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ORIGINAL RESEARCH

Knowledge Domain and Emerging Trends in Heart Failure and Anxiety Comorbidity: A Scientometric Analysis

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Objective: The high prevalence of anxiety disorders among heart failure (HF) patients significantly impacts clinical outcomes, yet a comprehensive analysis of the global research landscape is lacking. This study explores research trends, knowledge structure, and emerging hotspots in the field of HF and anxiety comorbidity over the past decade.

Methods: A bibliometric analysis was conducted on 1,475 publications from the Web of Science Core Collection (2015–2024). A total of 1,475 English-language publications, including articles and reviews, were analyzed. CiteSpace and VOSviewer were used to analyze collaboration networks, references, and keywords. The search tool for the retrieval of interacting genes database was applied to construct a protein-protein interaction (PPI) network of HF and anxiety comorbidity. R with clusterProfiler was applied to perform kyoto encyclopedia of genes and genomes pathway enrichment analysis. Cytoscape was applied to visualize both the PPI network and the significant pathways.

Results: Annual publications increased steadily, peaking in 2021. The United States of America and China emerged as the most productive countries. Key contributors included Linkoping University and Harvard Medical School. Keyword analysis revealed evolving focuses from mortality and depression to self-care, cardiac rehabilitation, and psychological assessment tools. Gene intersection analysis identified 124 shared genes, with hub genes such as AKT1, TP53, and IL6 implicated in MAPK, FoxO, and JAK-STAT signaling pathways. These results suggest neuroendocrine and inflammatory mechanisms linking HF and anxiety.

Conclusion: This study offers the bibliometric and molecular insight into the HF and anxiety comorbidity landscape. While research output and mechanistic understanding have grown, gaps remain in standardized assessment and clinical translation. Future studies should focus on translating these mechanistic insights into strategies that improve integrated care and quality of life for patients living with the dual burden of heart failure and anxiety.

Keywords: heart failure, anxiety disorders, bibliometric analysis, gene enrichment, comorbidity

Introduction

Heart failure (HF) affects more than 64 million individuals globally. Studies indicate that approximately half of these patients also experience comorbid anxiety disorders.[1,2] Anxiety complicates HF management by worsening symptoms like dyspnea and fatigue, and is linked to poorer treatment adherence, higher hospitalization rates, and increased all cause mortality.[3,4] Guidelines and studies increasingly focus on the biopsychological framework in vascular care.[5–7]

Extensive research has explored the pathophysiological mechanisms underlying the association between heart failure and anxiety.[8] A range of pharmacological and behavioral interventions including selective serotonin reuptake inhibitors

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have been examined in both interventional and observational studies, with inconsistent findings regarding their safety, efficacy, and durability of effect.[9,10] Previous narrative reviews lack quantitative analysis of the field's evolution. To address this, bibliometrics offers a powerful solution.[11,12] However, existing scientometric studies on heart failure focus on isolated aspects and neglect its comorbidity with anxiety, presenting a critical knowledge gap.[13–15]

This study provides a comprehensive bibliometric analysis of the heart failure and anxiety comorbidity research landscape from 2015 to 2024, a period marking a significant increase in publication activity. It evaluates research productivity, collaboration networks, and and knowledge structure to identify core domains and emerging trends, thereby establishing evidence-based priorities to guide future research and integrated clinical care in psychocardiology.

Materials and Methods

Data Collection and Search Strategy

An advanced search was performed in the Web of Science (WoS) Core Collection database on April 12, 2025. The selection of WoS was based on its high-quality, curated metadata, which is critical for reliable bibliometric analysis, and its established status as a standard data source in the field, ensuring consistency and comparability. The scope was restricted to the WoS Core Collection database, specifically including the Science Citation Index Expanded and the Social Sciences Citation Index. Literature published between January 1, 2015, and December 31, 2024, was included. The search terms used were TS = (Heart Failure) AND TS = (Anxiety), which initially returned 1,619 records. Duplicate records were removed through an automated deduplication process followed by a blinded manual review, where two researchers independently checked the records and resolved any discrepancies through consensus.

After removing conference abstracts, proceedings papers, editorials, book chapters, and retracted publications, only articles and review articles were retained, yielding 1,507 records. A final refinement by language, limited to English, resulted in 1,475 publications, consisting of 1,273 original articles and 202 review articles.

Visualization Analysis

Descriptive statistics, co-occurrence analysis, co-citation analysis, and cluster analysis were carried out using CiteSpace 6.4.R1, VOSviewer 1.6.19, Scimago Graphic 1.0.25, and WPS Excel 2023. Reference and keyword analyses were mainly conducted through CiteSpace. The analysis was performed based on the following settings. The time span was set from January 2015 to December 2024, with each year treated as a separate time slice. For each slice, the top 10 most frequently cited or co-occurring items were selected (k = 10). Network pruning was carried out using Pathfinder, pruning sliced networks, and pruning the merged network. In the resulting visual maps, the size of each node reflected the frequency of publications or citations, while the thickness of the connecting lines represented the strength of the relationships between nodes.

Collaboration networks among journals, cited journals, institutions, countries, authors, and cited authors were analyzed and visualized using VOSviewer. In the resulting network maps, larger node diameters represent higher publication or citation counts, while thicker links indicate stronger co-occurrence relationships. Country collaboration networks were further mapped with Scimago Graphica, based on GML-format data exported from VOSviewer. Descriptive statistical analyses and visualizations, including donut charts, bar graphs, and column charts, were conducted using WPS Excel.

Identification of Comorbid Genes for HF and Anxiety

To identify genes potentially involved in both HF and anxiety disorders, genes related to each condition with a relevance score of 20 or higher were first retrieved from the GeneCards database (https://www.genecards.org/) based on the GeneCards scoring system, aiming to capture genes with a high confidence of association while filtering out less relevant entries. The shared genes between the two disease categories were then determined using the Bioinformatics Online Analysis and Visualization Cloud Platform (http://www.bioinformatics.com.cn/).

Protein-Protein Interaction (PPI) Network Between HF and Anxiety

To construct the PPI network related to the comorbidity of HF and anxiety, the intersecting genes were imported into the STRING database (https://cn.string-db.org/) with the organism set to Homo sapiens and the minimum required interaction score set at high confidence (0.700). Disconnected nodes were excluded from the analysis. The resulting PPI network was then exported in TSV format and visualized using Cytoscape version 3.7.2 (https://cytoscape.org/).

Signaling Pathway Enrichment Analysis of HF and Anxiety Comorbidity

To explore the potential biological mechanisms underlying the comorbidity of HF and anxiety, kyoto encyclopedia of genes and genomes (KEGG) pathway enrichment analysis was conducted on the intersecting genes using R version 4.4.2 and the clusterProfiler package version 4.6.2. The Benjamini-Hochberg method was applied to correct for multiple testing, and only pathways with a false discovery rate (FDR) below 0.05 were considered statistically significant. Pathways directly related to human diseases were excluded from the results. The top 20 enriched pathways were selected and used to construct a gene-pathway regulatory network, which was subsequently visualized in Cytoscape.

Results

Annual Trends in Publications and Citations

Between 2015 and 2024, the number of publications in this field exhibited a generally increasing trend. In the initial phase, publication growth remained modest, with 98 articles in 2015 and an annual output of approximately 100 articles through 2018. A significant increase began in 2019 reaching 146 publications followed by 177 in 2020 and peaking at 200 in 2021 which marked the highest number over the past decade. In the subsequent years, the number of publications slightly decreased to 182 in 2022, followed by a modest recovery to 192 in 2023. As of 2024, a total of 147 articles have been published, indicating sustained research activity in this area (Figure 1).

The number of citations increased steadily and markedly from 2015 to 2024, rising from 92 to 5942. Prior to 2017, citation counts remained relatively low, but a clear upward trajectory became evident starting in 2018. In 2020, citations exceeded 2900, followed by 3988 in 2021 and 4881 in 2022. A modest increase was observed in 2023 with 4897 citations, reaching a peak in 2024. Overall, the rise in citation frequency generally mirrored the growth in publication output, although the rate of increase in citations became more pronounced in recent years as shown in Figure 1.

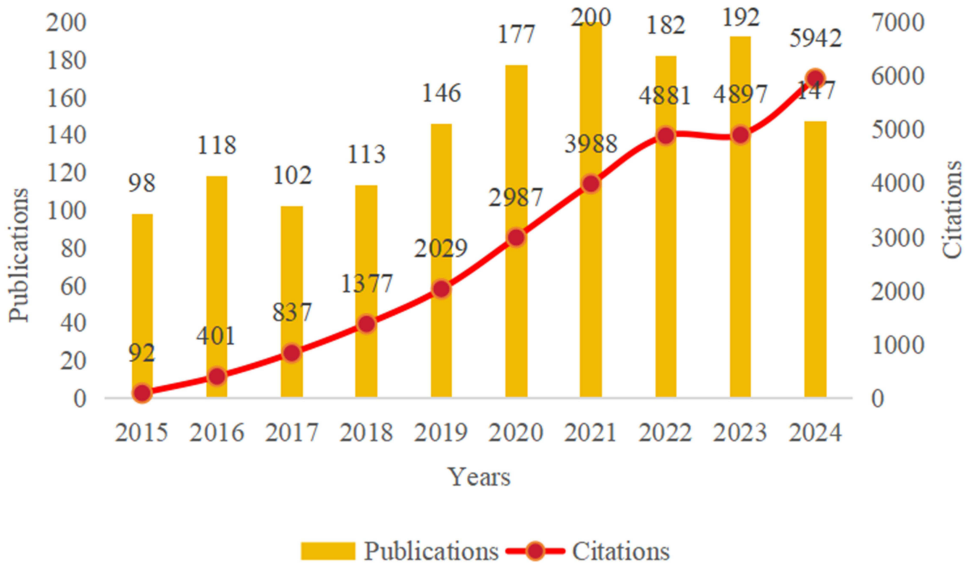

Figure 1 Time Sequence of Relevant Papers of all Types of Publications and Citations on Heart Failure and Anxiety Comorbidity Published from 2015 to 2024 in Web of science (WoS).

Journal Collaboration Network and Publication Overview

Analysis of the journal collaboration network using VOSviewer reveals that *European Journal of Cardiovascular Nursing, Journal of Cardiovascular Nursing, PLOS ONE*, and *Medicine* occupy central positions in the research landscape, indicated by their prominent node sizes and strong interconnections (Figure 2A). In terms of publication output, *European Journal of Cardiovascular Nursing* leads with 57 articles, followed by *Journal of Cardiovascular Nursing* (44 articles), *PLOS ONE* and *Heart & Lung* (32 articles each), and *Medicine* (27 articles). Overall, scholarly contributions are concentrated in a limited number of high-output journals, reflecting their pivotal role in disseminating research within this field (Table 1).

Among the top 10 journals by publication volume, *PLOS ONE* exhibited the highest average citations per article (18.22), followed by *Medicine* (16.30) and the *Journal of Cardiac Failure* (15.32). In terms of journal impact factor, the *Journal of Cardiac Failure* ranked first (IF = 6.7), followed by the *Journal of Psychosomatic Research* (IF = 3.5) and *ESC Heart Failure* (IF = 3.2) (Figure 2B). With regard to total citations, the *European Journal of Cardiovascular Nursing* led with 827 citations, followed by *PLOS ONE* (583), *Journal of Cardiovascular Nursing* (533), *Medicine* (440), and *Heart & Lung* (421). Notably, despite publishing only 19 articles, the *Journal of Cardiac Failure* demonstrated a remarkable citation impact, with an average of 15.32 citations per article.

Based on the Journal Citation Reports (JCR) classification (Figure 2C), among the top 10 journals, only the *Journal of Cardiac Failure* is ranked in Quartile 1 (Q1). *PLOS ONE, ESC Heart Failure, Journal of Clinical Medicine, BMJ Open*, and *Journal of Psychosomatic Research* fall into Quartile 2 (Q2), while the remaining journals are primarily categorized in Quartile 3 (Q3).

National Collaboration Network and Publication Overview

The national collaboration network generated using CiteSpace demonstrates that the United States of America (USA), China, Germany, the United Kingdom, and Italy occupy central positions in the field, as indicated by their larger node sizes and dense interconnections, which reflect robust international collaboration. The network is organized into six distinct clusters, each representing a separate research community. Cluster 1 (green) is the largest and includes multiple European nations, alongside major contributors such as the USA and China (Figure 3A). The USA has established robust collaborative relationships with several countries, including China, Germany, South Korea, Turkey, the Netherlands, Italy, Brazil, and Malaysia. Serving as the central hub within the global collaboration network, the USA exhibits both the highest frequency and the widest scope of international cooperation (Figure S1).

An analysis of publication trends from 2015 to 2024 shows that the USA consistently leads in the number of publications. China, Germany, the United Kingdom, Italy, Australia, the Netherlands, Sweden, Denmark, and Canada also rank among the top 10 contributing countries. Most of these countries demonstrated an upward trajectory in publication volume, peaking around 2021 (Figure 3B). A comparative analysis of publication trends between the USA and China over the past decade indicates that the USA has consistently maintained a leading position in terms of publication volume. The number of publications from the USA increased from 37 in 2015 to a peak of 64 in 2021, followed by a modest decline in subsequent years, although it remained the most prolific contributor. In contrast, China demonstrated a marked upward trend, with the number of publications rising from 4 in 2015 to a peak of 48 in 2023, and slightly declining to 39 publications in 2024 (Figure 3C).

Institutional Collaboration Network and Publication Overview

The institutional collaboration network, constructed using VOSviewer, reveals that Linköping University, the University of Southern Denmark, Odense University Hospital, the University of Copenhagen, and Harvard Medical School serve as key hubs within the global research landscape. These institutions are represented by larger nodes and exhibit dense interconnections, indicating their pivotal role in driving international collaboration in this field (Figure 4A). Cluster analysis further delineates distinct groups of inter-institutional partnerships. The green cluster—the largest—comprises Linköping University, Karolinska Institutet, and the University of Kentucky. The yellow cluster includes the University

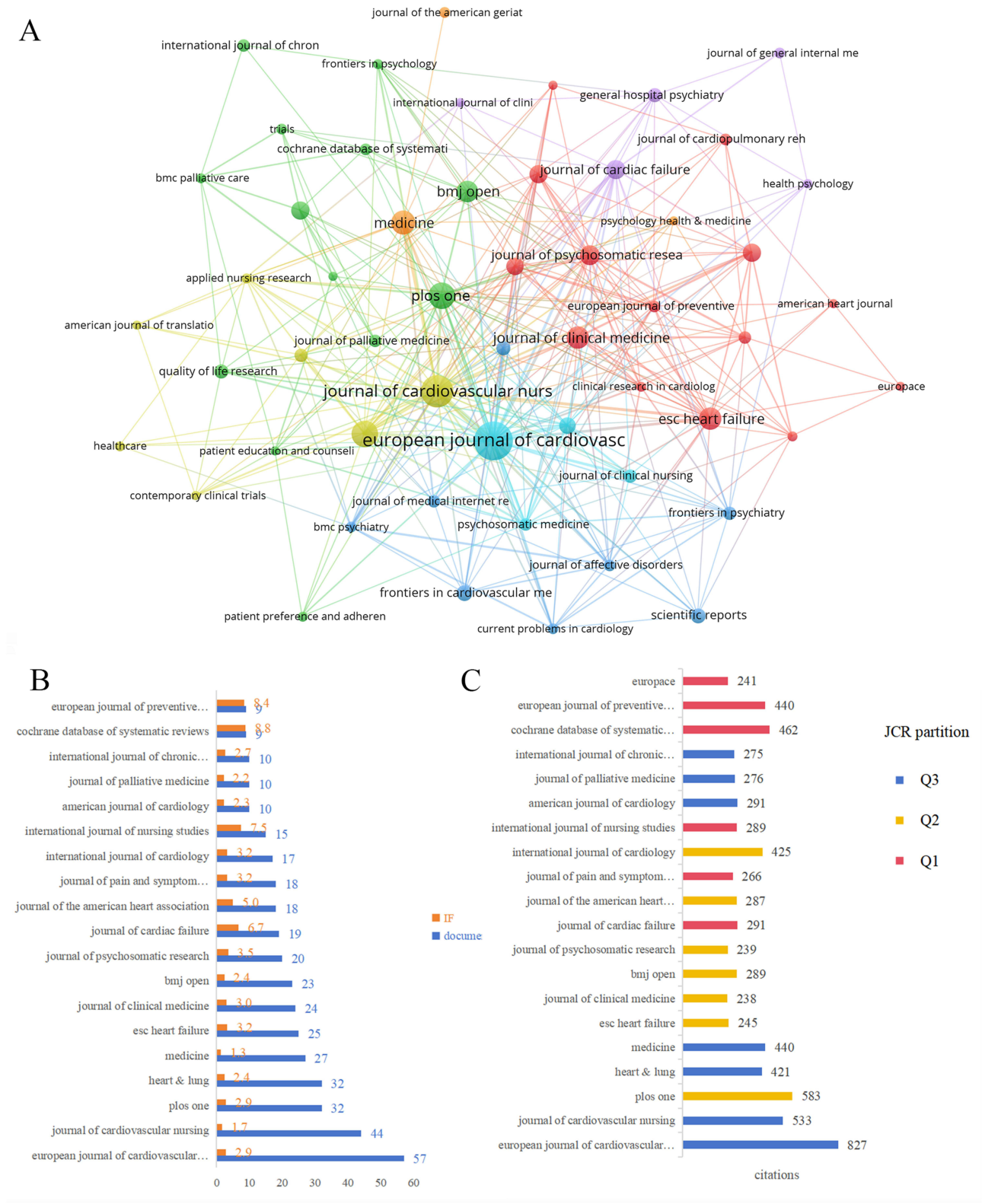

Figure 2 Journal Collaboration Network and Publication Overview on Heart Failure and Anxiety Comorbidity Published from 2015 to 2024 in Web of science (WoS). (**A**) The Cooperation Network of Journal. (**B**) The Number of Publications in the Journal and Journal Impact Factors. (**C**) Journal Citation Reports Classification and Total Citations.

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Table 1 Top 10 Journals Related to Heart Failure and Anxiety Research

Rank	Journal Name	Documents	Citations	Avg. Citations	IF	JCR
1	European Journal of Cardiovascular Nursing	57	827	14.51	2.9	Q3
2	Journal of Cardiovascular Nursing	44	533	12.11	1.7	Q3
3	PLOS ONE	32	583	18.22	2.9	Q2
4	Heart & Lung	32	421	13.16	2.4	Q3
5	Medicine	27	440	16.30	1.3	Q3
6	ESC Heart Failure	25	245	9.80	3.2	Q2
7	Journal of Clinical Medicine	24	238	9.92	3.0	Q2
8	BMJ Open	23	289	12.57	2.4	Q2
9	Journal of Psychosomatic Research	20	239	11.95	3.5	Q2
10	Journal of Cardiac Failure	19	291	15.32	6.7	Q1

of Southern Denmark, the University of Copenhagen, and Odense University Hospital. The red cluster is dominated by leading North American institutions such as Yale University and the University of California, San Francisco.

In terms of research productivity and academic impact, Linköping University and the University of Southern Denmark each produced 39 publications, representing the highest output among institutions in this field. Odense University Hospital followed with 28 publications, while the University of Copenhagen contributed 27. Harvard Medical School, Karolinska Institutet, and the University of Kentucky each published 25 articles. The University of Göttingen accounted for 24 publications, and both Copenhagen University Hospital and Tilburg University contributed 22 articles each (Figure 4B and Table 2).

In terms of total citation count, the University of Copenhagen ranked first with 1,863 citations, followed by Harvard Medical School with 719 citations. When considering average citations per article, the University of Copenhagen also led with a mean of 69.00 citations per publication, surpassing Harvard Medical School (28.76) and the Karolinska Institute (25.92). As illustrated in the bubble plot, Linköping University and the University of Southern Denmark exhibited the largest bubble sizes, suggesting a central role within the collaborative research network. The bubble corresponding to the University of Copenhagen appeared closest to green, indicating its leading position in citation performance.

Author Collaboration Network and Publication Overview

The author collaboration network, visualized using VOSviewer, identified eight distinct clusters, each delineated by a unique color. Among these, the green, red, and blue clusters emerged as the most prominent, characterized by a high density of nodes and strong intra-cluster connectivity. *Herrmann-Lingen Christoph* occupies a central and highly influential position within the overall network, as indicated by the largest node size and the highest degree of linkage with other authors. *Jaarsma Tiny, Lee Christopher S., Strömberg Anna*, and *Moser Debra K*. are situated at the cores of separate clusters, each demonstrating substantial publication output and extensive collaborative networks. In contrast, the cyan cluster, anchored by *Pedersen Susanne S*., is comparatively smaller and exhibits limited cross-cluster interaction, suggesting more localized collaborative activity (Figure 5A).

Based on the combined analysis of publication volume and total citation count, *Herrmann-Lingen Christoph, Jaarsma Tiny*, and *Lee Christopher S*. emerged as the most prolific authors, with 20, 16, and 15 publications, respectively, as indicated by the taller bars in the chart. *Herrmann-Lingen Christoph and Jaarsma Tiny* exhibited comparable citation performance, with 323 and 321 total citations, respectively, denoted by the darker shading of their bars. Although *Lee Christopher S*. had a similar publication count, his total citations (258) were relatively lower, as reflected by a lighter color. *Stromberg Anna* and *Pedersen Susanne S*. also contributed 15 publications each. However, *Stromberg Anna* demonstrated a higher citation impact (305 vs 233 citations), as illustrated by a more intense color gradient. Notably, despite publishing fewer articles (n = 11), *Denollet Johan* received the highest number of total citations (335), which is represented by the darkest bar color, highlighting his markedly higher citation impact compared to peers with similar publication output (Figure 5B and Table 3).

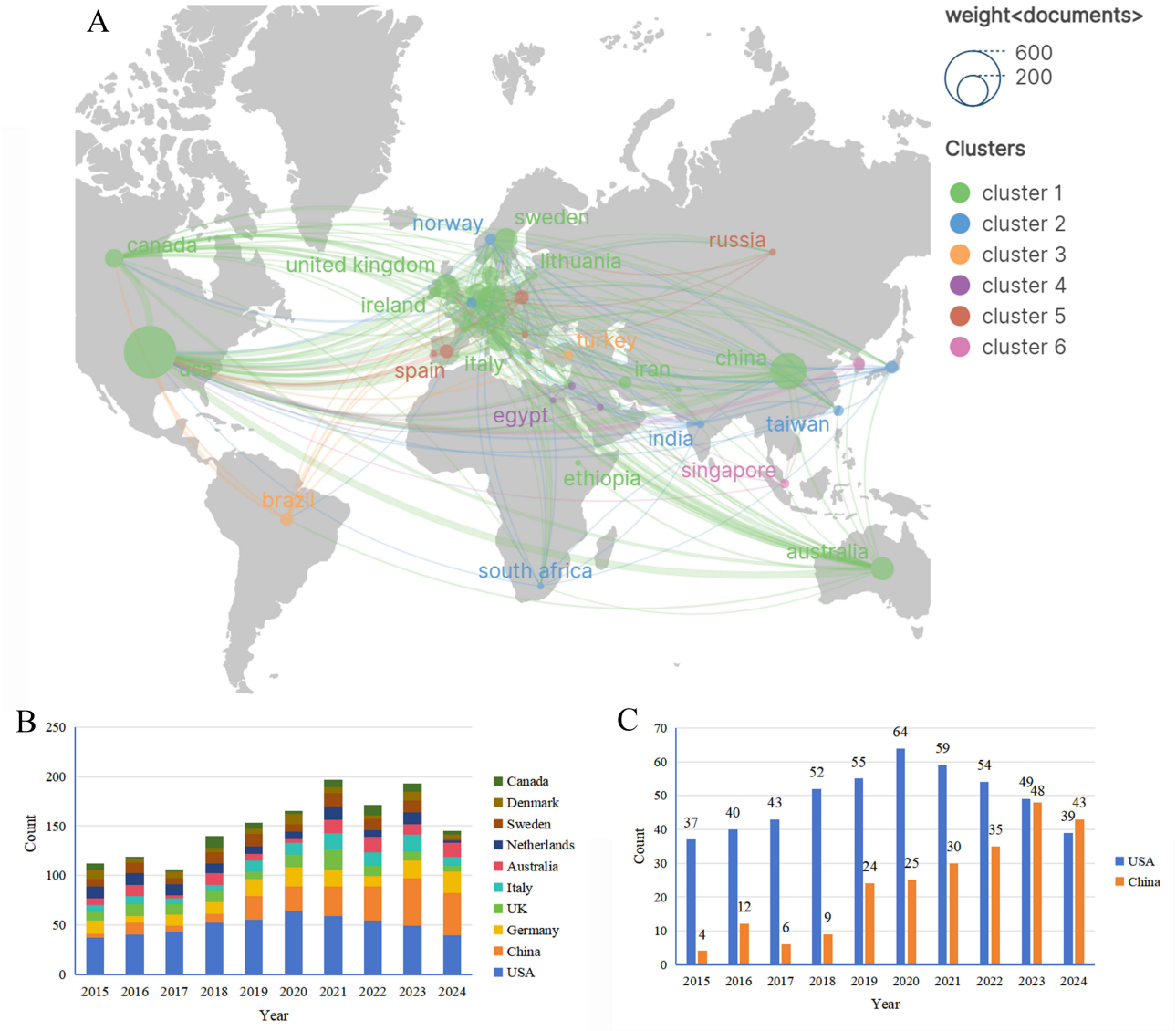

Figure 3 National Collaboration Network and Publication Overview on Heart Failure and Anxiety Comorbidity Published from 2015 to 2024 in Web of science (WoS). (**A**) The National Collaboration Network. (**B**) Analysis of National Publication Trends from 2015 to 2024. (**C**) Comparison of the Number of Publications between the United States of America (USA) and China from 2015 to 2024.

When assessed by average citations per publication, *Denollet Johan* ranks highest with 30.45 citations per article, indicating a substantial scholarly impact despite a lower publication count. He is followed by *Berg Selina Kikkenborg* (21.09), *Strömberg Anna* (20.33), *Jaarsma Tiny* (20.06), and *Vellone Ercole* (19.29). These findings suggest that, beyond their steady publication output, these authors consistently produce high-impact work within the cardiovascular and multidisciplinary healthcare fields (Table 3).

Keyword Co-Occurrence Analysis and Burst Detection

A keyword co-occurrence network and clustering analysis generated using CiteSpace identified 13 major clusters (Figure 6A). Each cluster reflects specific research focuses and temporal trends. Cluster 0, centered on coronary artery disease, includes terms such as atrial fibrillation, mental health, and risk, and was predominantly active in the early years of the study period. Cluster 1 focuses on palliative care, with keywords including health status, blood pressure, and quality of life, peaking around 2016. Cluster 2, related to risk factors, features terms like prevalence and emerged mainly during the middle phase of the timeline. Cluster 3 is anchored by HF and represents a continuously active research theme

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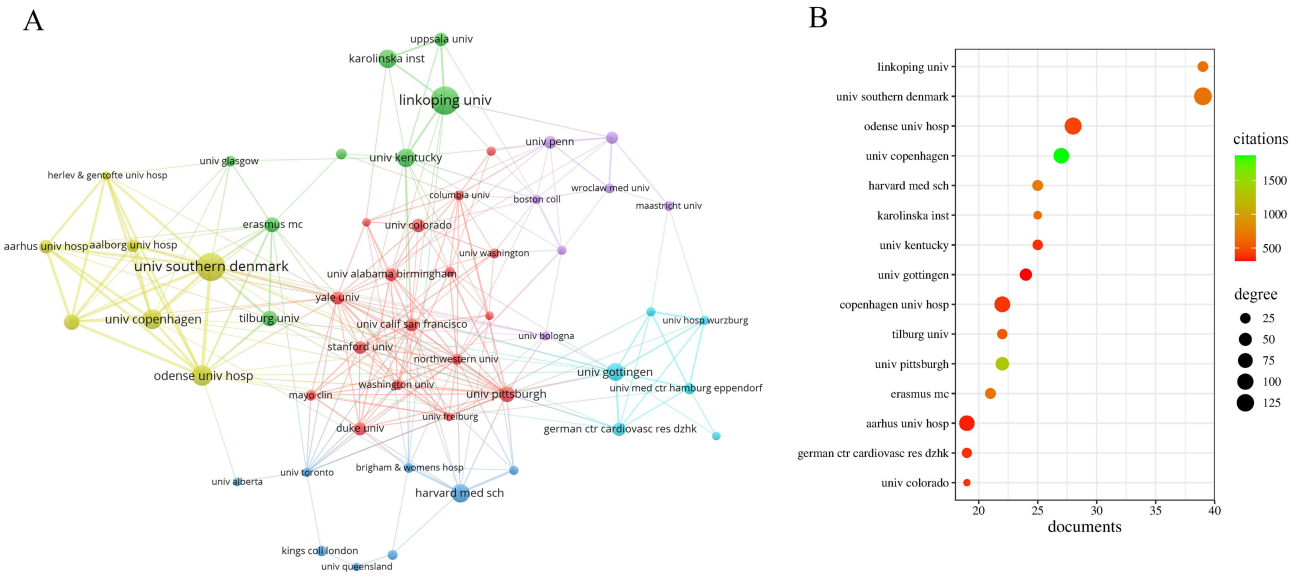

Figure 4 Institutional Collaboration Network and Publication Overview on Heart Failure and Anxiety Comorbidity Published from 2015 to 2024 in Web of science (WoS). (**A**) The Institutional Collaboration Network. (**B**) The Number of Publications and Citations of the Institution.

throughout the study period. Cluster 4 focuses on symptoms and anxiety associated with hospitalization and exhibits a temporally diffuse distribution. Cluster 5 emphasizes diagnosis and the use of questionnaires. Cluster 6 explores self care, predictors, and health status reported by patients. Cluster 7 addresses chronic obstructive pulmonary disease and associated psychological distress. Cluster 8 highlights cardiac rehabilitation and exercise capacity, suggesting growing scholarly attention in recent years. Cluster 9 is associated with HF with reduced ejection fraction and its underlying physiological mechanisms. Cluster 10, focused on cardiovascular disease, represents a relatively independent area of research. Cluster 11 involves meta-analyses and their validation processes. Cluster 12 pertains to lung transplantation and its management strategies, with increasing activity in recent years (Figure 6B).

Analysis of keyword citation bursts (Figure 6C) revealed that, in 2015, research interest was notably concentrated on topics such as implantable cardioverter defibrillators (6.13), chronic obstructive pulmonary disease (5.94), major depression (5.56), Type D personality (4.00), depression scales (3.92), myocardial infarction (3.48), and mechanical circulatory support (2.80). In 2016, the emergence of keywords such as posttraumatic stress disorder (3.23) and congestive heart failure (2.78) indicated an increasing emphasis on the psychological dimensions of cardiovascular disease and the chronic burden of HF. Between 2017 and 2019, the appearance of terms like primary care (3.43), mechanical circulatory support (3.28), and natriuretic peptides (3.18) reflected a growing research focus on community centered management and cardiovascular biomarkers. From 2021 onward, the prominence of keywords including stroke (4.44), PHQ-9 (4.09), burden (3.96), exercise capacity (2.87),

Table 2 Top Organizations Related to Heart Failure and Anxiety Research

Rank	Organization	Documents	Citations	Avg. Citations
1	Linkoping University	39	667	17.10
2	University of Southern Denmark	39	671	17.21
3	Odense University Hospital	28	440	15.71
4	University of Copenhagen	27	1863	69.00
5	Harvard Medical School	25	719	28.76
6	Karolinska Institute	25	648	25.92
7	University of Kentucky	25	377	15.08
8	University of Gottingen	24	309	12.88
9	Copenhagen University Hospital	22	395	17.95
10	Tilburg University	22	534	24.27

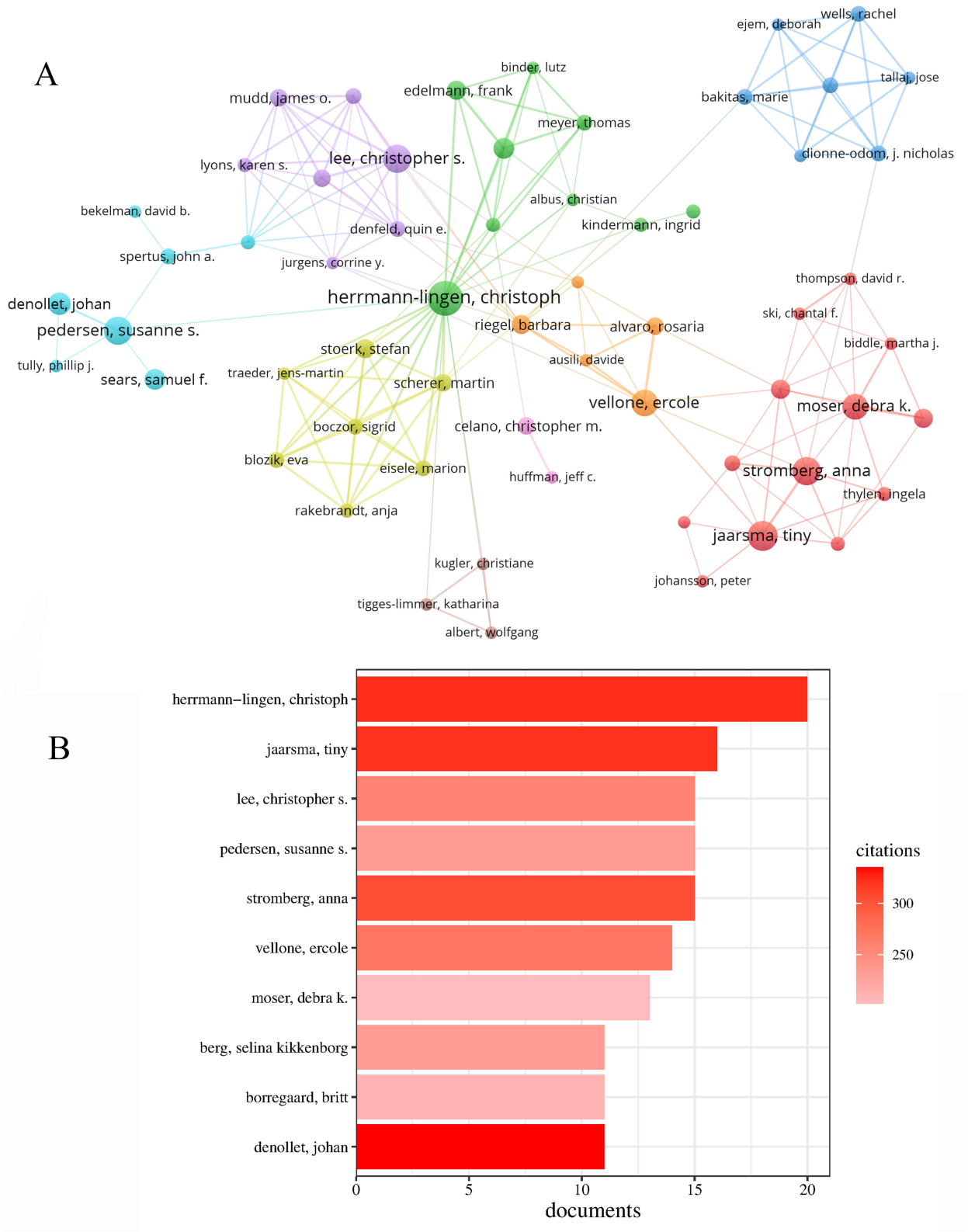

Figure 5 Author Collaboration Network and Publication Overview on Heart Failure and Anxiety Comorbidity Published from 2015 to 2024 in Web of science (WoS). (**A**) The Author Collaboration Network. (**B**) The Number of Publications and Citations.

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Table 3 Top 10 Authors Related to Heart Failure and Anxiety Research

Rank	Author	Documents	Citations	Avg. Citations
1	Herrmann-Lingen, Christoph	20	323	16.15
2	Jaarsma, Tiny	16	321	20.06
3	Lee, Christopher S.	15	258	17.20
4	Pedersen, Susanne S.	15	233	15.53
5	Stromberg, Anna	15	305	20.33
6	Vellone, Ercole	14	270	19.29
7	Moser, Debra K.	13	202	15.54
8	Berg, Selina Kikkenborg	11	232	21.09
9	Borregaard, Britt	11	209	19.00
10	Denollet, Johan	11	335	30.45

hypertension (3.10), and functional capacity (3.01) suggests a continued shift toward integrated cardiovascular care with an emphasis on functional status and comorbid conditions.

As shown in Table 4, HF was the most frequently occurring keyword, with a total of 727 mentions, underscoring its position as the core subject within the research field. The term diagnosis demonstrated the highest betweenness centrality value of 0.38, followed by reliability at 0.36 and exercise at 0.29, suggesting their critical roles as conceptual bridges in the knowledge network. Additional keywords with prominent centrality included health related quality of life at 0.23, predictors at 0.22, and psychological distress at 0.21, highlighting their integrative significance in the evolving framework of HF research.

Key Gene Screening and PPI Network Analysis

A total of 614 genes associated with HF and 384 genes linked to anxiety were retrieved from the GeneCards database. Intersection analysis revealed 124 overlapping genes that may be implicated in both conditions (Table S1). PPI network was then constructed based on these shared genes using the STRING database (Figure 7A). According to their connectivity within the network, the top 20 hub genes were identified: AKT1 (35), TP53 (33), INS (32), CTNNB1 (31), IL6 (26), TNF (25), PTEN (23), ACTB (22), ALB (22), ESR1 (22), BDNF (20), IL1B (20), KRAS (19), MAPK1 (19), BRAF (18), EP300 (18), IGF1 (18), IL10 (18), TGFB1 (18), and IFNG (17) (Figure 7B). These hub genes may play key roles in the shared pathophysiological mechanisms of HF and anxiety, offering potential targets for further functional research and therapeutic development.

Key Signaling Pathways Associated with HF and Anxiety

KEGG enrichment analysis demonstrated that the genes shared between HF and anxiety were significantly enriched in 81 signaling pathways. After removing those directly associated with specific diseases, 20 major functional pathways were selected for further investigation (Figure 8A). Ranked by descending gene count, these pathways include the MAPK signaling pathway, FoxO signaling pathway, cAMP signaling pathway, mTOR signaling pathway, thyroid hormone signaling pathway, lysosome pathway, HIF-1 signaling pathway, phospholipase D signaling pathway, cellular senescence, JAK-STAT signaling pathway, neurotrophin signaling pathway, T cell receptor signaling pathway, growth hormone synthesis, secretion and action, C-type lectin receptor signaling pathway, apoptosis, insulin signaling pathway, prolactin signaling pathway, sphingolipid signaling pathway, longevity regulating pathway, and longterm depression pathway.

Among these pathways, the C-type lectin receptor signaling pathway, apoptosis, and JAK-STAT signaling pathway showed the lowest p-values, indicating the highest level of statistical significance. In the bubble plot, these three pathways are highlighted by distinct green nodes, emphasizing their potential biological relevance. In the pathway gene interaction network, the top 20 key genes were identified based on both gene count and connectivity degree. These genes include AKT1, HRAS, MAPK1, PIK3CA, KRAS, SOS1, INS, BRAF, IGF1, TP53, CREBBP, EP300, TNF, TSC2, IL6, PTPN11, TSC1, GNAS, IL10, and PTEN (Figure 8B).

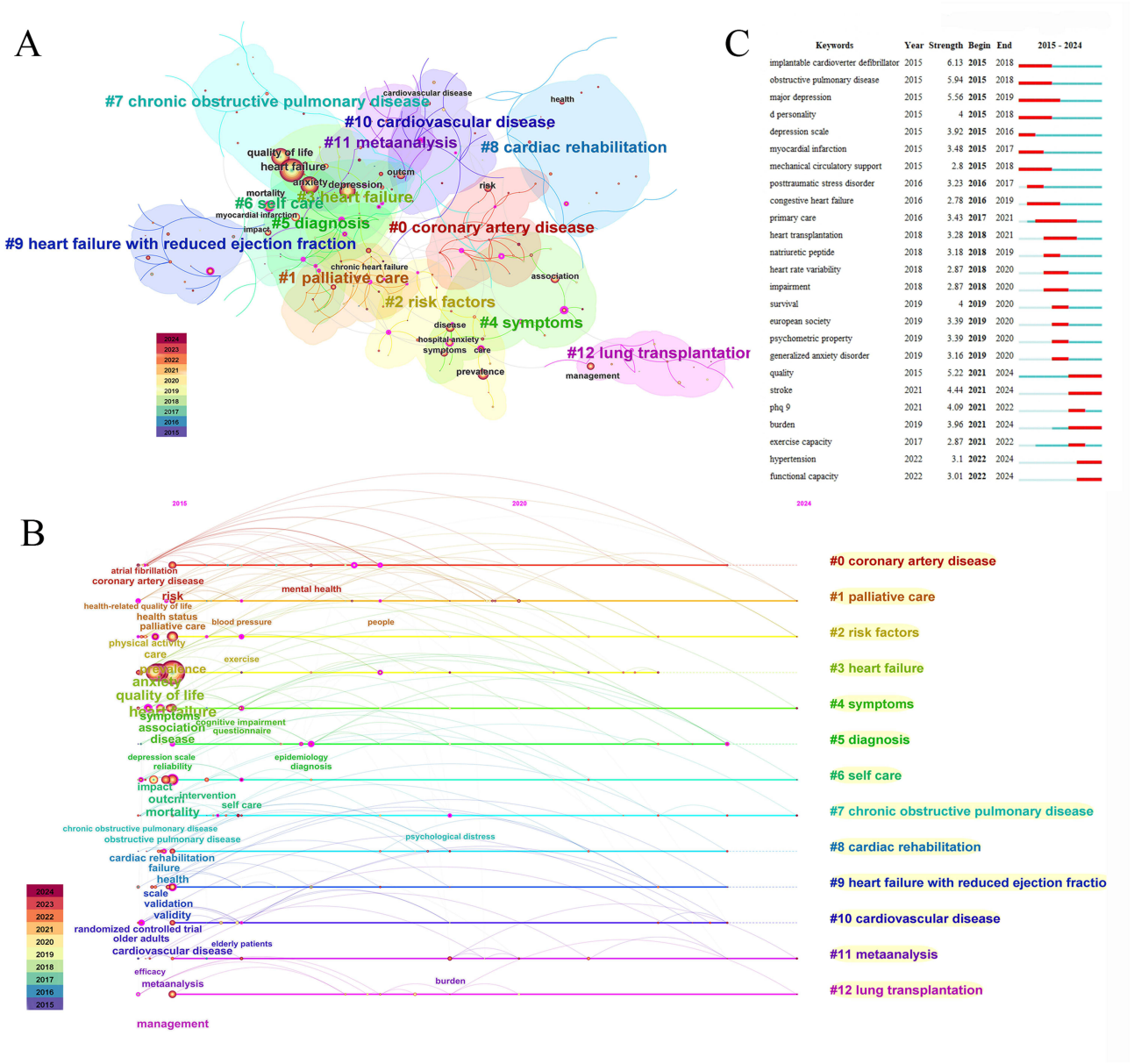

Figure 6 Keyword Co-occurrence Analysis and Burst Clustering of Heart Failure and Anxiety Comorbidity Published from 2015 to 2024 in Web of science (WoS). (**A**) Keywords Co-occurrence Network and Clustering Analysis. (**B**) The Keywords of Heart Failure and Anxiety Comorbidity are Sorted into Chronological Order. (**C**) Top 25 Keywords with the Strongest Citation Bursts.

These findings underscore key molecular targets and signaling pathways potentially mediating the comorbidity between HF and anxiety, providing a foundation for future mechanistic exploration and therapeutic development.

Discussion

This comprehensive bibliometric analysis captures the dynamic progression of research on HF and anxiety between 2015 and 2024, characterized by a marked increase in publication output. Co-citation analysis, burst detection, and clustering techniques were utilized via CiteSpace to delineate temporal patterns, collaborative structures, thematic evolution, and potential molecular mechanisms. Distinct geographic and institutional collaboration networks were identified, alongside a notable thematic transition from epidemiological surveillance to clinical application. This trajectory distinguishes the field from HF and depression research.

Table 4 Top 10 Keywords by Frequency and Top 10 Keywords by Centrality

Rank	Keyword	Count	Keyword	Centrality
1	Heart failure	727	Diagnosis	0.38
2	Quality of life	484	Reliability	0.36
3	Anxiety	431	Exercise	0.29
4	Depression	381	Older adults	0.23
5	Mortality	227	Health-related quality of life	0.23
6	Prevalence	209	Predictors	0.22
7	Outcome	187	Psychological distress	0.21
8	Risk	180	Heart rate variability	0.21
9	Disease	171	Acute coronary syndrome	0.20
10	Association	168	Health status	0.19

Research Productivity and Collaborative Networks

A progressive increase in annual publication output was observed from 2015 to 2024, culminating in a peak of 200 publications in 2021. This mirrors broader trends in psychocardiology. Therefor, this growth trajectory was found to exceed the 73% increase documented for heart failure and depression research during a comparable period.[13] Scholarly output was predominantly disseminated through nursing journals, contrasting with the cardiology journal dominance reported in broader psychocardiology analyses.[16]

The national contribution analysis is consistent with previous findings suggesting that North America and Europe are leading the way in psychocardiology research.[16,17] Although China started relatively late, its rapid growth in research output highlights the increasing global interest in this field. Examination of international collaboration demonstrates that the USA, leading both in breadth and depth of partnerships, has engaged in extensive cooperation with multiple countries, underscoring the critical role of global collaboration in accelerating research progress.

Institutionally, Universities in North America and Europe were identified as central nodes. Herrmann-Lingen Christoph emerged as the most prolific author, differing from the principal investigators noted in heart failure and depression research networks.[7] Notably, Angermann and Ertl (2018) called for routine mental health screening in HF care

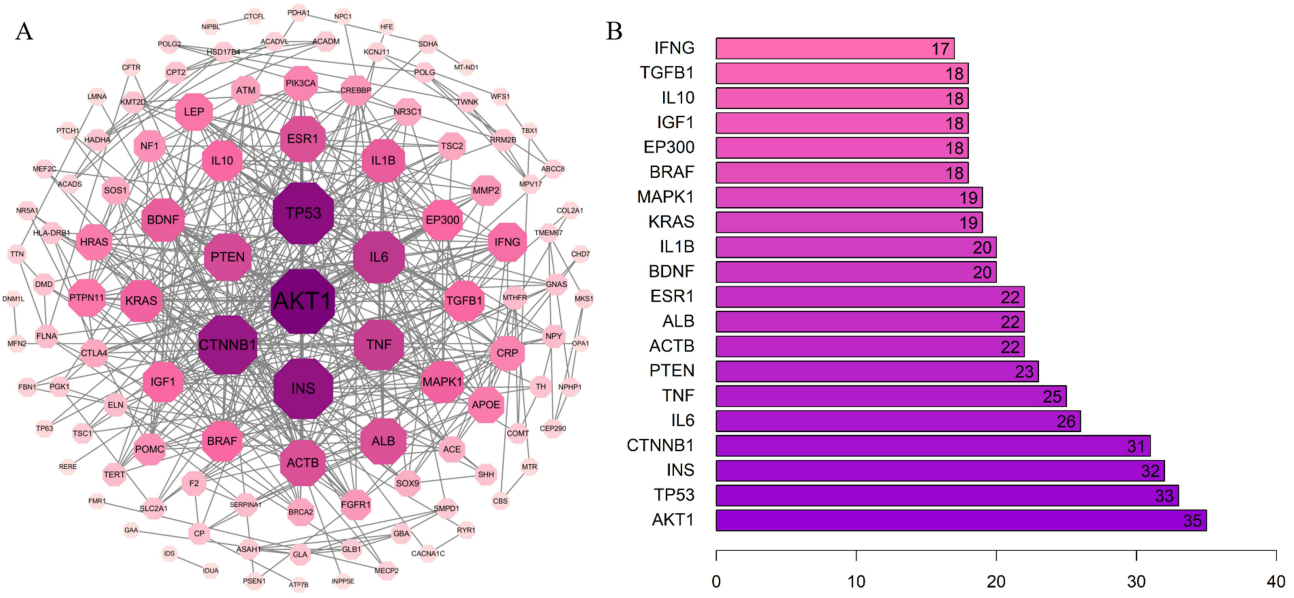

Figure 7 Key Gene Screening and Protein–protein Interaction (PPI) network Analysis of Heart Failure and Anxiety Comorbidity. (**A**) Protein–protein Interaction (PPI) Network of Heart Failure and Anxiety Comorbidity. (**B**) The Top 20 Hub Genes.

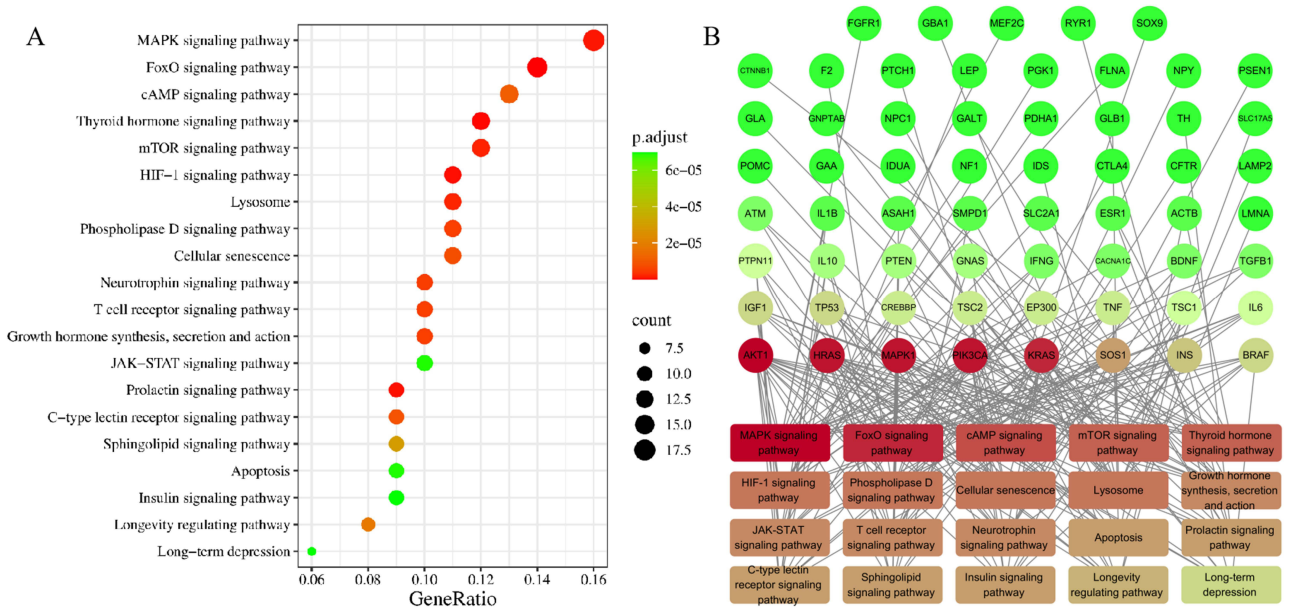

Figure 8 Key Signaling Pathways Associated with Heart Failure and Anxiety. (**A**) Bubble Plot of the Major Functional Pathways. (**B**) Pathway Gene Interaction Network.

and advocated for collaborations across psychosomatic and cardiology departments.[18] Our network maps provide visual confirmation that this interdisciplinary collaboration is now being increasingly realized.

Knowledge Domain Evolution and Field Development

Thematic evolution was quantified through keyword burst detection and co-occurrence mapping. Three sequential phases were discernible, beginning with a focus on mortality metrics and device therapy from 2015 to 2018, followed by an emphasis on self care behaviors during 2019 to 2021, and culminating in the recent prioritization of standardized assessment tools and functional status from 2022 to 2024. This progression from epidemiological observation to intervention implementation aligns conceptually with established frameworks for comorbid cardiovascular and behavioral research,[19] demonstrates accelerated translation of guideline recommendations.[5] Crucially, the concept of diagnosis achieved the highest betweenness centrality, distinguishing this domain from heart failure and depression research where the central concept is typically prognosis.[13] This divergence may reflect the unique diagnostic complexities of anxiety identification in heart failure populations. The persistent emergence of concept of burden as a high burst keyword underscores significant unmet clinical needs, reinforcing calls for implementation science approaches articulated in recent scientific statements.[8]

The Underlying Mechanisms Linking HF and Anxiety

In this study, gene analyses related to HF and anxiety were performed, resulting in the identification of 124 overlapping genes potentially involved in both conditions. Among these, AKT1, TP53, and IL6 were mainly recognized as central hub genes based on network connectivity. Enrichment analysis revealed involvement in key signaling pathways such as the MAPK, FoxO, and JAK-STAT pathways, suggesting common mechanisms that may be associated with inflammation, oxidative stress, and neuroendocrine dysfunction.[16] These findings are consistent with previously proposed biological frameworks, such as those described by Angermann, which emphasize systemic inflammation and neurocardiac interactions as core contributors to the comorbidity of HF and anxiety.[18]

The MAPK signaling pathway, one of the key pathways identified, serves as a prime example of this mechanistic convergence. In the heart, MAPK pathways activated by stress, particularly p38 MAPK and JNK, are established contributors of cardiomyocyte apoptosis, hypertrophy, and maladaptive remodeling in failing hearts.[20] In the central nervous system, the same pathways are activated by psychological stress and are critically involved in mediating synaptic

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plasticity, neuroinflammation, and behaviors resembling anxiety.[21] This dual role establishes the MAPK cascade as a fundamental shared signaling axis that transduces both cardiovascular and psychological stress into cellular pathology.

The JAK-STAT signaling pathway, another hub in our network, provides a direct molecular link between systemic inflammation and the brain and heart axis. Inflammatory cytokines such as IL-6, a key hub gene we identified, activate cardiac JAK-STAT signaling, promoting myocardial inflammation, fibrosis, and dysfunction in heart failure.[22] Circulating IL-6 can access the brain to activate the JAK-STAT pathway within key regions like the hippocampus and prefrontal cortex, disrupting neurogenesis and neurotransmitter balance, sustaining anxiety states.[23] Our identification of this pathway powerfully reinforces the cytokine hypothesis of depression and anxiety in somatic disease.

The enrichment of the FoxO signaling pathway integrates these mechanisms. FoxO transcription factors are crucial regulators of cellular metabolism, oxidative stress response, and autophagy. In cardiomyocytes, FoxO activity influences survival and hypertrophy.[24] In the brain, it regulates neuronal resilience and stress resistance, with its dysfunction being implicated in mood disorders.[25] This suggests that deficits in core cellular maintenance and stress adaptation processes, governed by pathways like FoxO, may underlie the vulnerability to both cardiac and emotional dysfunction.

Neuroendocrine dysregulation and inflammatory responses have been recognized as contributors to the development and progression of.[26] Chronic anxiety has been shown to activate the hypothalamic pituitary adrenal axis, resulting in sustained elevations of cortisol levels. This neurohormonal imbalance promotes myocardial fibrosis and oxidative stress, accelerating cardiac dysfunction.[27–29] The upregulation of proinflammatory cytokines such as IL6 and TNF contributes to persistent low grade systemic inflammation. This inflammatory milieu impairs cardiovascular integrity and amplifies anxiety related symptomatology, reinforcing a maladaptive cycle of neuroendocrine and inflammatory interaction.[30,31]

Anxiety has been associated with heightened activation of the sympathetic nervous system and suppression of parasympathetic tone. This autonomic imbalance is typically reflected by a reduction in heart rate variability and an elevation in circulating catecholamines, which may confer an increased risk of myocardial ischemia and arrhythmia.[32–34] In addition, self management behaviors are often impaired in patients with anxiety, as evidenced by reduced adherence to medical therapy and decreased physical activity, both of which may also contribute to a worsened prognosis in individuals with HF.[35,36] Research hotspots focusing on self care and cardiac rehabilitation have underscored the potential of behavioral interventions, such as structured exercise therapy. It may improve clinical outcomes by restoring autonomic balance in patients with coexisting heart failure and anxiety.[33,37–39]

Beyond the inflammatory and stress axes, hub genes like BDNF and IGF1 have emerged as critical mediators.[40] Reduced BDNF expression is linked to both hippocampal atrophy in anxiety and cardiomyocyte apoptosis.[41,42] The mTOR signaling pathway, implicated in our analysis, is a key downstream effector of growth factors like BDNF and IGF1, regulating cellular growth, survival, and protein synthesis. Dysregulation of mTOR signaling may represent a convergent node where impaired neurotrophic support compromises both neuronal and cardiac cellular integrity.[43] The MAPK, JAK-STAT, and FoxO pathways, along with key hub genes, form a plausible multiscale network linking psychological distress to cardiac pathology. Future studies could validate the clinical relevance of these targets, with IL-6 targeting strategies and BDNF augmentation interventions.

Research Gaps and Clinical Implications

Although anxiety exerts a substantial influence on the clinical outcomes of patients with heart failure, its recognition and management in routine clinical settings remain insufficiently addressed. The identification of anxiety symptoms is often more complex than that of depressive symptoms, largely due to the heterogeneity of clinical presentations and the inherent limitations of existing diagnostic instruments. It is therefore recommended that future research be directed toward the development and validation of more sensitive and specific assessment tools, as well as targeted intervention strategies aimed at improving psychological health in this population. Furthermore, the integration of mental health services into standard heart failure care should be prioritized, and multidisciplinary collaboration among cardiologists, psychiatrists, nurses, and rehabilitation specialists should be strengthened. Such efforts are essential to improving not only mental health outcomes but also overall quality of life and longterm prognosis in individuals living with heart failure.

Limitations

The analysis was based solely on data extracted from the Web of Science, which does not include all relevant journals, especially those written in languages other than English or those available only through databases including Scopus, PubMed, Embase, and Google Scholar. As a result, the exclusion of pertinent literature may have occurred, introducing potential biases related to language and database selection. To enhance comprehensiveness, future investigations should consider the inclusion of clinical trial records and real world evidence, particularly from underrepresented regions, in order to better evaluate the translational relevance of scientometric findings.

Conclusions

This scientometric review provides a structured overview of research on the comorbidity between heart failure and anxiety, covering trends in publications, collaboration networks, thematic evolution, and molecular mechanisms. Early studies focused on epidemiological associations, while subsequent research shifted toward behavioral interventions such as self care and rehabilitation. Recent efforts have emphasized standardized psychological assessment, functional outcomes, and personalized treatment approaches. Despite this progress, clinical translation remains limited. Standardized tools for anxiety assessment in heart failure populations are lacking, and comprehensive intervention frameworks are underdeveloped. Future research should prioritize the validation of diagnostic instruments and targeted therapies, supported by multicenter longitudinal studies. Bridging mechanistic findings with clinical practice will be essential to improve patient outcomes in this high risk population.

Data Sharing Statement

No publicly available datasets were used or generated specifically for this study. The datasets generated and/or analyzed during the current study are available from the corresponding author (Lin Li) on reasonable request.

Ethics Statement

This study utilized exclusively legally sourced, publicly available data and/or observations of public behavior that did not involve interaction with individuals, and was therefore exempt from ethical approval as per Article 32(1) of China's "Ethical Review Measures for Life Sciences and Medical Research Involving Humans" (issued February 18, 2023).

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Disclosure

The authors report no conflicts of interest in this work.

References

1. Hamatani Y, Iguchi M, Ikeyama Y. et al. Prevalence, temporal change, and determinants of anxiety and depression in hospitalized patients with heart failure. *J Card Fail*. 2022;28(2):181–190. doi:10.1016/j.cardfail.2021.07.024
2. Al Shamiri MQ, Almushawah AA, Alsomali AH, et al. The prevalence of depression and anxiety in heart failure patients in Saudi Arabia: an original study. *Cureus*. 2023;15(4):e36997. doi:10.7759/cureus.36997
3. Polikandrioti M, Koutelekos I, Panoutsopoulos G, et al. Hospitalized patients with heart failure: the impact of anxiety, fatigue, and therapy adherence on quality of life. *Arch Med Sci Atheroscler Dis*. 2019;4(1):e268–e279. doi:10.5114/amsad.2019.90257
4. Abou Kamar S, Oostdijk B, Andrzejczyk K, et al. Temporal evolution of anxiety and depression in chronic heart failure and its association with clinical outcome. *Int J Cardiol*. 2024;411:132274. doi:10.1016/j.ijcard.2024.132274
5. McDonagh TA, Metra M, Adamo M, et al. ESC Scientific Document Group. Focused update of the 2021 ESC guidelines for the diagnosis and treatment of acute and chronic heart failure. *Eur Heart J*. 2023;44(37):3627–3639. doi:10.1093/eurheartj/ehad195
6. Chen CY, Wang CL. Psychiatric comorbidity and psychosocial factors matter in heart failure. *Acta Cardiol Sin*. 2016;32(1):62–64. doi:10.6515/acs20150723a

7. Chernoff RA, Messineo G, Kim S, et al. Psychosocial interventions for patients with heart failure and their impact on depression, anxiety, quality of life, morbidity, and mortality: a systematic review and meta-analysis. *Psychosom Med*. 2022;84(5):560–580. doi:10.1097/PSY.0000000000001073
8. Levine GN, Cohen BE, Commodore-Mensah Y, et al. Psychological health, well-being, and the mind-heart-body connection: a scientific statement from the American Heart Association. *Circulation*. 2021;143(10):e763–e783. doi:10.1161/CIR.0000000000000947
9. IsHak WW, Hamilton MA, Korouri S, et al. Comparative effectiveness of psychotherapy vs antidepressants for depression in heart failure: a randomized clinical trial. *JAMA Network Open*. 2024;7(1):e2352094. doi:10.1001/jamanetworkopen.2023.52094
10. Rashid S, Qureshi AG, Noor TA, et al. Anxiety and depression in heart failure: an updated review. *Curr Probl Cardiol*. 2023;48(11):101987. doi:10.1016/j.cpcardiol.2023.101987
11. Synnestvedt MB, Chen C, Holmes JH. CiteSpace II: visualization and knowledge discovery in bibliographic databases. *AMIA Annu Symp Proc*. 2005;2005:724–728.
12. Zhao Y, Chen GY, Fang M. Research trends of rheumatoid arthritis and depression from 2019 to 2023: a bibliometric analysis. *J Multidiscip Healthc*. 2024;17:4465–4474. doi:10.2147/JMDH.S478748
13. Ying H, Zhang X, He T, et al. A bibliometric analysis of research on heart failure comorbid with depression from 2002 to 2021. *Heliyon*. 2023;9(2):e13054. doi:10.1016/j.heliyon.2023.e13054
14. Dong X, Xie Y, Xu J, et al. Global historical retrospect and future prospects on biomarkers of heart failure: a bibliometric analysis and science mapping. *Heliyon*. 2023;9(2):e13509. doi:10.1016/j.heliyon.2023.e13509
15. Wang H, Shi J, Shi S, Bo R, Zhang X, Hu Y. Bibliometric analysis on the progress of chronic heart failure. *Curr Probl Cardiol*. 2022;47(9):101213. doi:10.1016/j.cpcardiol.2022.101213
16. Lam MI, Chen P, Xie XM, et al. Heart failure and depression: a perspective from bibliometric analysis. *Front Psychiatry*. 2023;14:1086638. doi:10.3389/fpsyt.2023.1086638
17. Papamichail A, Kourek C, Briasoulis A, et al. Targeting key inflammatory mechanisms underlying heart failure: a comprehensive review. *Int J Mol Sci*. 2023;25(1):510. doi:10.3390/ijms25010510
18. Angermann CE, Depression EG. Anxiety, and cognitive impairment: comorbid mental health disorders in heart failure. *Curr Heart Fail Rep*. 2018;15(6):398–410. doi:10.1007/s11897-018-0414-8
19. Manolis TA, Manolis AA, Melita H, Manolis AS. Neuropsychiatric disorders in patients with heart failure: not to be ignored. *Heart Fail Rev*. 2023;28(4):821–858. doi:10.1007/s10741-022-10290-2
20. Rose BA, Force T, Wang Y. Mitogen-activated protein kinase signaling in the heart: angels versus demons in a heart-breaking tale. *Physiol Rev*. 2010;90(4):1507–1546. doi:10.1152/physrev.00054.2009
21. Peng Z, Wang H, Zhang R, et al. Gastrodin ameliorates anxiety-like behaviors and inhibits IL-1β level and p38 MAPK phosphorylation of hippocampus in the rat model of posttraumatic stress disorder. *Physiol Res*. 2013;62(5):537–545. doi:10.33549/physiolres.932507
22. Fischer P, Hilfiker-Kleiner D. Survival pathways in hypertrophy and heart failure: the gp130-STAT axis. *Basic Res Cardiol*. 2007;102(5):393–411. doi:10.1007/s00395-007-0674-z
23. Hodes GE, Pfau ML, Leboeuf M, et al. Individual differences in the peripheral immune system promote resilience versus susceptibility to social stress. *Proc Natl Acad Sci USA*. 2014;111(45):16136–16141. doi:10.1073/pnas.1415191111
24. Sengupta A, Molkentin JD, Paik JH, DePinho RA, Yutzey KE. FoxO transcription factors promote cardiomyocyte survival upon induction of oxidative stress. *J Biol Chem*. 2011;286(9):7468–7478. doi:10.1074/jbc.M110.179242
25. Polter A, Yang S, Zmijewska AA, et al. Forkhead box, class O transcription factors in brain: regulation and behavioral manifestation. *Biol Psychiatry*. 2009;65(2):150–159. doi:10.1016/j.biopsych.2008.08.005
26. Murphy SP, Kakkar R, McCarthy CP, Januzzi JL. Inflammation in heart failure. *J Am Coll Cardiol*. 2020;75(11):1324–1340. doi:10.1016/j.jacc.2020.01.014
27. Golbidi S, Frisbee JC, Laher I. Chronic stress impacts the cardiovascular system: animal models and clinical outcomes. *Am J Physiol Heart Circ Physiol*. 2015;308(12):H1476–98. doi:10.1152/ajpheart.00859.2014
28. Chen GY, Liu XY, Yan XE, et al. Total flavonoids of rhizoma drynariae treat osteoarthritis by inhibiting arachidonic acid metabolites through AMPK/NFκB pathway. *J Inflamm Res*. 2023;16:4123–4140. doi:10.2147/JIR.S418345
29. Chen GY, Ji XY, Li Y, Zheng SS, Jin Q, Tao QW. Mechanisms of total glucosides of paeony in alleviating methotrexate-induced liver injury. *Drug Des Devel Ther*. 2025;19:3407–3423. doi:10.2147/DDDT.S521740
30. Altamura M, D'Andrea G, Angelini E, et al. Psychosomatic syndromes are associated with IL-6 pro-inflammatory cytokine in heart failure patients. *PLoS One*. 2022;17(3):e0265282. doi:10.1371/journal.pone.0265282
31. Lu H, Yang Q, Zhang Y. The relation of common inflammatory cytokines with anxiety and depression and their values in estimating cardiovascular outcomes in coronary heart disease patients. *J Clin Lab Anal*. 2022;36(6):e24404. doi:10.1002/jcla.24404
32. Chalmers JA, Heathers JA, Abbott MJ, Kemp AH, Quintana DS. Worry is associated with robust reductions in heart rate variability: a transdiagnostic study of anxiety psychopathology. *BMC Psychol*. 2016;4(1):32. doi:10.1186/s40359-016-0138-z
33. Chung WH, Lin YN, Wu MY, Chang KC. Sympathetic modulation in cardiac arrhythmias: where we stand and where we go. *J Pers Med*. 2023;13(5):786. doi:10.3390/jpm13050786
34. Osei J, Vaccarino V, Wang M, et al. Stress-induced autonomic dysfunction is associated with mental stress-induced myocardial ischemia in patients with coronary artery disease. *Circ Cardiovasc Imaging*. 2024;17(6):e016596. doi:10.1161/CIRCIMAGING.124.016596
35. Müller-Tasch T, Löwe B, Lossnitzer N, et al. Anxiety and self-care behaviour in patients with chronic systolic heart failure: a multivariate model. *Eur J Cardiovasc Nurs*. 2018;17(2):170–177. doi:10.1177/1474515117722255
36. Toback M, Clark N. Strategies to improve self-management in heart failure patients. *Contemp Nurse*. 2017;53(1):105–120. doi:10.1080/10376178.2017.1290537
37. Besnier F, Labrunée M, Pathak A, et al. Exercise training-induced modification in autonomic nervous system: an update for cardiac patients. *Ann Phys Rehabil Med*. 2017;60(1):27–35. doi:10.1016/j.rehab.2016.07.002
38. Hsu CY, Hsieh PL, Hsiao SF, Chien MY. Effects of exercise training on autonomic function in chronic heart failure: systematic review. *Biomed Res Int*. 2015;2015:591708. doi:10.1155/2015/591708
39. Pearson MJ, Smart NA. Exercise therapy and autonomic function in heart failure patients: a systematic review and meta-analysis. *Heart Fail Rev*. 2018;23(1):91–108. doi:10.1007/s10741-017-9662-z

40. Arjunan A, Sah DK, Woo M, Song J. Identification of the molecular mechanism of insulin-like growth factor-1 (IGF-1): a promising therapeutic target for neurodegenerative diseases associated with metabolic syndrome. *Cell Biosci*. 2023;13(1):16. doi:10.1186/s13578-023-00966-z
41. Zhu G, Sun X, Yang Y, et al. Reduction of BDNF results in GABAergic neuroplasticity dysfunction and contributes to late-life anxiety disorder. *Behav Neurosci*. 2019;133(2):212–224. doi:10.1037/bne0000301
42. Agrimi J, Spalletti C, Baroni C, et al. Obese mice exposed to psychosocial stress display cardiac and hippocampal dysfunction associated with local brain-derived neurotrophic factor depletion. *EBioMedicine*. 2019;47:384–401. doi:10.1016/j.ebiom.2019.08.042
43. Wang X, Liu R, Liu D. The role of the MAPK signaling pathway in cardiovascular disease: pathophysiological mechanisms and clinical therapy. *Int J Mol Sci*. 2025;26(6):2667. doi:10.3390/ijms26062667