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Exploring the landscape of exosomes in heart failure: a bibliometric analysis

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Background: Exosomes, which carry bioactive RNAs, proteins, lipids, and metabolites, have emerged as novel diagnostic markers and therapeutic agents for heart failure (HF). This study aims to elucidate the trends, key contributors, and research hotspots of exosomes in HF.

Methods: We collected publications related to exosomes in HF from the Web of Science Core Collection. Using VOSviewer, CiteSpace, Excel, and SRplot software, we performed a visualization analysis of authors, countries, institutions, keywords, and references.

Results: The publications on exosomes in the field of HF has grown rapidly. China (*N* = 245, 42.683%) and the United States (*N* = 170, 29.617%) are the leading contributors in this area. Wang L (*N* = 14, 2.443%) is the most prolific author in the field. Key areas of exosome research in HF include mesenchymal stem cells (MSCs), angiogenesis, and microRNAs. Additionally, keywords and references analysis reveal that exosome research in HF is primarily focused on the role of exosomes in intercellular communication in HF, the value of miRNAs in exosomes as diagnostic markers, and the therapeutic mechanisms of MSC-derived exosomes.

Conclusion: Exosomes are receiving increasing attention in the field of HF. Mapping the development landscape of exosomes in HF will help researchers accelerate progress in this area.

Keywords: bibliometric analysis, citeSpace, exosome, heart failure, VOSviewer

Introduction

Heart failure (HF) is a progressive condition caused by various factors such as hypertension, cardiomyopathy, valvular heart disease, congenital heart disease, and arrhythmias, characterized by a decline in the heart's ability to pump and/or fill with blood[1,2]. HF affects approximately 64 million people worldwide, with a prevalence ranging from about 1% to 6% across different countries[3]. Due to an aging population and the effective management of acute coronary syndromes, the prevalence and incidence of HF among individuals over 50 years old are steadily increasing with age[4].

Exosomes are nanoscale extracellular vesicles (EVs) with a diameter ranging from 30-150 nm[5]. They play a crucial role in intercellular communication by transferring bioactive molecules, including circular RNAs, microRNAs, long non-coding RNAs, proteins, and metabolites[6,7]. Significant progress has been made in the use of exosomes for diagnosis, therapy, and targeted drug delivery in cardiovascular disease (CVD) research[8]. HF patients can influence central inflammatory responses by modulating the expression of miR-214-3p, let-7g-5p, and let-7i-5p in circulating exosomes. Therefore, monitoring changes in circulating exosomes can help researchers identify targeted therapeutic strategies for HF[9,10]. While some researchers have explored the mechanisms by which exosomes improve cardiac function in HF treatment, as well as their use in HF diagnosis, therapy, and targeted drug delivery, there is a lack of visualization analysis of the application trends, leading authors, and research hotspots of exosomes in HF[11,12].

Bibliometrics, which emerged in the early 20th century, is an efficient and quantitative method for literature research[13]. Visualizing exosome-related publications in HF can quickly reveal the development status of countries or institutions, the

HIGHLIGHTS

- This study is the first bibliometric analysis of exosome research in the field of heart failure.
- In recent years, the number of publications and citations related to exosomes in heart failure has increased significantly.
- China and the United States are leading countries in exosome research for heart failure.
- A comprehensive analysis indicates that future key areas in heart failure research include exploring the role of exosomes in cell communication, developing improved exosome-based therapies, and identifying better diagnostic biomarkers for the disease.

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distribution patterns of author groups, and research hotspots[14,15]. Based on bibliometric findings, researchers can identify valuable research topics and potential collaborators, accelerating the exploration of exosomes in the mechanisms of HF. For clinicians, this analysis highlights exosomes' potential as biomarkers for disease progression and risk assessment tools, as well as the latest advancements in exosome-based therapies for HF.

This study constructs a scientific knowledge map of exosomes in the field of HF by CiteSpace and VOSviewer. Finally, based on the results of the bibliometric analysis, we will discuss the primary application areas and current advancements of exosomes in HF, with the aim of providing a foundation and guidance for future research in HF and exosome studies.

Methods

Data sources and search strategy

The Web of Science Core Collection (WoSCC) offers the most comprehensive and highest level of evidence available, adhering to Bradford's Law and Garfield's Law. The plain text format derived from WoSCC can be directly used for visualization with software such as VOSviewer and CiteSpace. We retrieved publications related to exosomes and HF from the WoSCC database spanning from 1 January 2004, to 13 August 2024. The search formula was: TS = (exosome) OR TS = (exosomes) OR TS = (exosomal) AND TS = (heart failure) OR TS = (cardiac failure) OR TS = (myocardial failure) OR TS = (right sided heart failure) OR TS = (left sided heart failure) OR TS = (congestive heart failure) OR TS = (acute heart failure) OR TS = (chronic heart failure). To minimize bias during literature retrieval, data inclusion, and deduplication, at least two researchers independently conducted the literature search and inclusion process. In cases of disagreement, a third researcher was consulted for judgment. Additionally, all included publications were retrieved from the database on the same day.

Inclusion and exclusion criteria

Publications that fully met the following criteria were included in the subsequent analysis, while others were excluded: 1. Publications related to exosomes and acute or chronic HF article and review. 2. Publications written in English. 3. Publications published between 2004 and 2024. Exclusion criteria: Publications that were clearly unrelated to exosomes and acute or chronic HF, non-English publications, other types of publications aside from articles and review, and publications from before 2004 were excluded from the subsequent bibliometric analysis.

Data visual software and statistical analysis

After collecting all data from the WoSCC database, we thoroughly reviewed all included data, removing duplicates and correcting spelling errors to ensure compatibility with subsequent software processing and data analysis. Several bibliometric and visualization tools were employed, including Microsoft Excel 2019, SRplot, VOSviewer, and CiteSpace. We created the graphical abstract using BioRender (www.biorender.com). Publication statistics and citation trend charts were generated using Microsoft Excel 2019 (Microsoft, USA). SRplot (www.bioinformatics.com.cn) was used to illustrate the global distribution of publications and the publication status of the top 10 countries and institutions[16]. Detailed journal classification information was obtained from the 2023 Journal Citation Reports (http://clarivate.com/products/web-of-science). Finally, we conducted bibliometric analysis and visualization of countries/regions, institutions, keywords, and references using VOSviewer (version 1.6.20)[17] developed by Professors Van Eck and Waltman from Leiden University, and CiteSpace (version 6.2. R4)[13,18] developed by Professor Chaomei Chen from the College of Computing and Informatics at Drexel University, based on the Java platform. In VOSviewer, the value of Total Link Strength is related to the number of connections a node has; the higher the value, the more collaborators are indicated. In CiteSpace, centrality is a metric that measures the importance of a node. A higher centrality value for a node indicates greater importance, represented by a larger circle with a purple outer ring. Citation bursts are detected using the Kleinberg algorithm, which identifies terms with a high rate of frequency change over a specific period from a large set of keywords. CiteSpace can detect burst terms and burst literature, allowing insight into research frontiers, shifts in research focus, and the latest trends, and helping to predict future developments in the field.

Result

Global publication distribution and citation trends

As shown in Figure 1, a preliminary search in the WoSCC database identified 623 publications. After applying exclusion criteria based on publication date, article type, and language, 574 publications were selected for bibliometric analysis. Currently, research on exosomes in HF spans across 61 countries or regions worldwide. According to Figure 2A, most publications on exosomes in the field of HF originate from East Asia, North America, and Western Europe. Additionally, Figure 2B illustrates the overall trend in the annual number of publications and total citations in the field of engineered organs. The 574 published papers have been cited 21 784 times in the WoSCC database (excluding self-citations, which amount to 19 670), with an H-index of 69. Research on exosomes in HF was relatively scarce between 2004 and 2014. From 2015 onwards, particularly between 2015 and 2021, there has been a rapid increase in the number of annual publications and total citations. Despite a slowdown in publication and citation growth rates during the COVID-19 pandemic between 2021 and 2023, interest in this field remains strong.

Contributions of countries and institutions

A bibliometric analysis of publications from different countries on exosomes in HF revealed that the top ten countries in terms of total publication count are shown in Table 1 and Figure 3A. China leads with 245 publications (42.683%), followed by the United States with 170 publications (29.617%). The other eight countries each contributed between 10 and 40 publications, indicating that China and the United States dominate this field. In terms of total citations, the United States holds a clear advantage with 9352 citations, followed by China with 5857 citations, while the majority of the other eight countries have fewer than 2000 citations. The H-index of China and the United States are

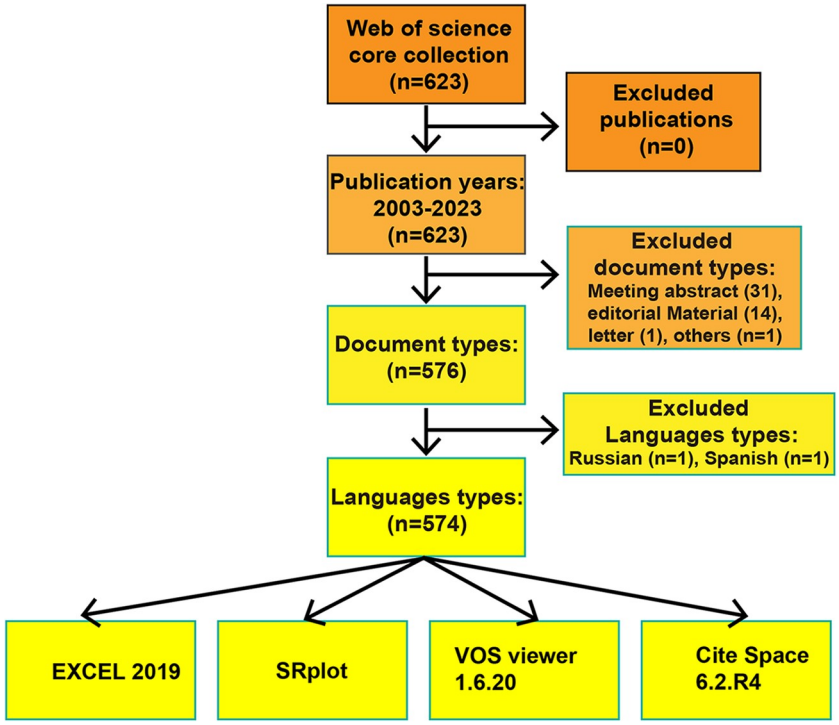

Figure 1. Flowchart for search process.

39 and 49, respectively, while the other countries have H-index ranging between 10 and 20.

Subsequently, we conducted a collaborative country analysis of all publications from the 61 countries using CiteSpace to explore international cooperation. The larger the circle, the higher the number of publications. The larger the purple outer ring, the higher the centrality. The centrality of the nodes represents the degree of collaboration between countries. The United States has the highest centrality at 0.57, significantly higher than that of the United Kingdom (0.17), Germany (0.16), and China (0.12), suggesting that the United States plays a bridging role in international cooperation (Fig. 3B). Overall, China and the United States hold pivotal positions in this field. However, it is noteworthy that the academic impact of Chinese publications is relatively low, indicating a need for more high-quality, innovative research articles.

Table 1

Top 10 countries by publications, H-index, and citations

Rank	Countries	Publications	Total citations	Average citations	H-index
1	Peoples R China	245(42.683%)	5,857	23.91	39
2	USA	170 (29.617%)	9,352	55.01	49
3	Italy	38 (6.620%)	1,067	28.08	16
4	England	26 (4.530%)	2,080	80.38	17
5	Canada	25 (4.355%)	957	39.28	15
6	Germany	24 (4.181%)	2,124	88.5	13
7	Iran	23 (4.007%)	483	21	11
8	Netherlands	21 (3.659%)	1,955	93.1	14
9	Japan	19 (3.310%)	1,182	62.21	14
10	France	18 (3.136%)	823	45.72	11

To investigate the contributions of the top 952 institutions in the study of exosomes in HF, we conducted a bibliometric analysis of the publications from these institutions. As shown in Table 2 and Figure 3C, Harvard University, Nanjing Medical University, and Shanghai Jiao Tong University lead with 15 publications each (2.613%). The other eight institutions have published between 11 and 14 papers each, suggesting no clear leading institution in this field. Harvard University and Harvard Medical School have the

Table 2

Top 10 institutions by publications, H-index, and citations

Rank	Countries	Publications	Total citations	Average citations	H-index
1	Harvard University	15 (2.613%)	1,430	95.33	10
2	Nanjing Medical University	15 (2.613%)	337	22.47	9
3	Shanghai Jiao Tong University	15 (2.613%)	249	16.6	10
4	Pennsylvania Commonwealth System of Higher Education Pcshe	14 (2.439%)	509	36.36	8
5	Institut National De La Sante Et De La Recherche Medicale Inserm	13 (2.265%)	730	56.15	9
6	Cedars Sinai Medical Center	12 (2.091%)	628	52.33	9
7	University System of Georgia	12 (2.091%)	320	26.67	7
8	Assistance Publique Hopitaux Paris Aphp	11 (1.916%)	450	40.91	8
9	Harvard Medical School	11 (1.916%)	1,251	113.73	7
10	Soochow University China	11 (1.916%)	384	34.91	6

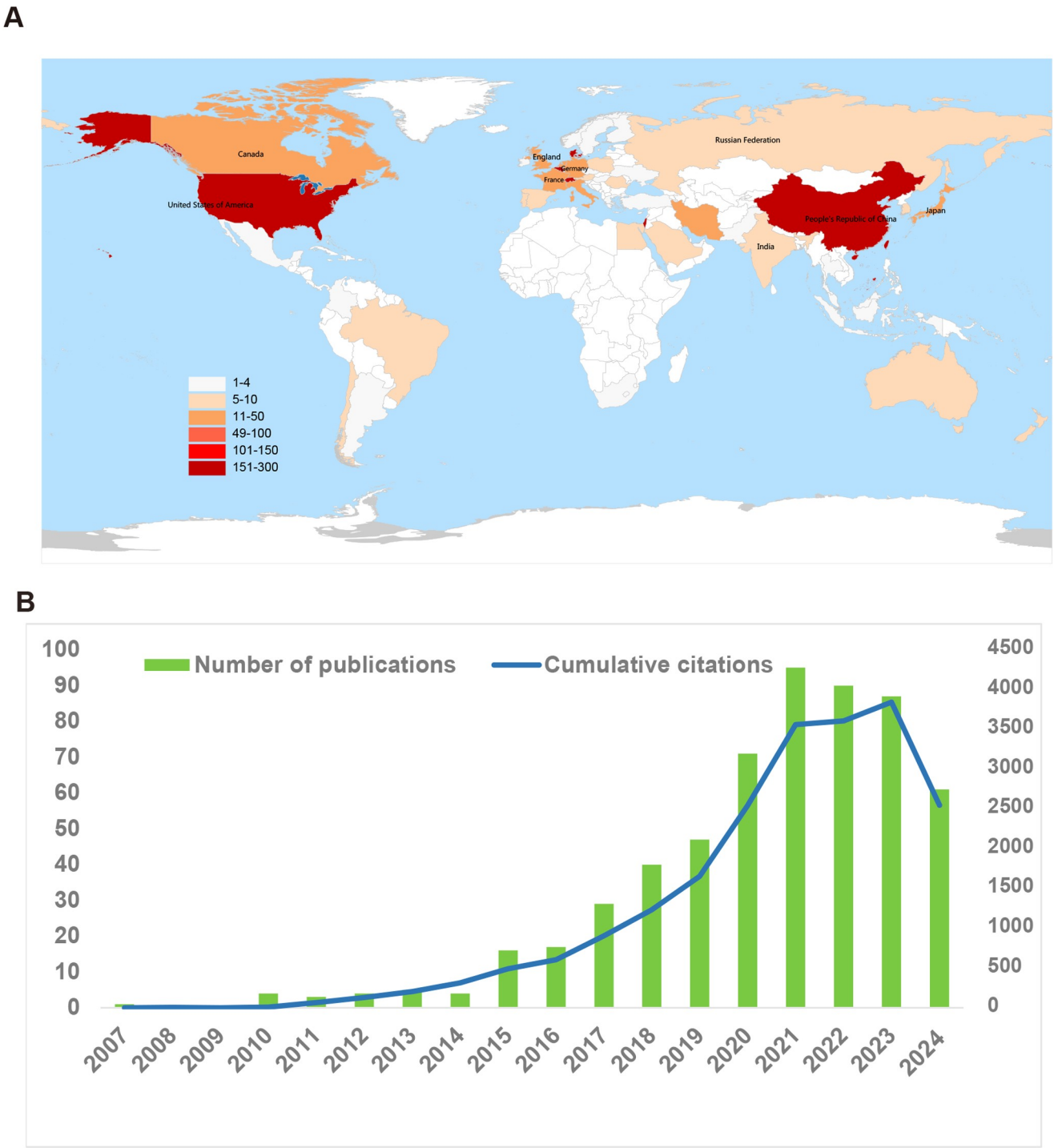

Figure 2. Global publication distribution and citation trends. (A) Geographic publication distribution of exosomes in HF. (B) Trends in the publications of exosomes in HF.

highest total citation counts, with 1430 and 1251 citations, respectively. Among the top 10 institutions in terms of total publications, five are located in the United States, highlighting the leadership of the United States in this field. Additionally, as shown in Figure 3D, The larger the circle, the higher the number of publications. The larger the purple outer ring, the higher the centrality. The centrality of the nodes represents the degree of collaboration between institutions. Assistance Publique – Hôpitaux de Paris, Shanghai Jiao Tong University, The Institute of Medical Biology, and Cedars-Sinai Medical Center have high centrality values of 0.38, 0.29, 0.28, and 0.27, respectively, indicating their key roles in institutional collaboration and communication.

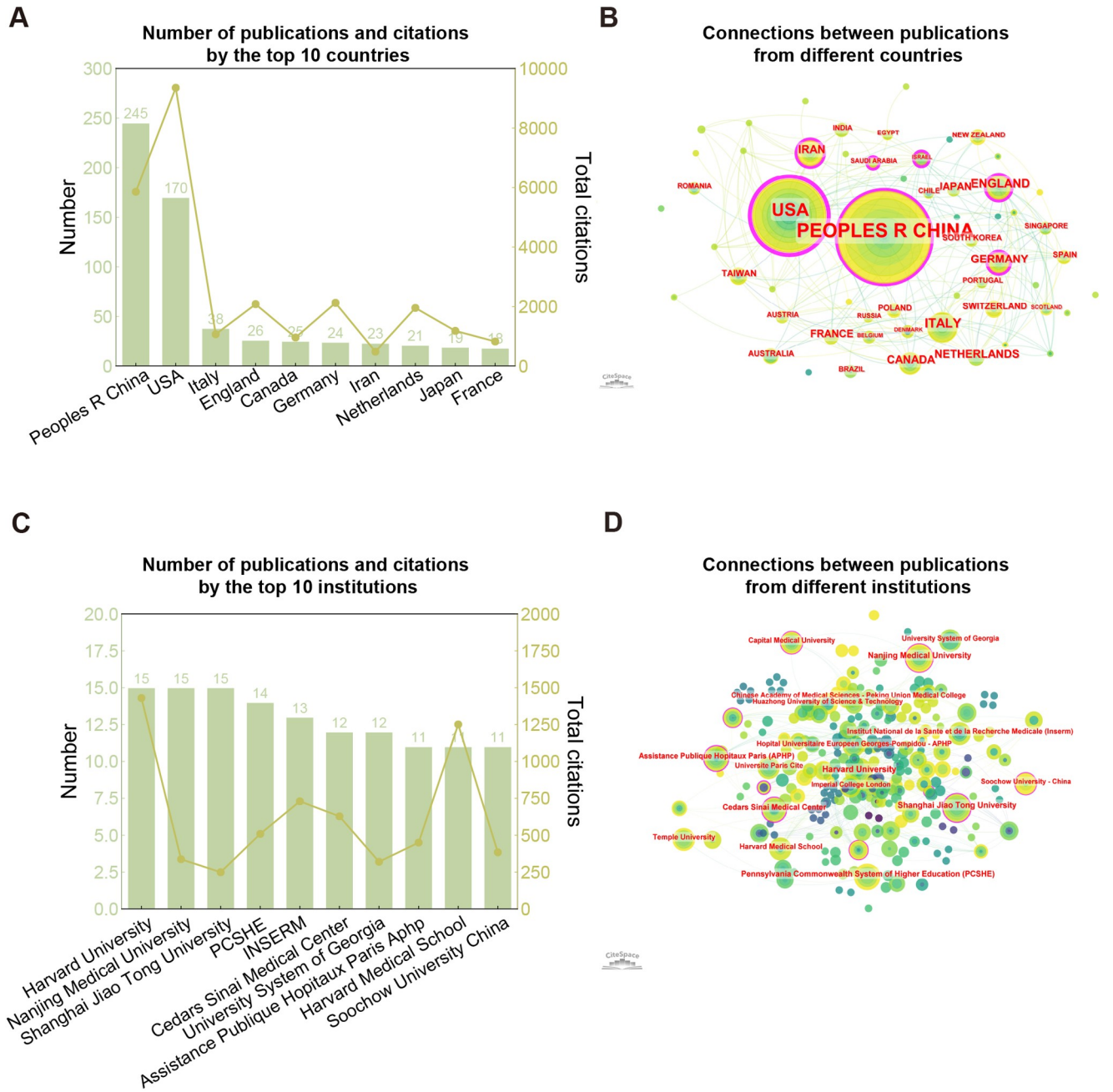

Figure 3. Distribution of publications and citations in country and institution. (A) Number of publications and citations by the top 10 countries. (B) Connections between publications from different countries. (C) Number of publications and citations by the top 10 institutions. (D) Connections between publications from different institutions. PCSHE: Pennsylvania Commonwealth System of Higher Education. INSERM: Institut National De La Sante Et De La Recherche Medicale.

Contributions of authors and journal

A total of 3376 researchers have studied exosomes and contributed to the field of HF. As shown in Table 3, Wang L ($N = 14$, 2.443%) and Wang Y ($N = 12$, 2.094%) published the most publications, but did not widen the gap with the next eight. Moreover, Marbán E ($N = 585$), Kishore R ($N = 456$), and Menasché P ($N = 410$) had more than 400 citations, indicating their significant contributions to the field. Co-citation analysis of authors can reveal international collaboration and influence among researchers. Table 4 shows the top 10 co-cited authors. Similarly, VOSviewer visualized co-cited authors with more than 20 citations and divided them into four clusters (Fig. 4A). Each cluster represents the close collaborative relationships within that group. Based on the clustering results, Zhang Y, Wang XH, Barile L, and Davidson SM may be the most influential members of their respective international research communities.

Research on exosomes in HF has been published in 261 journals. Table 5 lists the top 10 journals by publication volume and their latest 2023 JCR classification. *International Journal of Molecular Sciences* ($N = 28$) and *Frontiers in Cardiovascular Medicine*

Table 3

Top 10 authors of publications, total citations, and H-index

Rank	Author	Publications	Total citations	H-index
1	Wang L	14 (2.443%)	390	8
2	Wang Y	12 (2.094%)	336	7
3	Kishore R	8 (1.396%)	456	5
4	Marbán E	8 (1.396%)	585	8
5	Menasché P	8 (1.396%)	410	7
6	Zhang JY	8 (1.396%)	285	7
7	Zhang Y	8 (1.396%)	272	6
8	Li X	7 (1.222%)	71	4
9	Li Y	7 (1.222%)	60	4
10	Xu B	7 (1.222%)	162	6

(*N* = 46) had the largest number of publications, while the 8th to 10th ranked journals published 10-15 articles, respectively. These journals are well-known in the fields of cardiovascular, biomedical, and multidisciplinary research. Co-citation analysis of journals can reveal the relationship and influence of journals. Table 6 shows the top 10 co-citation journals. In terms of total citations, *Circulation Research* (*N* = 2634), *Circulation* (*N* = 1823), *Cardiovascular Research* (*N* = 1102), and *PLOS ONE* (*N* = 1005) each had more than 1000 citations. VOSviewer visualized journals with more than 20 co-citations and divided them into six clusters (Fig. 4B). Each cluster represents journals in closely related fields. The yellow cluster is the largest, representing cardiovascular journals including *Circulation Research*, *Journal of the American College of Cardiology*, and *Circulation*. The red cluster has several nodes pointing to comprehensive journals such as *Proceedings of the National Academy of Sciences* and *PLOS ONE*. The blue cluster is mainly related to stem cell and exosome research, represented by *Journal of Extracellular Vesicles* and *Stem Cell Research & Therapy*. The green cluster is related to biomedical journals such as *Theranostics* and *Cardiovascular Research*. The light blue cluster involves pathology, while the purple cluster is mainly related to clinical medicine.

Keywords analysis of clusters and bursts

Keyword analysis provides valuable insights into the research hotspots of exosomes in HF studies. Table 7 lists the top 20 keywords, with "Exosomes" (*N* = 301), "Extracellular vesicles" (*N* = 204), and "Heart-failure" (*N* = 200) being the most frequently occurring. These keywords can be further categorized into two major groups: Exosome-mediated cellular interaction mechanisms following HF caused by various diseases. This includes keywords such as "Myocardial-infarction," "Acute myocardial infarction," "Cardiomyocytes," "Expression," "MicroRNAs," "Inflammation," "Angiogenesis," and "Cells." Therapeutic mechanisms involving stem cells and exosomes, with keywords like "Therapy," "Progenitor cells," "Stem-cells," "MicroRNA," and "Mechanisms." Co-occurrence analysis of these keywords reveals research directions and hotspots in the study of exosomes in HF, thus enhancing the clarity and success rate of specific research endeavors. Figure 5A illustrates the keyword network visualized through VOSviewer, which identifies seven clusters encompassing the mechanisms of HF, miRNAs and proteins within exosomes, intercellular communication, and the therapeutic potential of exosomes in HF. Figure 5B presents a more detailed cluster analysis of keywords using CiteSpace, highlighting a total of 11 clusters. Each cluster represents a representative summary of the keyword. Noteworthy clusters include "stem cell," "biomarker," "extracellular vesicle," "oxidative stress," and "cardiac hypertrophy." The network clustering diagram (Fig. 5C) marks the initial appearance of each keyword, followed by the frequency of subsequent occurrences, demonstrating the evolution of each cluster. Clustering analysis of the keywords is conducted to generate clustering modules. Then, the keywords within each cluster are sorted in chronological order based on their year of first appearance, forming a timeline chart for the clusters. Currently, the most prominent clusters are #0 "cardiac hypertrophy," #1 "cardiac regeneration," followed by #2 "biomarker" and #3 "extracellular vesicles." Burst analysis of keywords reveals trends in their popularity and temporal distribution (Fig. 5D). The red line segments indicate the duration of high-frequency occurrence for the keyword, while "strength" represents the frequency of the keyword's occurrence. Early bursts (2010-2016) focused on exosome-mediated cellular interactions within endothelial and cardiac cells. Mid-term bursts (2016-2019) centered on exosomes secreted by mesenchymal stem cells (MSCs) for the treatment of HF. In recent years (2019-2024), bursts have concentrated on the mechanisms by which exosomes improve cardiac cell fibrosis and cardiac function.

Table 4

Top 10 co-cited authors of total citations

Rank	Author	Citations	Total link strength
1	Barile L	179	5,668
2	Lai RC	147	3,997
3	Wang XH	136	4,108
4	Bang C	125	3,621
5	Ibrahim S	122	3,929
6	Sahoo S	111	3,365
7	Zhang Y	111	3,110
8	Thery C	108	3,070
9	Khan M	102	3,224
10	Wang Y	94	2,753

Table 5

Top 10 journals of publications, JCR

Rank	Countries	Publications	JCR (2022)
1	International Journal of Molecular Sciences	28 (4.878%)	Q1
2	Frontiers in Cardiovascular Medicine	26 (4.530%)	Q2
3	Cells	13 (2.265%)	Q2
4	Journal of Molecular and Cellular Cardiology	11 (1.916%)	Q1
5	American Journal of Physiology Heart and Circulatory Physiology	10 (1.742%)	Q1
6	Circulation Research	10 (1.742%)	Q1
7	Frontiers in Cell and Developmental Biology	10 (1.742%)	Q2
8	Frontiers in Cell and Developmental Biology	10 (1.742%)	Q1
9	Frontiers in Physiology	10 (1.742%)	Q2
10	Journal of Cellular and Molecular Medicine	10 (1.742%)	Q2

Highly cited publications and references analysis

Table 8 lists the top 10 most-cited publications in this area. Among them, the study by Jia, GH *et al*, titled "Diabetic Cardiomyopathy:

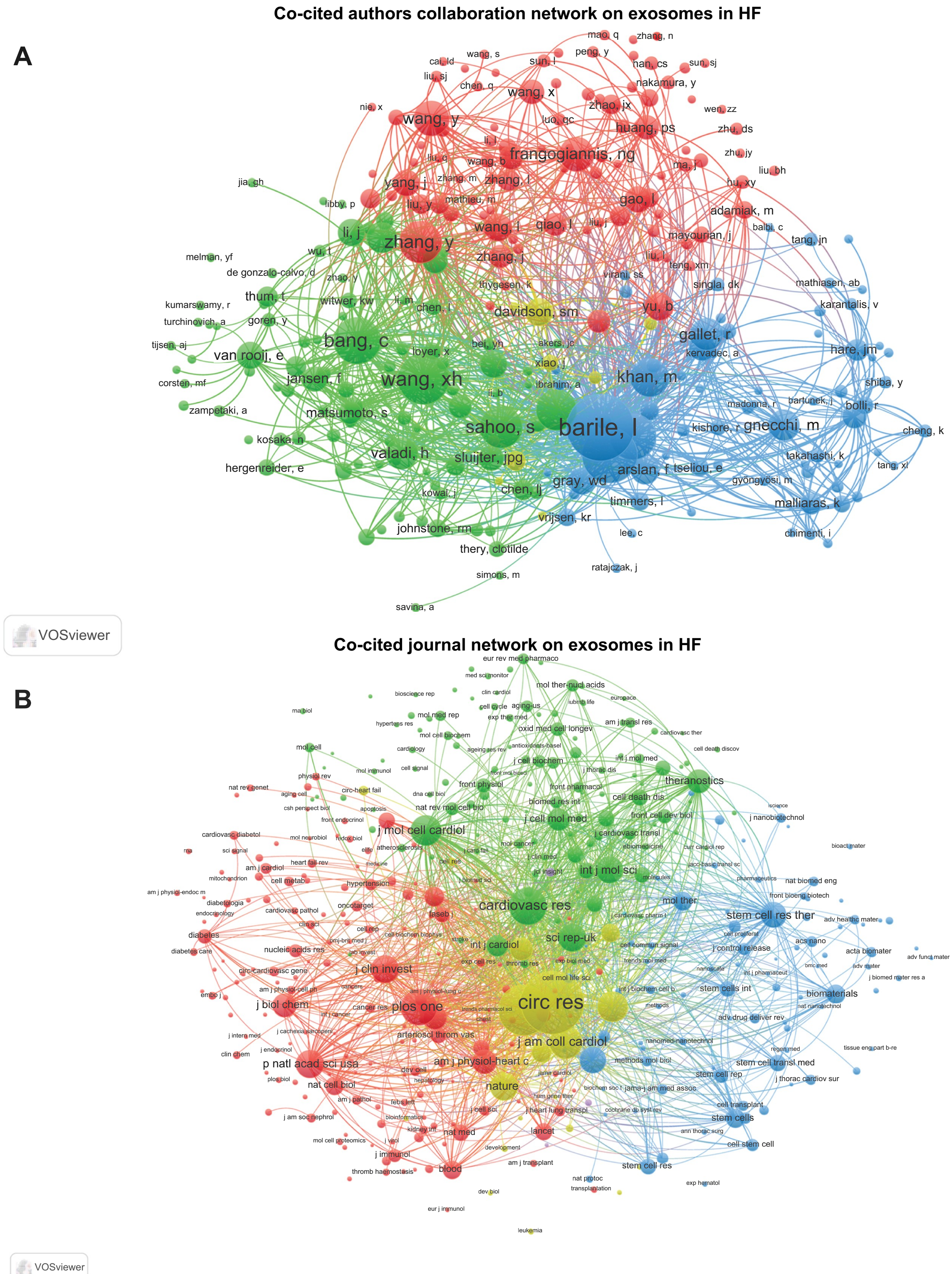

Figure 4. Visualization of co-authors and co-cited journals. (A) Co-cited authors collaboration network on exosomes in HF. (B) Co-cited journal network on exosomes in HF.

An Update of Mechanisms Contributing to This Clinical Entity," has been cited 1052 times. This work highlights alterations in adenosine monophosphate-activated protein kinase, peroxisome proliferator-activated receptors, O-linked N-acetylglucosamine, protein kinase C, microRNA, and exosome pathways during the progression of HF due to diabetic cardiomyopathy. The second most-cited publication, by Creemers, EE *et al* (2012), "Circulating microRNAs: novel biomarkers and extracellular communicators in cardiovascular disease?" explored the potential of miRNAs as novel diagnostic markers in the cardiovascular system, underscoring the crucial role of exosomes in intercellular communication.

Co-cited references analysis of exosome-related publications in HF research provides insights into the field's key publications. Table 9 presents the top 10 co-cited references in this field, most of which focus on studies where exosomes derived from various cell types mitigate myocardial injury and improve cardiac function via miRNAs. Through VOSviewer analysis of the interconnectedness of these cited articles, we identified three major international collaboration clusters (Fig. 6A). Key references include the studies by Ibrahim AGE in 2014, Gallet R in 2017, and Bang C in 2014. CiteSpace's keyword cluster analysis of cited references revealed 15 keyword clusters, such as "non-coding RNA," "mesenchymal stem," "circulating RNA" (related to exosome source cells and contents), and "myocardial regeneration," "cardiovascular diseases" (related to the causes and symptoms of HF) (Fig. 6B). Clustering analysis of the co-cited references is conducted to generate clustering modules. Then, the co-cited references within each cluster are sorted in chronological order based on their year of first appearance, forming a timeline chart for the clusters (Fig. 6C). Temporal analysis further shows that "myocardial regeneration," "non-coding RNA," "mesenchymal stem," and "circulating RNA" are the most frequently co-occurring keywords. Analyzing the burst of co-cited references helps identify emerging topics and their duration in exosome research within HF studies (Fig. 6D). The red line segments indicate the duration of high-frequency occurrence for the co-cited references, while "strength"

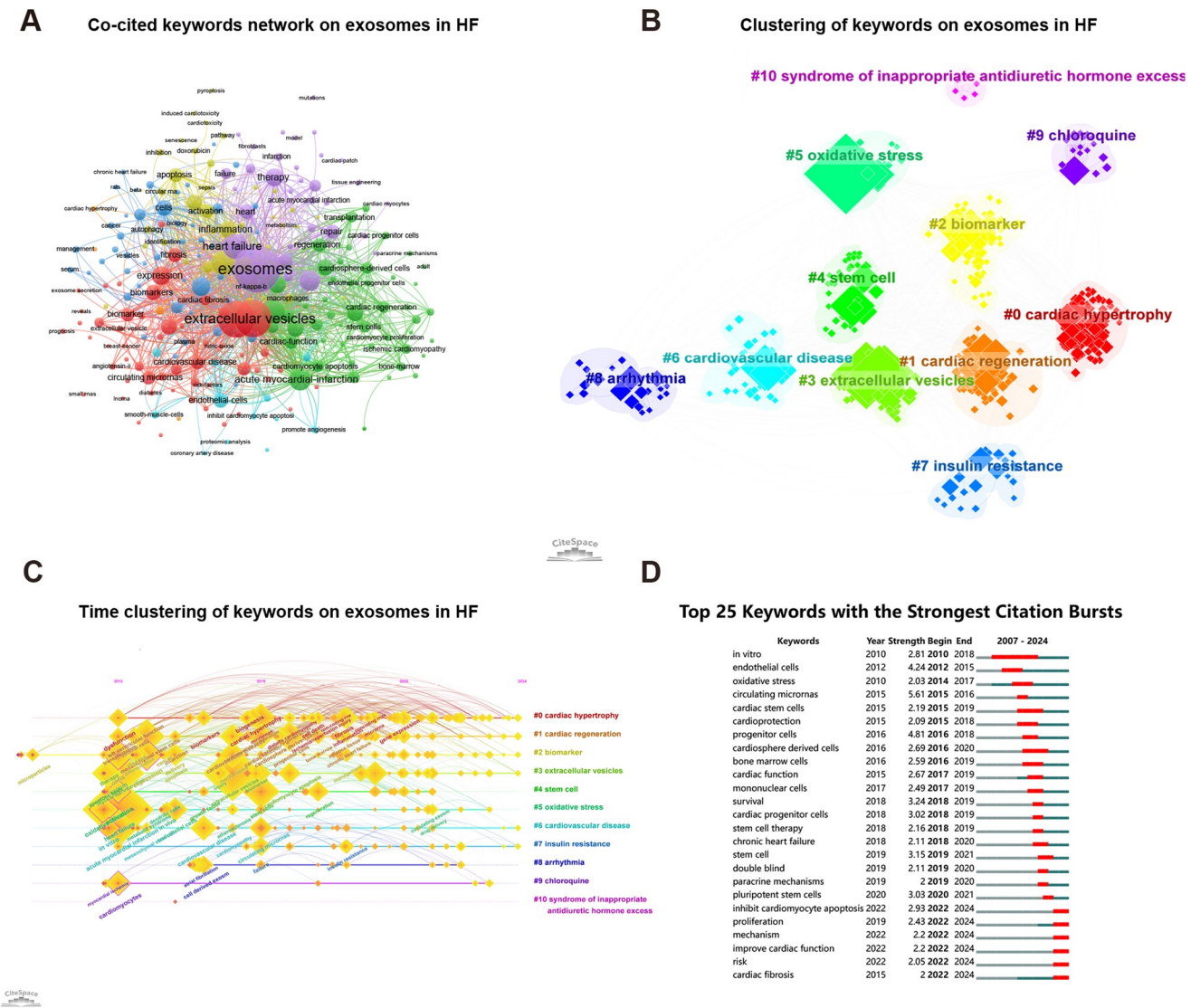

Figure 5. Hot keywords on exosomes in HF. (A) Co-cited network on exosomes in HF by VOSviewer. (B) Clustering on exosomes in HF keywords by CiteSpace. (C) Time clustering on exosomes in HF by CiteSpace. (D) Top 25 keywords with the strongest citation burst by CiteSpace.

Table 6

Top 10 co-cited journal of total citations

Rank	Journal	Total citations	Total link strength	JCR (2023)
1	Circulation Research	2,634	258,557	Q1
2	Circulation	1,823	181,936	Q1
3	Cardiovascular Research	1,102	121,934	Q1
4	PLOS one	1,005	100,623	Q1
5	Journal of the American College of Cardiology	870	87,719	Q1
6	European Heart Journal	776	78,004	Q1
7	Journal of Molecular and Cellular Cardiology	764	84,378	Q1
8	PNAS	675	69,290	Q1
9	Scientific Reports	668	72,201	Q1
10	Nature	666	71,167	Q1

represents the frequency of the co-cited references 's occurrence. Most of the prominent research was concentrated between 2014 and 2020. Notably, Khan M's 2015 study, "Embryonic stem cell-derived exosomes promote endogenous repair mechanisms and enhance cardiac function following myocardial infarction," stands out for its investigation into the therapeutic mechanism where embryonic stem cell-derived exosomes deliver miR290-295 to cardiac progenitor cells, enhancing cardiac regeneration.

Discussion

Research trend of exosomes in heart failure

The number of publications and citations related to exosomes in the field of HF has seen rapid growth (Fig. 2). It is noteworthy that while China leads in the number of publications, it still lags behind the United States in terms of citation counts, H-index, and the strength of research institutions (Fig. 3). Most of these publications originate from China and the United States, likely due to the intense competition between the two countries in stem cell research, with exosomes secreted by stem cells considered a promising approach for HF treatment. Significant support is provided by the National Institutes of Health (NIH) and the National Heart, Lung, and Blood Institute (NHLBI) in the United States, as well as China's "National Key R&D Program" and various innovation funds. Besides, CVD is a major public health issue in both countries, and exosomes have garnered widespread attention as potential diagnostic and therapeutic markers due to their role in intercellular communication. However, this geographic concentration also poses limitations, including: limited involvement of smaller research institutions in other regions, a lack of focus on specific needs of other populations and regions, and high research barriers that can impede clinical translation.

Table 7

Top 20 keywords of publications

Rank	keywords	Counts	Rank	keywords	Counts
1	Exosomes	301	11	Therapy	60
2	Extracellular vesicles	204	12	Angiogenesis	59
3	Heart-failure	200	13	Inflammation	59
4	Heart failure	106	14	Progenitor cells	53
5	Exosome	97	15	Stem-cells	53
6	Myocardial-infarction	93	16	MicroRNA	52
7	Acute myocardial infarction	85	17	Mesenchymal stem cells	51
8	Myocardial infarction	75	18	Cells	49
9	MicroRNAs	66	19	Mechanisms	48
10	Expression	66	20	cardiomyocytes	47

Interestingly, the *International Journal of Molecular Sciences* has published the most research on exosomes and HF, while the other top 10 journals in terms of publication volume are ranked in Q1 or Q2 of the JCR (Table 5). Revolutionary discoveries or more impactful publications in this field are often found in top cardiovascular journals such as *Circulation Research, Circulation*, and *Cardiovascular Research*, highlighting the growing attention on exosomes in the exploration of mechanisms, biomarkers, and therapeutic developments for CVDs (Table 6). This suggests that for clinical researchers to publish high-quality findings, more in-depth exploration of exosome therapeutic mechanisms or additional foundational experiments to validate the functions of exosome contents are needed. A co-occurrence analysis of keywords (Fig. 5) from the 574 included publications revealed that exosomes are recognized as biomarkers for HF caused by various etiologies. Clustering and burst analyses using VOSviewer and CiteSpace suggest that the therapeutic mechanisms of exosomes may involve cardiac regeneration, reduction of oxidative stress, inflammation, and anti-apoptotic effects. Subsequent clustering and burst analyses of the references indicate that high-quality and influential co-cited references were generally published between 2014 and 2020 (Fig. 6). Most of these papers focus on the biology of exosomes, their functions, and the preclinical evaluation of their therapeutic potential in CVDs. For example, a seminal paper by Ruenn Chai Lai *et al*, published in 2010, demonstrated that MSCs mediate their cardioprotective paracrine effects via exosome secretion[19]. Similarly, a 2015 study by Mohsin Khan *et al* showed that exosomes derived from embryonic stem cells enhance neovascularization, improve cardiomyocyte survival, and reduce post-infarction fibrosis[20]. In summary, current research on exosomes in HF can be categorized into three main areas, providing valuable insights for clinicians and clinical researchers: exploring the therapeutic potential of exosomes derived from MSCs, identifying high-quality exosomal biomarkers for HF, and investigating the role of exosomes in cellular communication within HF.

Advances in the study of exosomes in heart failure

HF often represents the terminal stage of various CVDs, including coronary artery disease, valvular heart disease, hypertension, and arrhythmogenic cardiomyopathy, which typically manifest after years of disease progression[21-23]. HF imposes a significant societal burden, with total healthcare costs in the United States projected to rise from $20.9 billion in 2012 to $53.1 billion by 2030[1]. Exosomes were first discovered in 1946 in platelet-free serum and have since been identified in the supernatants of various types of living cells. EVs are generally classified into three categories based on their size: apoptotic bodies (200 to 5000 nm in diameter), microvesicles (100 to 800 nm), and exosomes (30 to 150 nm)[24]. Exosomes, which contain RNA, DNA, proteins, and metabolites, are derived from cells through exocytosis. They are taken up by target cells, facilitating the

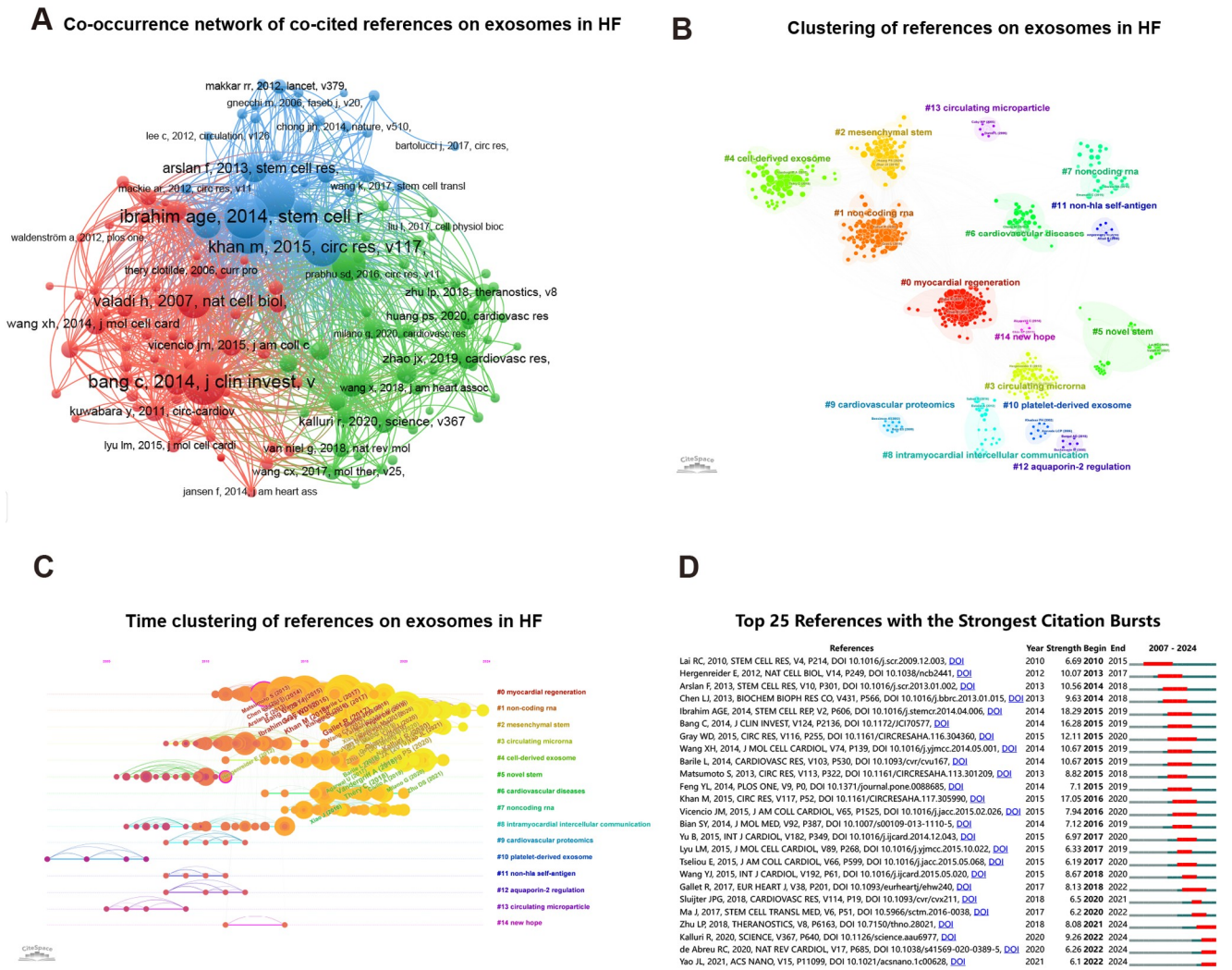

Figure 6. Hot references on exosomes in HF. (A) Co-occurrence network of co-cited references on exosomes in HF by VOSviewer. (B) Clustering of references on exosomes in HF. (C) Time clustering of references on exosomes in HF by CiteSpace. (D) Top 25 references with the strongest citation bursts by CiteSpace.

transfer of biological signals between cells locally or over long distances[25]. Exosomes present a unique opportunity to explore cellular communication mechanisms in HF, and they can also serve as biomarkers, vaccines, and drug delivery vehicles, opening new avenues for therapeutic interventions and prognostic targets in HF (Table 10)[26].

Advances in the study of exosomes derived from MSCs

Recent studies have shown that exosomes derived from MSCs can accumulate in the heart and vasculature, exerting significant inhibitory effects on apoptosis, inflammation, and cardiac remodeling, while promoting angiogenesis during tissue repair (Fig. 7)[27,28]. Abha Banerjee *et al* found that MSC-Exo can increase IL-10 secretion and M2 polarized macrophages, playing a significant role in alleviating diabetes-induced cardiomyopathy[29]. Fang Yan *et al* discovered that miR–129-5p carried by MSC-derived exosomes inhibits tumor necrosis factor receptor-associated factor 3 (TRAF3) expression, thereby reducing apoptosis and oxidative stress in HF[30]. Yuto Nakamura *et al* found that adiponectin stimulation of MSCs increases exosome release, enhancing the therapeutic effects in a mouse model of pressure-overload-induced HF[31]. Additionally, strategies such as utilizing biomaterial carriers, modifying exosomes with cell membranes, and other optimization techniques have been shown to enhance the retention and therapeutic efficacy of MSC-derived exosomes in damaged cardiac tissue[32,33]. For instance, cardiac fibrosis is recognized as a major cause of mortality in HF. Jianping Yuan *et al* developed a microneedle patch loaded with exosomes containing miR-29b to prevent post-myocardial infarction cardiac fibrosis[34]. George Cheng and colleagues embedded MSC-derived exosomes into a hyaluronic acid hydrogel to create and test an injectable ExoGel. The ExoGel therapy reduced the pericardial cavity size and preserved wall thickness in a rat model of transverse aortic constriction (TAC)-induced HF[35]. Yan et al incorporated human endometrial MSC-derived exosomes (hEMSC-Exo) into a polypyrrole-chitosan (PPY-CHI) matrix enhances the regenerative potential of this conductive biomaterial, resulting in an injectable hydrogel with

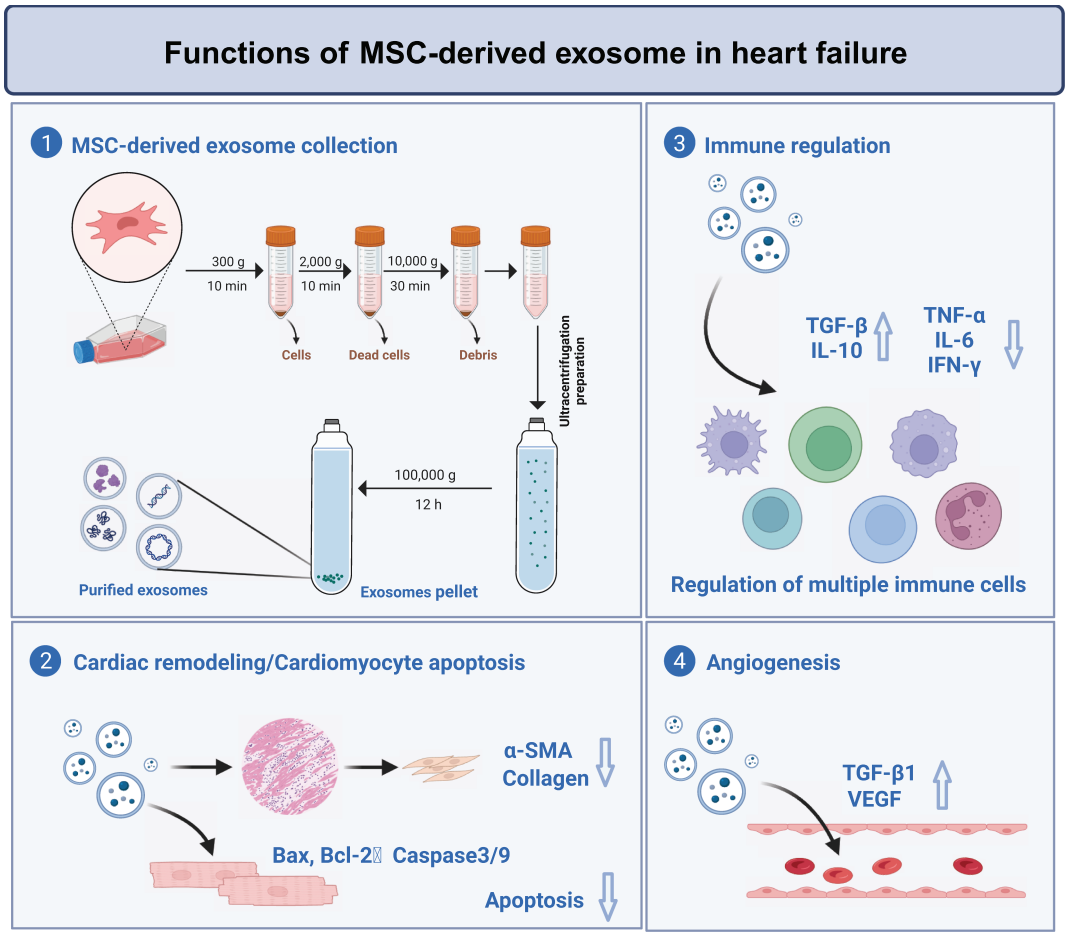

Figure 7. Function of MSC-derived exosomes in the treatment of heart failure. Exosomes can be isolated from mesenchymal stem cell supernatant by gradient centrifugation. Exosomes are secreted into the bull's eye and blood vessels, exerting a significant inhibitory effect on cardiomyocyte apoptosis, immune cell infiltration and cardiac remodeling, and promoting angiogenesis during tissue repair. The figure was created by BioRender (www.biorender.com).

therapeutic benefits. The PPY-CHI/hEMSC-Exo hydrogel combines the cardiac regenerative capacity of hEMSC-Exo with the conductive properties of PPY-CHI, improving cardiac function by promoting angiogenesis, inhibiting apoptosis, and resynchronizing electrical conduction[36].

Advances in studying exosomes as biomarkers in heart failure

Another significant contribution of exosomes in HF is their potential as biomarkers, offering new tools for the diagnosis and treatment of HF. For example, in 2018, Tao Wu *et al* identified circulating exosomal miR-92b-5p as negatively correlated with left ventricular fractional shortening and left ventricular ejection fraction, while positively correlated with left atrial diameter, left ventricular diastolic diameter, and left ventricular systolic diameter, making it a diagnostic marker for patients with reduced ejection fraction HF[37]. Cardiac fibrosis, a hallmark of pathological cardiac remodeling in HF patients, has also been linked to specific exosomal biomarkers. Lu Wang *et al* discovered that the levels of miR-425 and miR-744 in plasma exosomes could potentially serve as biomarkers for predicting cardiac fibrosis and HF[38]. Additionally, exosomes hold promise as screening indicators in various diseases and complications in pre-clinical and clinical trials[39]. In HF induced by diabetes, Jiung-Pang Huang *et al* identified that exosomal microRNAs miR-30d-5p and miR-126a-5p are associated with HF with preserved ejection fraction (HFpEF) and could serve as non-invasive diagnostic biomarkers[40]. In a 2024 study involving 12 HF patients with or without depression, Ruting Wang found that miR-144-3p, identified through serum exosomal RNA screening, is a potential biomarker for diagnosing HF with depression syndrome[41]. Another study found a correlation between the exosomal miRNA profile and patients with chronic heart failure (CHF) and hyperuricemia (HUA). Elevated exosomal miR-27a-5p combined with decreased exosomal miR-139-3p may serve as a novel molecular marker for the precise diagnosis of CHF with coexisting HUA[42].

Research progress on the role of exosomes in intercellular communication in heart failure

During the progression of CVDs, exosomes play a crucial role in intercellular communication, transporting proteins, lipids, non-coding RNAs, and mRNAs, thereby influencing angiogenesis and myocardial regeneration[43]. In the process of cardiac fibrosis, various types of cells can secrete exosomes that regulate the biological behavior of fibroblasts by activating or inhibiting

Table 8

Top 10 cited publications

Rank	Title	Journal	Author	JCR (2023)	Citations
1	Diabetic Cardiomyopathy: An Update of Mechanisms Contributing to This Clinical Entity	Circulation Research	Jia, GH	Q1	1,052
2	Circulating MicroRNAs Novel Biomarkers and Extracellular Communicators in Cardiovascular Disease?	Circulation Research	Creemers, EE	Q1	826
3	Cardiac fibroblast-derived microRNA passenger strand-enriched exosomes mediate cardiomyocyte hypertrophy	Journal of Clinical Investigation	Bang, C	Q1	783
4	Exosomes Mediate the Cytoprotective Action of Mesenchymal Stromal Cells on Hypoxia-Induced Pulmonary Hypertension	Circulation	Lee, C	Q1	622
5	Diabetic cardiomyopathy: a hyperglycaemia- and insulin-resistance-induced heart disease	Diabetologia	Jia, GH	Q1	509
6	Circulating Extracellular Vesicles in Human Disease	New England Journal of Medicine	Shah, R	Q1	459
7	Mesenchymal stem cell exosome: a novel stem cell-based therapy for cardiovascular disease	Regenerative Medicine	Lai, RC	Q3	434
8	Plasma Exosomes Protect the Myocardium from Ischemia-Reperfusion Injury	Journal of The American College of Cardiology	Vicencio, JM	Q1	415
9	Blockade of exosome generation with GW4869 dampens the sepsis-induced inflammation and cardiac dysfunction	Biochimica Et Biophysica Acta-Molecular Basis of Disease	Essandoh, K	Q1	316
10	Enabling a robust scalable manufacturing process for therapeutic exosomes through oncogenic immortalization of human ESC-derived MSCs	Journal of Translational Medicine	Chen, TS	Q1	291

intracellular signaling pathways through their contents. A comprehensive understanding of the interactions between fibroblasts and other cell types during cardiac remodeling will be key to developing breakthrough therapies[44]. In a 2024 study, Vandana Mallaredy found that circulating plasma exosomes increase significantly following HF, contributing to left ventricular dysfunction, cardiac hypertrophy, and fibrosis. This phenomenon may be due to the elevated expression of serum miR-331-5p post-HF, which promotes fibroblast-to-myofibroblast transition by targeting homeobox protein hox-C8, a key regulator of fibrosis[23]. Lei Zhao *et al* studied tRNA-derived small RNAs in the epicardial adipose tissue of HF patients, identifying tRF-Tyr-GTA-010 and tRF-Tyr-GTA-011 as potential regulators of sphingolipid and adrenergic signaling pathways through targeting genes that primarily promote calcium ion transport, potentially exerting protective effects[45]. Recent research has also found that exosomes from M2 macrophages can reverse the decline in cardiac function in diet-induced myocardial infarction mice by inhibiting type I interferon signaling in bone marrow cells[46]. Furthermore, myocardial injury during HF triggers fibrosis. Yuling Xu *et al* discovered that limb bud and heart expression in cardiomyocytes is upregulated under hypoxic conditions and promotes cardiac fibroblast activation via exosome secretion[47].

Table 9

Top 10 co-cited references

Rank	Title	Journal	Author	JCR (2023)	Citations
1	Cardiac fibroblast-derived microRNA passenger strand-enriched exosomes mediate cardiomyocyte hypertrophy	Journal of Clinical Investigation	Bang C	Q1	112
2	Exosomes as critical agents of cardiac regeneration triggered by cell therapy.	Stem Cell Reports	Ibrahim AGE	Q1	110
3	Exosome secreted by MSC reduces myocardial ischemia/reperfusion injury.	Stem Cell Research	Lai RC	Q4	101
4	Embryonic stem cell-derived exosomes promote endogenous repair mechanisms and enhance cardiac function following myocardial infarction.	Circulation Research	Khan M	Q1	97
5	Extracellular vesicles from human cardiac progenitor cells inhibit cardiomyocyte apoptosis and improve cardiac function after myocardial infarction.	Cardiovascular Research	Barile L	Q1	85
6	Exosomes secreted by cardiosphere-derived cells reduce scarring, attenuate adverse remodelling, and improve function in acute and chronic porcine myocardial infarction.	European Heart Journal	Gallet R	Q1	85
7	Exosome-mediated transfer of mRNAs and microRNAs is a novel mechanism of genetic exchange between cells.	Nature Cell Biology	Valadi H	Q1	85
8	Identification of therapeutic covariant microRNA clusters in hypoxia-treated cardiac progenitor cell exosomes using systems biology.	Circulation Research	Gray WD	Q1	71
9	Mesenchymal stem cell-derived exosomes increase ATP levels, decrease oxidative stress and activate PI3K/Akt pathway to enhance myocardial viability and prevent adverse remodeling after myocardial ischemia/reperfusion injury.	Stem Cell Research	Arslan F	Q4	68
10	Circulating p53-responsive microRNAs are predictive indicators of heart failure after acute myocardial infarction.	Circulation Research	Matsumoto S	Q1	57

Table 10

Role of exosomes in heart failure

Type of Exosomes	Component	Biological function	Roles of exosomes	Year	References
Human iPSC	Exosomes loaded with Nec-1	Exosomes carrying Nec-1 alleviate oxidative stress and mitochondrial dysfunction in HF by targeting the PARP1/AIFM1 axis.	Treatment of HF	2024	[31]
Rat bone marrow	Hsp27	EVs from STZ-induced type 1 diabetic rats contained lower levels of Hsp27. Overexpression of Hsp27 in MSCs effectively improved STZ-induced heart failure in rats.	Treatment of HF; Prognostic markers of HF	2024	[32]
Mouse bone marrow fibroblast progenitor cells	miR-21a-5p	Exacerbating cardiac fibrosis via the miR-21a-5p/ITGAV/Col1 α signaling pathway.	Mechanism studies	2024	[33]
Mouse blood	miR-331-5p	miR 331-5p targets HOXC8, a key regulator of fibrosis.	Treatment of HF	2024	[34]
Human bone marrow	NA	Inhibits ferroptosis and restores cardiac function in myocardial tissue by regulating the UL3/Hippo pathway.	Prognostic markers of HF	2024	[35]
Human blood	miR-144-3p	miR-144-3p is a potential biomarker for diagnosing depression in HF patients.	Prognostic markers of HF	2024	[36]
Human blood	BDNF	BDNF is a potential biomarker for HF with cognitive impairment.	Prognostic markers of HF	2024	[37]
Mouse fat	NA	Increase ATP levels, block myocardial cell apoptosis, and enhance cardiac function.	Treatment of HF	2023	[38]
Human epicardial adipose tissue	tRF-Tyr-GTA-010 and tRF-Tyr-GTA-011	Protective effect by modulating sphingolipid and adrenaline signaling pathways by targeting genes that promote calcium transport.	Mechanism studies	2023	[39]
Human blood	92 types miRNA	92 differentially expressed miRNAs in patients with DCM-HF patients.	Mechanism studies	2023	[40]
Mouse fibroblasts	NA	Long-term low-dose SFN treatment of fibroblasts enhances the release of anti-remodeling cardiomyocyte and effectively prevents the onset of HF.	Mechanism studies	2023	[41]
Mouse blood, cardiomyocytes	miR-22-3p	Exosomes secreted by cardiomyocytes inhibit tumor ferroptosis sensitivity in ischemic HF.	Mechanism studies	2023	[42]
Rat bone marrow	NA	Attenuating cardiomyocyte apoptosis and inflammatory responses by inactivating the Hippo-YAP pathway in HF.	Treatment of HF	2023	[43]
Rat blood	AGT, renin, and ACE	SHR Exosome induced hypertrophy of H9c2 cells.	Mechanism studies	2023	[44]
Mouse fibroblasts	miR-29b	Microneedle patch containing exosomes containing miR-29b improves cardiac fibrosis.	Mechanism studies	2023	[29]
Mouse myocardium	miR-494-3p	Cardiomyocyte pressure overload produces exosomes containing miR-494-3p and promotes myocardial fibrosis	Mechanism studies	2023	[45]
Rat blood	NA	Exosomes induced by ischemic preconditioning from normal rats can restore cardioprotection in heart failure after myocardial infarction.	Mechanism studies	2023	[46]
Mouse cardiomyocytes	NA	LBH upregulation of cardiomyocytes under hypoxia promotes cardiac fibroblast activation via exosome secretion.	Mechanism studies	2022	[47]
Rat blood	miR-22-3p	miR-22-3p in exosomes increases the risk of HF after downregulating FURIN.	Mechanism studies	2022	[48]
Rat blood	miR-30d-5p and miR-126a-5p	miR-30d-5p and miR-126a-5p were consistently associated with significant decreases in exosome expression, cardiac expression, and cardiac output.	Prognostic markers of HF	2022	[49]
Human blood	miR-27a	The survival rate of patients with high miR-27a expression was significantly higher than that of patients with low expression.	Prognostic markers of HF	2022	[50]
Mouse bone marrow	miR-129-5p	miR-129-5p protects the heart from failure by targeting TRAF3 and subsequent NF-κB signaling.	Treatment of HF	2022	[25]
NA	NA	ExoGel was injected into the pericardial cavity of rats with heart failure. ExoGel therapy reduced LV cavity size and preserved wall thickness.	Treatment of HF	2022	[30]
Rat blood	miR-214-3p	Enhanced inflammatory response in the RVLM, which may further contribute to sympathetic hyperactivity in HF.	Prognostic markers of HF	2022	[51]
Mouse and human cortical bone stem cells	NA	Exosome contents are involved in fibroblast migration.	Mechanism studies	2021	[52]
Human embryonic stem cells	FGF2	Promoting myocardial angiogenesis to alleviate TAC-induced HF.	Treatment of HF	2021	[53]
Human blood	miR-320a	miR-320a promotes cardiac fibroblast proliferation by regulating PIK3CA/Akt/mTOR signaling pathway.	Prognostic markers of HF	2021	[54]
Rat bone marrow	miR-30e	Inhibit LOX1 expression in rats, downregulate NF-κB p65/Caspase-9 signaling activity in rats, and improve HF.	Treatment of HF	2021	[55]
Human umbilical cord	miR-1246	Targeting PRSS23 and inhibiting the activation of Snail/α-SMA signaling alleviates hypoxia-induced myocardial tissue damage.	Treatment of HF	2021	[56]
Mouse blood	miR-340-3p,miR-3103-3p	Both α-AR and β-AR agonists can alter the small RNA content of circulating blood exosomes.	Mechanism studies	2021	[57]

(*Continued*)

Table 10
(Continued).

Type of Exosomes	Component	Biological function	Roles of exosomes	Year	References
Human blood	miR-31-5p, miR-126-5p, miR-106a-5p, miR-378i and miR-181c-5p	Lower ApoA-I levels are associated with increased risk of HF incidence and HF rehospitalization.	Prognostic markers of HF	2021	[58]
Mouse cortical bone	VEGFA	Production of VEGFA-enriched exosomes that exert excellent pro-angiogenic, anti-fibrotic and cardioprotective effects	Treatment of HF	2021	[59]
Human iPSCs	miR22	Exosomes containing miR22 are a potential source of cardiac recovery.	Treatment of HF	2020	[60]
Human adipose tissue	let-7 family	Relieve left ventricular function, fibrosis, and improve heart function.	Treatment of HF	2020	[26]
Mouse bone marrow	NA	Reduced cardiac hypertrophy and fibrosis.	Treatment of HF	2020	[61]
Human blood	miR-222-3p, miR-497-5p and miR-21-5	miR-222-3p, miR-497-5p, and miR-21-5p, which bind to Ago1, were significantly increased, whereas let-7a-5p was significantly decreased in HF patients.	Prognostic markers of HF	2020	[62]
Human blood	circ_0097435	Involved in regulating myocardial cell injury.	Prognostic markers of HF	2020	[63]
Human cardiac fibroblasts	NA	Inducing a HF phenotype in cardiomyocytes.	Prognostic markers of HF	2019	[64]
Human myocardium	miR -21-5p	miR-21-5p enhances Akt kinase activity by inhibiting phosphatase and tensin homolog.	Mechanism studies	2019	[65]
Human blood	miR-92b-5p	miR-92b-5p can be used as a biomarker for the diagnosis of HFrEF.	Prognostic markers of HF	2018	[66]
Human blood	piR-020009 and piR-006426	piR-020009 and piR-006426 are potential biomarkers for HF	Prognostic markers of HF	2018	[67]
Human plasma, cardiac fibroblasts	miR-425 and miR-744	miR-425 and miR-744 levels may serve as biomarkers for predicting cardiac fibrosis and heart failure.	Prognostic markers of HF	2018	[68]
H9c2 cell supernatant	miR-217	Cardiomyocyte-derived exosomes containing miR-217 enhanced fibroblast proliferation.	Mechanism studies	2018	[69]
Human blood	miR-92b-5p	Serum miR-92b-5p is a potential biomarker for the diagnosis of DCM-HF.	Prognostic markers of HF	2018	[70]
Rat cardiomyocytes, cardiac fibroblasts	miR-27a, miR-28-3p and miR-34a	MI-induced local increase in microRNAs may lead to oxidative stress by inhibiting Nrf2 translation in HF.	Mechanism studies	2018	[71]
Human blood	miR-146a	miR-146a as a biomarker for HF.	Prognostic markers of HF	2017	[72]
Dog blood	miR-9, miR-495 and miR-599	miRNA expression levels are associated with disease states.	Mechanism studies	2017	[73]
Human cardiac fibroblasts	NA	Ang II treatment enhances exosome release by activating AT1R and AT2R	Mechanism studies	2015	[74]
Human pericardial fluid	miR-21-5p, miR-451a, miR-125b-5p, let-7b-5p and miR-16-5p	MicroRNAs can act as paracrine signaling factors by mediating local crosstalk between cardiac cells.	Mechanism studies	2015	[75]
Rat cardiac fibroblasts	miR-21	miR-21 may be a paracrine signaling mediator of cardiomyocyte hypertrophy and has the potential to be a therapeutic target.	Mechanism studies	2014	[76]
Human blood	NO	Cardiodepressant effects of exosomes in sepsis.	Mechanism studies	2007	[77]

ACE: angiotensin converting enzyme; AT1R: Ang II receptor type 1; ATP: Adenosine triphosphate; AGT: angiotensinogen; AGO1: Argonaute RISC Component 1; BDNF: Brain-derived neurotrophic factor; DCM: Dilated cardiomyopathy; FGF2: Fibroblast Growth Factor 2; HFrEF: Heart failure with reduced ejection fraction; HOXC8: Homeobox C8; iPSC: Induced pluripotent stem cells; LV: Left ventricle; LBH: Limb bud and heart; MI: Myocardial Infarction; MSC: Mesenchymal stem cells; NRF2: Nuclear factor erythroid 2-related factor 2; NO: Nitric oxide;NA: Not applicable; REN: renin; RVLM: Rostral ventrolateral medulla; SFN: Sulforaphane; SHR: Spontaneously hypertensive rats; STZ: Streptozocin; SFN: Sulforaphane; TAC: Transverse aortic constriction; TRAF3: Tumor necrosis factor receptor-associated factor 3; VEGFA: Vascular endothelial growth factor A; **β**-AR: Beta-Adrenergic Receptors; **α**-AR: Alpha-Adrenergic Receptors

Clinical implications of exosome research

Exosome-based therapies have the potential to revolutionize HF treatment, shifting conventional approaches toward more precise, personalized, and regenerative methods[48]. First, exosomes serve as biomarkers for precision diagnostics. By carrying specific proteins, miRNAs, and lncRNAs, they can reflect the pathological changes associated with HF, enabling early diagnosis, stratified patient management, and monitoring of therapeutic effectiveness. Secondly, exosomes offer a novel path for regeneration and repair. Exosome-based therapies can deliver growth factors, miRNAs, and other bioactive molecules to damaged cardiac cells, suppress inflammation, and activate cellular repair and regeneration mechanisms[49]. This approach may help restore damaged myocardial tissue, reduce fibrosis, and slow HF progression[50]. Thirdly, current treatments for HF primarily rely on medication and mechanical support; however, these methods cannot reverse myocardial damage and may lead to liver and kidney injury or be limited by the challenges of heart transplants. Stem cell and exosome therapies offer the potential for a more fundamental improvement in HF outcomes[51-53]. Unlike complex stem cell therapies, exosome production and storage are relatively simple, allowing for easier standardization with reduced risks of immune rejection and improved safety profiles, supporting their clinical translation and wider adoption. Exosomes can be delivered via minimally invasive methods, such as intravenous or subcutaneous injection, and even intranasal administration, enhancing patient

adherence[54]. This versatility positions exosome therapy as a promising tool in the future of HF treatment.

Research limitation

It is important to acknowledge certain limitations inherent in bibliometrics. First, due to the constraints of the analysis software, we only collected publications from the WoSCC database. Second, the differing algorithms and procedures of VOSviewer and CiteSpace lead to slight variations in the final results. Third, recently published high-quality studies may not be adequately reflected. Fourth, there was no detailed distinction made regarding the sources of exosomes or the differences introduced by various in vivo models. Fifth, as research on exosomes in the field of HF is gradually emerging, we must acknowledge that the sample size of this study is relatively small. Despite these limitations, this study still provides valuable insights into the application of exosomes in the field of HF.

Conclusions and future directions

In conclusion, through bibliometric analysis based on VOSviewer and CiteSpace, we have constructed a novel knowledge map of exosome research in the field of HF. This field has seen a continuous increase in the number of publications on exosomes in leading international journals, accompanied by growing collaboration and exchange among researchers. In exosome research for HF, the most promising approaches focus on developing novel diagnostic biomarkers, optimizing exosome-based therapies, and exploring the mechanisms of HF involving exosomes.

Future efforts should include large-scale, multicenter clinical studies to validate the specificity and sensitivity of exosomal biomarkers, integrate material science and gene editing to refine therapeutic strategies, and establish interdisciplinary teams of experts in molecular biology, cardiology, and pharmacology to advance the clinical application of exosome-based therapies.

Ethical approval

Not applicable.

Consent

Not applicable.

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Author contributions

H.L.: conceptualization, data curation, formal analysis, writing – original draft; Z.L., Q.F.: data curation; S.F.: conceptualization; T.X.: conceptualization, funding acquisition, writing – review & editing; All authors have read and approved the final version of the manuscript.

Conflicts of interest disclosure

All the authors declare to have no conflicts of interest relevant to this study.

Research registration unique identifying number (UIN)

Not applicable.

Guarantor

Tao Xiang and Shuiqiao Fu.

Provenance and peer review

The paper is not invited.

Data availability statement

The datasets used and/or analyzed during the current study are available from the corresponding author on reasonable request.

Assistance with the study

None.

Presentation

None

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