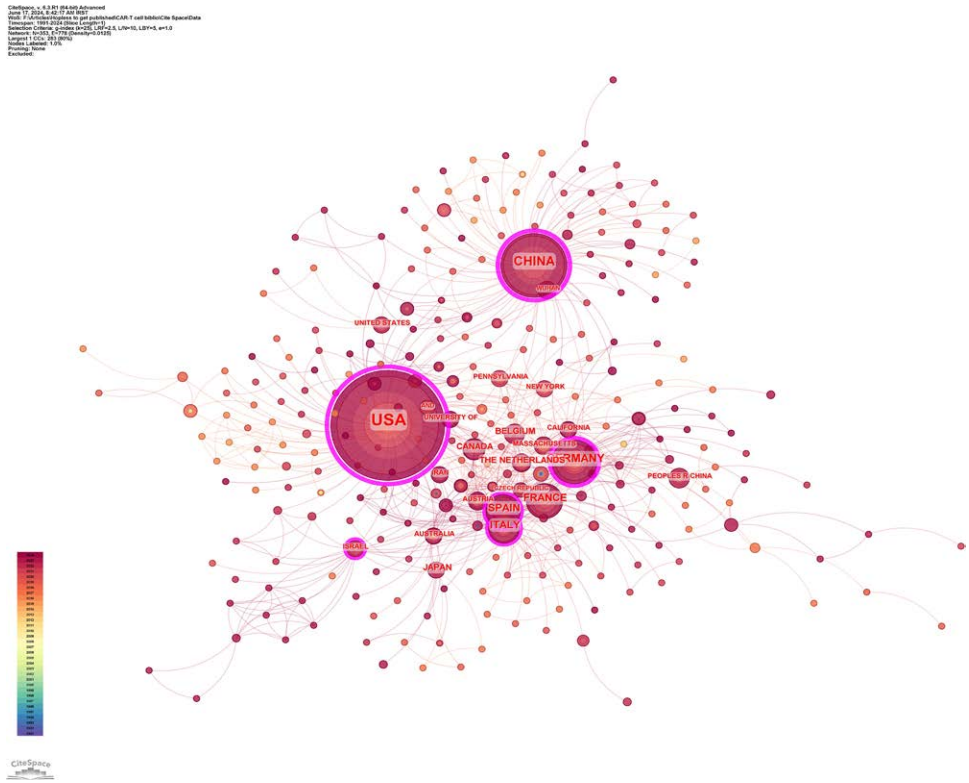

Figure 3. The co-occurrence map of countries and their centrality (purple ring).

One of the most notable adverse events is cardiovascular toxicity. Prior research has demonstrated that cardiovascular toxicities associated with immunotherapy represent a substantial risk of morbidity and mortality. As a result, the advancement and broad implementation of CAR-T cell therapy in clinical settings are ultimately limited.[32,33] The specific scope and nature of the cardiovascular toxicities linked to CAR-T cell therapy, however, are still poorly understood despite multiple investigations into this topic.[34–36]

Our study's results indicate a growing focus on assessing the cardiovascular implications of CAR-T therapy in recent years, as evidenced by an increasing number of publications. The surge in articles, especially after 2018, underscores the expanding interest and rapid progress in this field. This heightened research activity is likely driven by the positive therapeutic outcomes of CAR-T cell therapy in treating blood cancers, coupled with the need to address the associated cardiovascular issues. From 1990 to 2009, the annual number of publications was low, reflecting the early stage of CAR-T cell technology. Between 2009 and 2015, there was a gradual increase in publications, indicating rising interest in this topic. Since 2015, there has been a steady annual increase in the number of articles, signifying a substantial rise in attention to this area.

Table 2

Top 10 institutions in the field of CAR-T cell therapy and cardiovascular implications.

Number	Affiliation	Number of publications
1	Xuzhou Medical University	245
2	University of Pennsylvania	217
3	Memorial Sloan Kettering Cancer Center	214
4	Huazhong University of Science and Technology	196
5	Mayo Clinic	191
6	Xuzhou Medical University	182
7	Janssen Research and Development	160
8	Harvard Medical School	145
9	Jiangsu Key Laboratory of Bone Marrow Stem Cells	129
10	Zhejiang University	92

CAR-T = chimeric antigen receptor T cell.

The surge in the number of publications related to CAR-T therapy after 2018 can be attributed to the growing recognition and acceptance of this innovative treatment approach during that time period. For example, In 2017, the FDA approved 2 CAR-T therapy treatments for the management of advanced or treatment-resistant forms of lymphoma and acute lymphoblastic leukemia.[37] In 2018, CAR-T therapy for adult relapsed/refractory diffuse large B-cell lymphoma was confirmed.[38]

According to bibliometric trends, the need for standardized cardiac diagnostic techniques is growing along with the use of CAR-T cell treatments. Advanced imaging techniques, along with biomarkers and novel risk scores, are emerging as promising tools for early detection and management of adverse events.[39–41] Recent studies have used various statistical models for determining the prognosis of cardiovascular issues.[42–44] Furthermore, the improvements in artificial intelligence and machine learning models have deeply enhanced precision medicine in the cardiovascular field improving diagnostic, prognostic, and therapeutic strategies. These inventions emerge as valuable strategies to refine these risk assessments and develop predictive models tailored to this patient population.[13,45,46] In order to improve early detection and intervention techniques, future research should seek to evaluate and incorporate these novel approaches into clinical practice.

The United States had the highest number of publications, followed by China and Germany. As the leading contributor to research in CAR-T cell therapy, the United States plays a crucial role in shaping the current understanding and future advancements in this field. The high centrality of the USA in global research networks underscores its pivotal role in fostering international collaborations and disseminating innovative discoveries.

Renowned organizations like the Memorial Sloan Kettering Cancer Center, the University of Pennsylvania, and the National Institutes of Health have been at the forefront of CAR-T cell research.[47] Furthermore, 5 CAR-T cell treatments

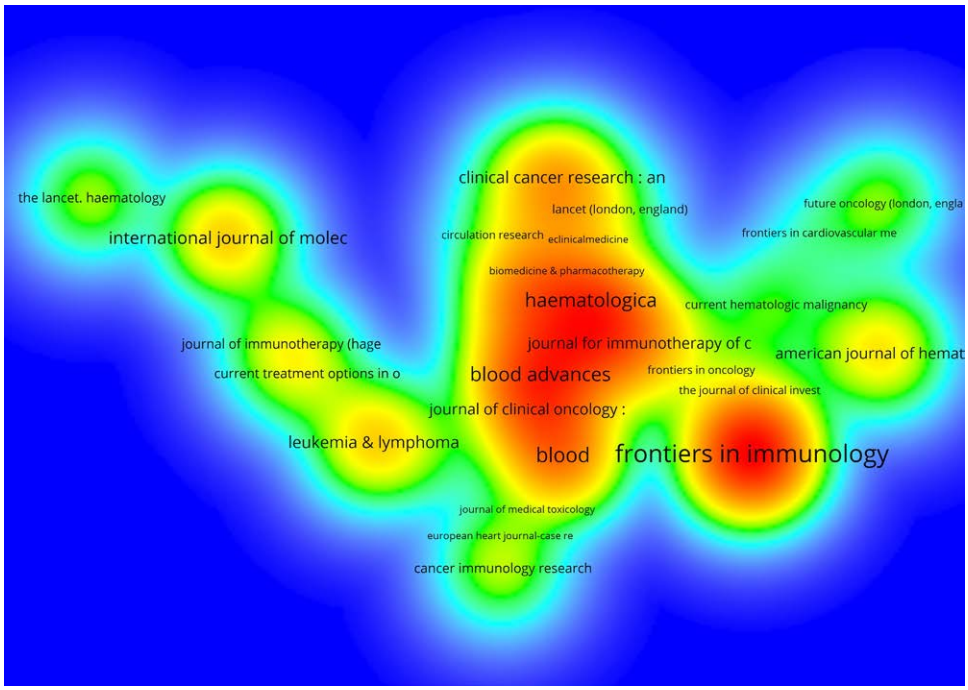

Figure 4. Density visualization of leading journals.

Table 3

Top 10 leading, cited and co-cited journals in the field of CAR-T cell therapy and cardiovascular outcomes.

	Top 10 leading journals	Impact factor	Quartile	Number of articles	Highly cited journals	Impact factor	Quartile	Number of citations	Highly co-cited journals	Impact factor	Quartile	Number of co-citations	Journals with high centrality	Impact factor	Quartile	Centrality
1	Frontiers in Immunology	7.3	Q1	35	Lancet Oncology	51.1	Q1	1397	New England Journal of Medicine	158.5	Q1	350	Annals of Internal Medicine	39.2	Q1	0.27
2	Blood	20.3	Q1	24	Journal of Clinical Oncology	45.4	Q1	612	Blood	20.3	Q1	223	Alimentary Pharmacology & Therapeutics	7.6	Q1	0.26
3	Haematologica	10.1	Q1	22	Journal of the National Cancer Institute	10.3	Q1	498	Journal of the American College of Cardiology	24.4	Q1	175	British Journal of Cancer	8.8	Q1	0.15
4	British Journal of Haematology	6.5	Q1	22	Cancer Immunology Research	10.1	Q1	441	Journal of Clinical Oncology	45.4	Q1	170	Blood	20.3	Q1	0.13
5	Blood Advances	7.6	Q1	20	Biology of Blood and Marrow Transplantation	4.3	Q2	126	Circulation	37.8	Q1	131	Biomed Research International	No IF	No Q	0.13
6	Journal of Hematology & Oncology	28.5	Q1	20	JACC: Cardio Oncology	11.1	Q1	120	Blood and Marrow Transplantation	4.3	Q2	106	Journal of Immunology	4.4	Q2	0.12
7	Blood Cancer Journal	12.8	Q1	18	International Journal of Molecular Sciences	5.6	Q1	90	JACC: Cardio Oncology	11.1	Q1	97	Anticancer Research	2	Q4	0.12
8	Clinical Lymphoma, Myeloma & Leukemia	2.7	Q3	16	Journal of the American College of Cardiology	24.4	Q1	81	Lancet	168.9	Q1	84	Annals of Oncology	50.5	Q1	0.11
9	International Journal of Molecular Sciences	5.6	Q1	15	European Journal of Cancer	8.4	Q1	80	Journal for Immunotherapy of Cancer	10.9	Q1	76	Cancer Immunology, Immunotherapy	5.8	Q1	0.09
10	The New England Journal of Medicine	158.5	Q1	14	Biomed Research International	No IF	No Q	66	Lancet Oncology	51.1	Q1	68	AAPS Pharm SciTech	3.3	Q2	0.08

CAR-T = chimeric antigen receptor T cell.

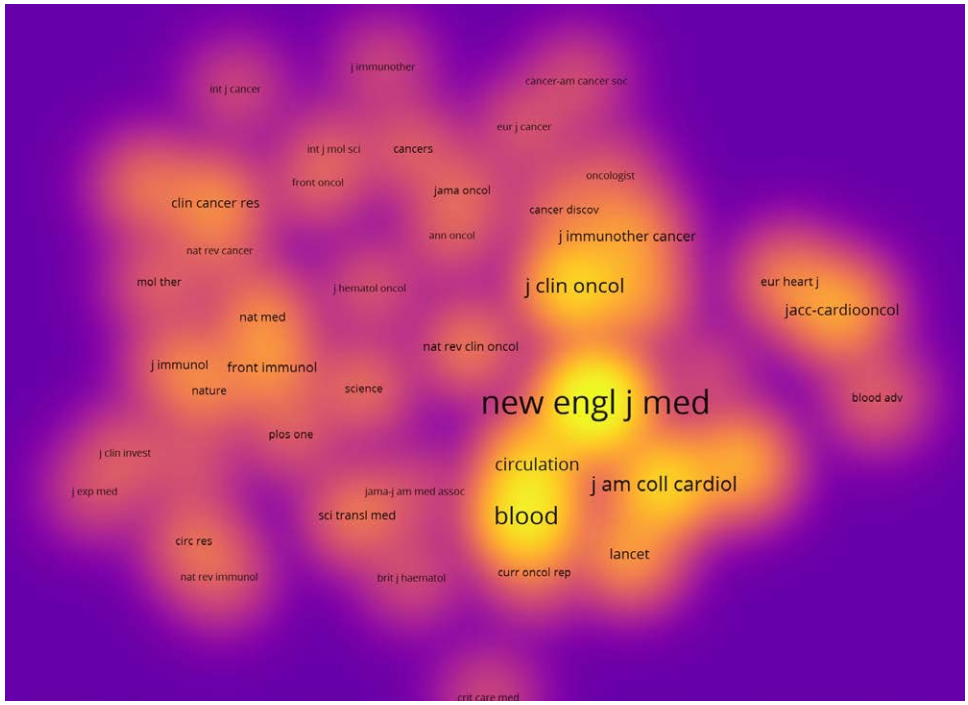

Figure 5. Density visualization of co-cited journals.

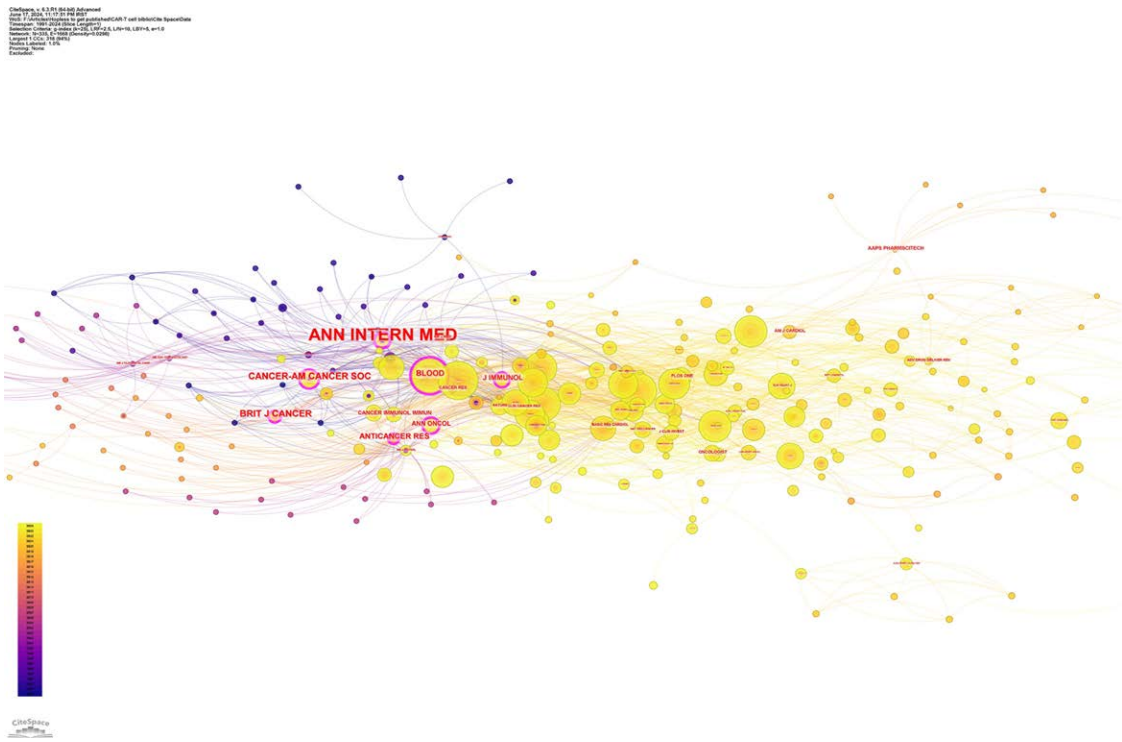

Figure 6. Network visualizing of journals with the highest centrality.

have been approved by the Food and Drug Administration (FDA) for commercialization in the US to date. Research in this field has significantly increased in China in the last few decades.[48] According to our research, developed countries make up the majority of the top countries with the highest publication outputs. The main driving force behind these advancements is the substantial cost needed for CAR-T therapy research and development.[49] Moreover, CAR-T cell therapy is an expensive treatment method. For instance, the cost of using Kymriah to treat acute lymphocytic leukemia is approximately $475,000.[50] The high costs associated with research and development, as well as clinical usage, impose limitations on the clinical promotion and implementation of this treatment. Addressing the challenge of reducing these expenses and making CAR-T cell treatment more accessible at a reasonable cost is a complex issue.[51,52]

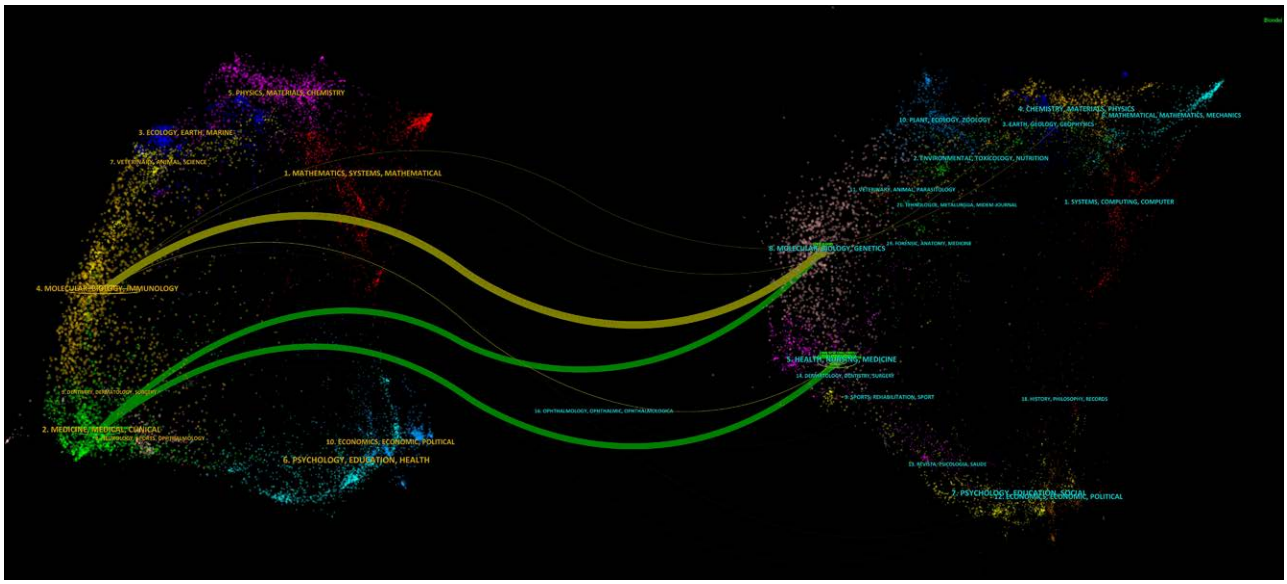

Figure 7. The dual-map overlay of journals on CAR-T cell therapy and cardiovascular implications. CAR-T = chimeric antigen receptor T cell.

Table 4

Top 10 authors and co-cited authors in the field of CAR-T cell therapy and cardiovascular implications.

Authors	Number of publications	Co-Cited authors	Number of co-citations
Usmani	17	Lee	78
Mailankody	17	Neelapu	66
Jagannath	16	Maude	63
Cohen	15	Ganatra	62
Einsele	15	Schuster	49
Cao	14	Alvi	44
van de Donk	14	Rosenberg	37
Shah	14	Lefebvre	35
Li	13	Locke	35
Xu	13	Brudno	33

CAR-T = chimeric antigen receptor T cell.

The cluster analysis revealed that "multiple myeloma" was the largest cluster, characterized by a dense network of connections. This indicates a substantial amount of research focused on multiple myeloma, showcasing significant enthusiasm for developing and enhancing CAR-T cell therapy for this particular blood cancer. Research within this cluster concentrates on understanding the disease's pathophysiology, therapeutic responses, and long-term outcomes of CAR-T cell therapy in patients with multiple myeloma.[53] Studies like the CARTITUDE-1 and KarMMa trials have shown that patients with poor prognoses can achieve better outcomes.[54–57]

The "combination therapy" cluster was identified as the second most crucial, focusing on research into various therapeutic combinations. This involves integrating CAR-T cell therapy with other treatments, such as chemotherapy, which improves the tumor environment for CAR-T cells by reducing immunosuppressive cells and promoting inflammation; radiotherapy, which enhances CAR-T effectiveness by causing DNA damage in cancer cells, leading to antigen release and immune activation; immune checkpoint inhibitors, which, when combined with CAR-T cells, have shown promising results, particularly in solid tumors; oncolytic viruses, which, when loaded onto CAR-T cells, have demonstrated synergistic effects in preclinical studies; and immunomodulatory drugs, which enhance CAR-T cell proliferation, persistence, and cytokine production. Research in this area underscores the potential of these combination strategies to increase the effectiveness and longevity of CAR-T cell therapy.[58–62]

The research conducted in the "#3 cardiovascular magnetic resonance assessment" cluster focuses on utilizing cardiovascular MRI to observe and measure the cardiovascular impacts of CAR-T cell treatment. This imaging technique is essential for identifying cardiotoxicity, evaluating heart performance, and providing guidance for therapeutic intervention to reduce cardiovascular risks.[63]

5. Limitations

Although, to the best of our knowledge, this is the first bibliometric study assessing the cardiac implications of CAR-T therapy, it is important to acknowledge certain limitations. First, our study relied exclusively on data from 2 databases, potentially overlooking relevant papers published elsewhere. Utilizing additional datasets might provide a more comprehensive view of the research landscape. Additionally, bibliometric data can be influenced by intrinsic biases, such as citation practices and publishing delays, which may impact the interpretation of research trends and the assessment of author impact. Moreover, tools like CiteSpace and VOSviewer cannot entirely replace systematic retrieval methods. The grouping of keywords and co-citation networks relies on computational processes, which, while generally reliable, may not accurately represent the complex relationships between study subjects. Our study presents a current snapshot of CAR-T cell therapy research, a field that is continually evolving. Ongoing advancements may alter the patterns and areas of focus we have identified. To overcome these limitations and gain a more comprehensive understanding, future research should incorporate longitudinal analyses and utilize multiple databases.

6. Conclusion

This comprehensive bibliometric analysis has provided a detailed assessment of the research landscape on CAR-T cell therapy and its cardiovascular implications. The study has identified the key countries, authors, journals, and institutions driving the progress in this field, as well as the emerging research hotspots and future directions. Understanding the research landscape and identifying key trends and gaps is important for

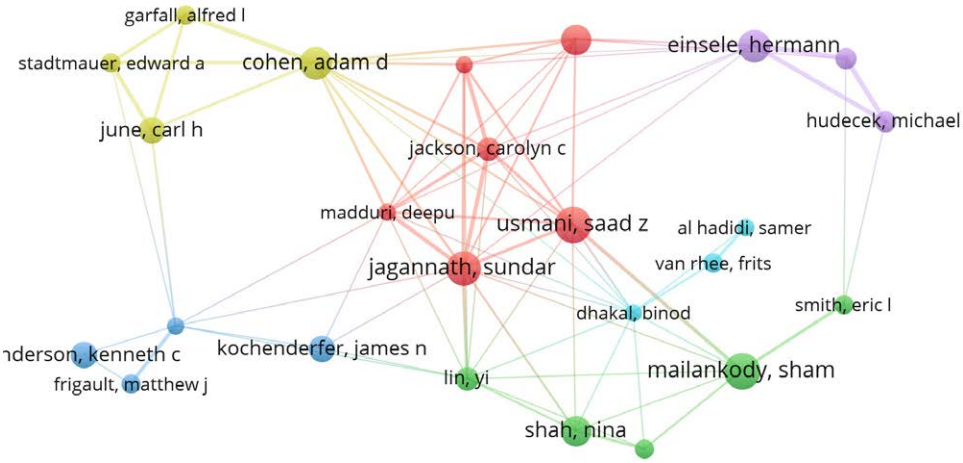

Figure 8. Network visualization of top 10 authors.

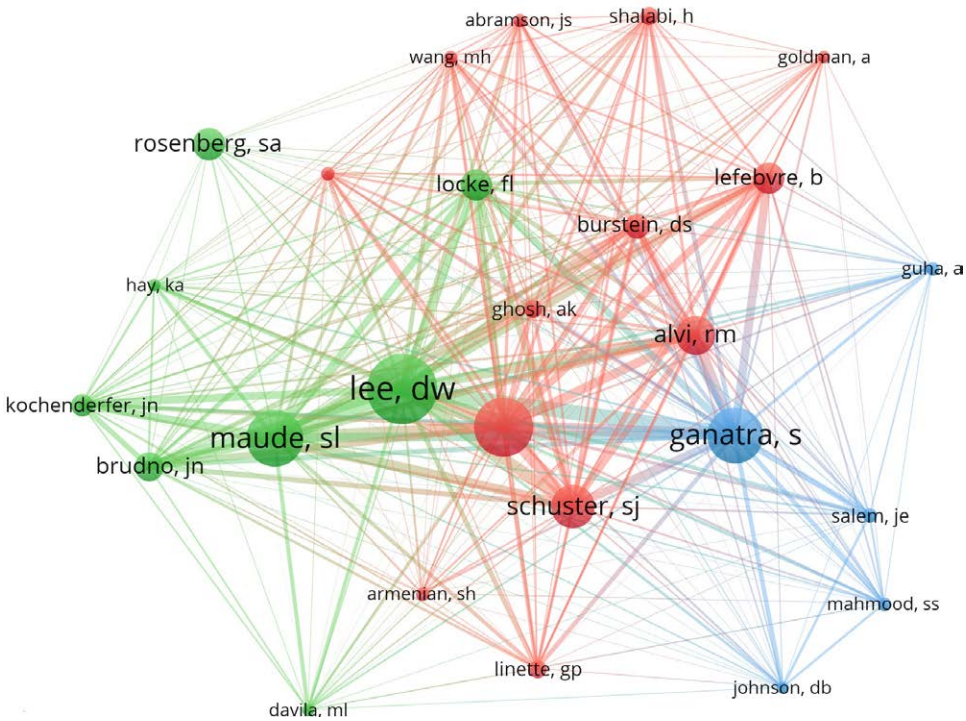

Figure 9. Network visualization of top 10 and co-cited authors.

the scientific community. As CAR-T cell therapy continues to evolve and gain widespread clinical application, the cardiovascular implications of this treatment cannot be overlooked. The findings from this bibliometric study underscore the need for a heightened focus on the cardiac safety and management of patients undergoing CAR-T therapy. By addressing the emerging research areas identified, the scientific community can work towards developing more effective strategies to mitigate the cardiovascular risks associated with CAR-T cell therapy, ultimately improving patient outcomes and quality of life.

Author contributions

Conceptualization: Ehsan Amini-Salehi, Sandeep Samethadka Nayak, Alexis Pudimat.
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Project administration: Ashraf Ahmed, Seyedeh Fatemeh Hosseini Jebelli.
Resources: Sandeep Samethadka Nayak.
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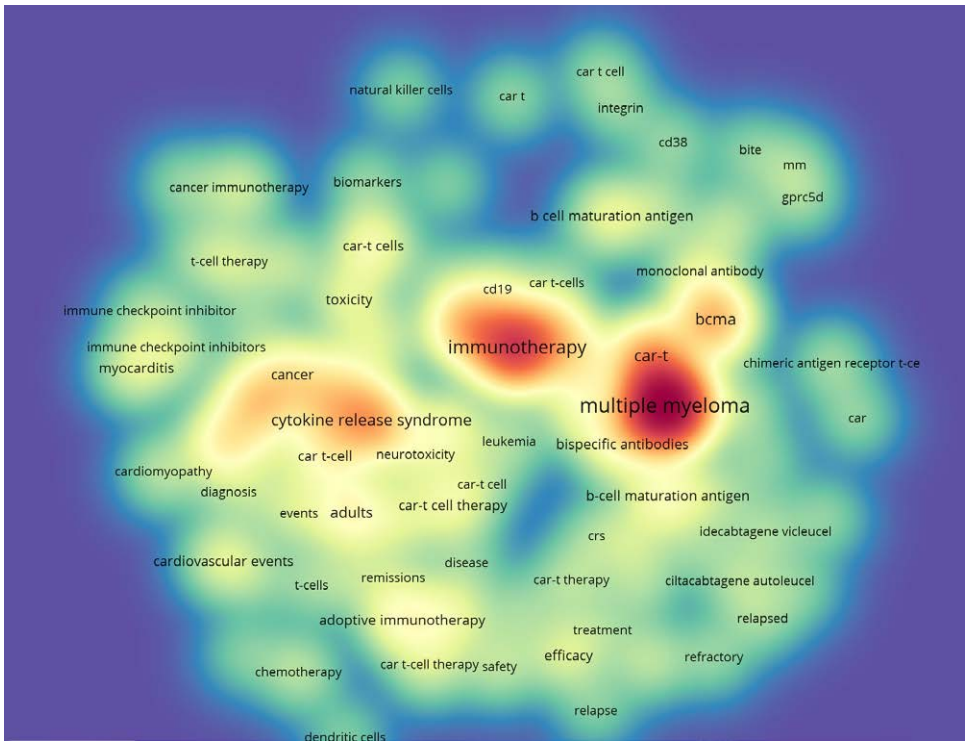

Figure 10. Density visualization of top keywords.

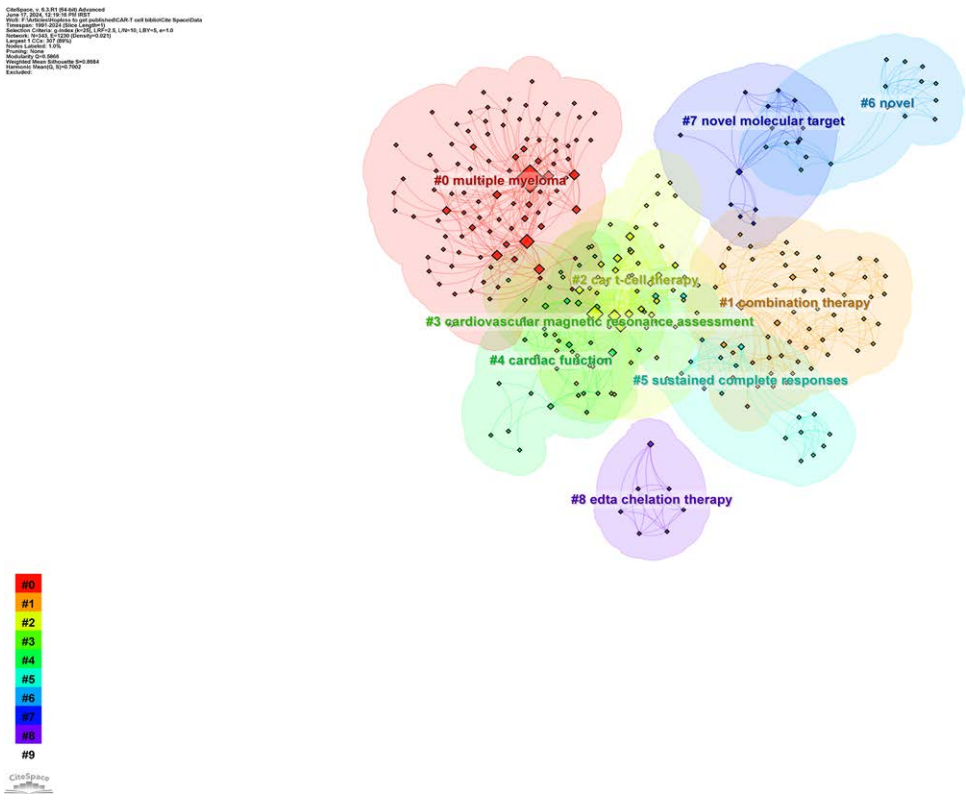

Figure 11. Cluster analysis of keywords in CAR-T cell therapy and cardiovascular outcomes. CAR-T = chimeric antigen receptor T cell.

References

[1] Ho M, Zanwar S, Paludo J. Chimeric antigen receptor T-cell therapy in hematologic malignancies: successes, challenges, and opportunities. Eur J Haematol. 2024;112:197–210.

[2] Zhang X, Zhu L, Zhang H, Chen S, Xiao Y. CAR-T cell therapy in hematological malignancies: current opportunities and challenges. Front Immunol. 2022;13:927153.

[3] Jogalekar MP, Rajendran RL, Khan F, Dmello C, Gangadaran P, Ahn BC. CAR T-Cell-Based gene therapy for cancers: new

perspectives, challenges, and clinical developments. Front Immunol. 2022;13:925985.
[4] Abbasi S, Totmaj MA, Abbasi M, et al. Chimeric antigen receptor T (CAR-T) cells: novel cell therapy for hematological malignancies. Cancer Med. 2023;12:7844–58.
[5] Chohan KL, Siegler EL, Kenderian SS. CAR-T cell therapy: the efficacy and toxicity balance. Curr Hematol Malig Rep. 2023;18:9–18.
[6] Lefebvre B, Kang Y, Smith AM, Frey NV, Carver JR, Scherrer-Crosbie M. Cardiovascular effects of CAR T cell therapy: a retrospective study. JACC CardioOncol. 2020;2:193–203.
[7] Camilli M, Maggio L, Tinti L, et al. Chimeric antigen receptor-T cell therapy-related cardiotoxicity in adults and children cancer patients: a clinical appraisal. Front Cardiovasc Med. 2023;10:1090103.
[8] Rao A, Stewart A, Eljalby M, et al. Cardiovascular disease and chimeric antigen receptor cellular therapy. Front Cardiovasc Med. 2022;9:932347.
[9] Oliveira OJ, Silva FF, Juliani F, Barbosa LCFM, Nunhes TV. Bibliometric method for mapping the state-of-the-art and identifying research gaps and trends in literature: an essential instrument to support the development of scientific projects. Scientometrics Recent Adv. 2019;85856:1.
[10] Nicolaisen J. Bibliometrics and citation analysis: from the science citation index to cybermetrics. J Am Soc Inf Sci Technol. 2010;61:205–7.
[11] Amini-Salehi E, Hasanpour M, Alotaibi A, et al. Global research trends on DPP-4 inhibitors and cardiovascular outcomes: a comprehensive bibliometric analysis. Ann Med Surg (Lond). 2025;87:2133–48.
[12] Alotaibi A, Contreras R, Thakker N, et al. Bibliometric analysis of artificial intelligence applications in cardiovascular imaging: trends, impact, and emerging research areas. Ann Med Surg (Lond). 2025;87:1947–68.
[13] Gadhachanda KR, Marsool MD, Bozorgi A, et al. Artificial intelligence in cardiovascular procedures: a bibliometric and visual analysis study. Ann Med Surg (Lond). 2025;87:2187–203.
[14] Wan Y, Shen J, Ouyang J, et al. Bibliometric and visual analysis of neutrophil extracellular traps from 2004 to 2022. Front Immunol. 2022;13:1025861.
[15] Meng T, Wang P, Ding J, et al. Global research trends on ventricular remodeling: a bibliometric analysis from 2012 to 2022. Curr Probl Cardiol. 2022;47:101332.
[16] Jiang J, Lyu W, Chen N. A bibliometric analysis of diffuse large B-cell lymphoma research from 2001 to 2020. Comput Biol Med. 2022;146:105565.
[17] Nayak SS, Amini-Salehi E, Ulrich MT, et al. Exploring the evolution of evidence synthesis: a bibliometric analysis of umbrella reviews in medicine. Ann Med Surg (Lond). 2025;87:2035–48.
[18] Alotaibi A, Mahapatro A, Mirchandani M, et al. Triglyceride-glucose index as a marker in cardiovascular diseases: a bibliometric study and visual analysis. Ann Med Surg (Lond). 2025;87:1487–505.
[19] Chen C. CiteSpace II: Detecting and visualizing emerging trends and transient patterns in scientific literature. J Am Soc Inf Sci Technol. 2006;57:359–77.
[20] Ma D, Guan B, Song L, et al. A bibliometric analysis of exosomes in cardiovascular diseases from 2001 to 2021. Front Cardiovasc Med. 2021;8:734514.
[21] Synnestvedt MB, Chen C, Holmes JH. CiteSpace II: visualization and knowledge discovery in bibliographic databases. AMIA Annu Symp Proc. 2005;2005:724–8.
[22] Mahapatro A, Bozorgi A, Obulareddy SUJ, et al. Glucagon-like peptide-1 agonists in cardiovascular diseases: a bibliometric analysis from inception to 2023. Ann Med Surg (Lond). 2024;86:6602–18.
[23] Maus MV, Grupp SA, Porter DL, June CH. Antibody-modified T cells: CARs take the front seat for hematologic malignancies. Blood. 2014;123:2625–35.
[24] Zhang T, Cao L, Xie J, et al. Efficiency of CD19 chimeric antigen receptor-modified T cells for treatment of B cell malignancies in phase I clinical trials: a meta-analysis. Oncotarget. 2015;6:33961–71.
[25] Topalian SL, Wolchok JD, Chan TA, et al. Immunotherapy: the path to win the war on cancer? Cell. 2015;161:185–6.
[26] Tang XJ, Sun XY, Huang KM, et al. Therapeutic potential of CAR-T cell-derived exosomes: a cell-free modality for targeted cancer therapy. Oncotarget. 2015;6:44179–90.
[27] Nigam M, Mishra AP, Deb VK, et al. Evaluation of the association of chronic inflammation and cancer: Insights and implications. Biomed Pharmacother. 2023;164:115015.
[28] Fotouhi M, Samami E, Mohseni S, et al. How prevalent is cancer in confirmed cases with coronaviruses and severe acute respiratory syndromes? Adv Exp Med Biol. 2021;1318:293–313.
[29] Bachanova V, Bishop MR, Dahi P, et al; CAR T-cell Consortium. Chimeric antigen receptor T cell therapy during the COVID-19 pandemic. Biol Blood Marrow Transplant. 2020;26:1239–46.
[30] Ghosh AK, Chen DH, Guha A, Mackenzie S, Walker JM, Roddie C. CAR T cell therapy-related cardiovascular outcomes and management: systemic disease or direct cardiotoxicity? JACC CardioOncol. 2020;2:97–109.
[31] Neelapu SS, Tummala S, Kebriaei P, et al. Chimeric antigen receptor T-cell therapy – assessment and management of toxicities. Nat Rev Clin Oncol. 2018;15:47–62.
[32] Stein-Merlob AF, Rothberg MV, Ribas A, Yang EH. Cardiotoxicities of novel cancer immunotherapies. Heart. 2021;107:1694–703.
[33] Pareek N, Cevallos J, Moliner P, et al. Activity and outcomes of a cardio-oncology service in the United Kingdom—a five-year experience. Eur J Heart Fail. 2018;20:1721–31.
[34] Ganatra S, Redd R, Hayek SS, et al. Chimeric antigen receptor T-cell therapy-associated cardiomyopathy in patients with refractory or relapsed non-hodgkin lymphoma. Circulation. 2020;142:1687–90.
[35] Shalabi H, Sachdev V, Kulshreshtha A, et al. Impact of cytokine release syndrome on cardiac function following CD19 CAR-T cell therapy in children and young adults with hematological malignancies. J ImmunoTher Cancer. 2020;8:e001159.
[36] Chen LR, Li YJ, Zhang Z, et al. Cardiovascular effects associated with chimeric antigen receptor T cell therapy in cancer patients: a meta-analysis. Front Oncol. 2022;12:924208.
[37] Chen YJ, Abila B, Mostafa Kamel Y. CAR-T: what is next?. Cancers (Basel). 2023;15:663.
[38] Braendstrup P, Levine BL, Ruella M. The long road to the first FDA-approved gene therapy: chimeric antigen receptor T cells targeting CD19. Cytotherapy. 2020;22:57–69.
[39] Patel NP, Doukas PG, Gordon LI, Akhter N. Cardiovascular toxicities of CAR T-cell therapy. Curr Oncol Rep. 2021;23:78.
[40] Chishinga N, Mapalo MT, Bodine CD. Risk stratification for immune effector cell-associated neurotoxicity syndrome in patients receiving chimeric antigen receptor T cell therapy. J Clin Oncol. 2024;42(16_suppl):e14534–e14534.
[41] Korell F, Entenmann L, Romann S, et al. Evaluation of all-cause mortality and cardiovascular safety in patients receiving chimeric antigen receptor T cell therapy: a prospective cohort study. eClinicalMedicine. 2024;69:102504.
[42] Shahzadi M, Rafique H, Waheed A, et al. Artificial intelligence for chimeric antigen receptor-based therapies: a comprehensive review of current applications and future perspectives. Ther Adv Vaccines Immunother. 2024;12:25151355241305856.
[43] Pay L, Yumurtaş A, Tezen O, et al. Efficiency of MVP ECG risk score for prediction of long-term atrial fibrillation in patients with ICD for heart failure with reduced ejection fraction. Korean Circ J. 2023;53:621–31.
[44] Hayıroğlu MI, Çınar T, Çiçek V, et al. A simple formula to predict echocardiographic diastolic dysfunction—electrocardiographic diastolic index. Herz. 2021;46:159–65.
[45] Hayıroğlu M, Altay S. The role of artificial intelligence in coronary artery disease and atrial fibrillation. Balkan Med J. 2023;40:151–2.
[46] Oikonomou EK, Sangha V, Dhingra LS, et al. Artificial intelligence–enhanced risk stratification of cancer therapeutics–related cardiac dysfunction using electrocardiographic images. Circ Cardiovasc Qual Outcomes. 2025;18:e011504.
[47] Wang V, Gauthier M, Decot V, Reppel L, Bensoussan D. Systematic review on CAR-T cell clinical trials up to 2022: Academic Center Input. Cancers (Basel). 2023;15:1003.
[48] Wei J, Guo Y, Wang Y, et al. Clinical development of CAR T cell therapy in China: 2020 update. Cell Mol Immunol. 2021;18:792–804.
[49] Ran T, Eichmüller SB, Schmidt P, Schlander M. Cost of decentralized CAR T-cell production in an academic nonprofit setting. Int J Cancer. 2020;147:3438–45.
[50] Pantin J, Battiwalla M. Upsetting the apple CAR-T (chimeric antigen receptor T-cell therapy) – sustainability mandates USA innovation. Br J Haematol. 2020;190:851–3.
[51] Borgert R. Improving outcomes and mitigating costs associated with CAR T-cell therapy. Am J Manag Care. 2021;27(13 Suppl):S253–61.
[52] Miao L, Zhang Z, Ren Z, Tang F, Li Y. Obstacles and coping strategies of CAR-T cell immunotherapy in solid tumors. Front Immunol. 2021;12:687822.
[53] Rendo MJ, Joseph JJ, Phan LM, DeStefano CB. CAR T-Cell therapy for patients with multiple myeloma: current evidence and challenges. Blood Lymphat Cancer. 2022;12:119–36.

[54] Puertas B, Mateos MV, González-Calle V. Anti-BCMA CAR T-cell therapy: changing the natural history of multiple myeloma. Hemasphere. 2022;6:e691.
[55] Sheykhhasan M, Ahmadieh-Yazdi A, Vicidomini R, et al. CAR T therapies in multiple myeloma: unleashing the future. Cancer Gene Ther. 2024;31:667–86.
[56] Berdeja JG, Madduri D, Usmani SZ, et al. Ciltacabtagene autoleucel, a B-cell maturation antigen-directed chimeric antigen receptor T-cell therapy in patients with relapsed or refractory multiple myeloma (CARTITUDE-1): a phase 1b/2 open-label study. Lancet. 2021;398:314–24.
[57] Munshi NC, Anderson LD, Jr., Shah N, et al. Idecabtagene vicleucel in relapsed and refractory multiple myeloma. N Engl J Med. 2021;384:705–16.
[58] Liu J, Jiao X, Ma D, Fang Y, Gao Q. CAR-T therapy and targeted treatments: emerging combination strategies in solid tumors. Med. 2024;5:530–49.
[59] Al-Haideri M, Tondok SB, Safa SH, et al. CAR-T cell combination therapy: the next revolution in cancer treatment. Cancer Cell Int. 2022;22:365.
[60] Zhong L, Li Y, Muluh TA, Wang Y. Combination of CAR-T cell therapy and radiotherapy: opportunities and challenges in solid tumors (Review). Oncol Lett. 2023;26:281.
[61] Lv Y, Luo X, Xie Z, et al. Prospects and challenges of CAR-T cell therapy combined with ICIs. Front Oncol. 2024;14:1368732.
[62] Wang AX, Ong XJ, D'Souza C, Neeson PJ, Zhu JJ. Combining chemotherapy with CAR-T cell therapy in treating solid tumors. Front Immunol. 2023;14:1140541.
[63] Voigt MB, Kravchenko D, Isaak A, Heine A, Holderried TAW, Luetkens JA. Cardiovascular magnetic resonance assessment of immunotherapy cardiotoxicity. Curr Cardiovasc Imaging Rep. 2023;16:103–15.