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A Bibliometric and Knowledge-map Analysis of Gut Microbiota in Cardiovascular Diseases from 2006 to 2024

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Abstract: Cardiovascular disease continues to be a leading cause of death and morbidity worldwide. The study employed bibliometric and knowledge-mapping analyses to explore research trends in cardiovascular disease, identifying emerging hotspots and offering new perspectives for scholars. The study conducted a comprehensive search within the WOSCC on December 28th, 2024, to retrieve articles and reviews that explore the association between gut microbiota and cardiovascular diseases. Citespace and VOSviewer were used to conduct the bibliometric and knowledge-map analysis. The analysis encompassed 1,680 studies published across 289 academic journals, authored by 9,865 researchers from 277 institutions spanning 103 countries/regions. The United States, China, Italy, and India emerged as the leading contributors, with the most cited institutions including the University of California system, INSERM, the Chinese Academy of Medical Sciences & Peking Union Medical College, and Southern Medical University (China). Among journals, Nutrients published the highest number of studies, while Nature, Gut, and the American Journal of Clinical Nutrition were the most frequently co-cited. The most prominent research focus centered on biochemistry and molecular biology, with four key cardiovascular conditions: heart failure, cardiometabolic disorders, infarction, and hypertension. GO and KEGG pathway analyses further revealed 30 critical biological processes and 21 signaling pathways linked to gut microbiota and cardiovascular disease. Additionally, PPI network analysis highlighted IFNG, IL10, TLR4, INS, TNF, IL6, IL1β, APOE, and AGT as potential core therapeutic targets for future research. Our analyses elucidated key research trends linking gut microbiota to cardiovascular diseases, highlighting metabolic modulation and prebiotic supplementation as promising therapeutic strategies.

Keywords: Gut microbiota; Cardiovascular diseases; Bibliometric; Knowledge map

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1. Introduction

Cardiovascular diseases are the leading cause of mortality, claiming 17.9 million lives annually, representing 31% of all deaths worldwide. Encompasses a range of conditions, including heart failure, atrial hypertension, coronary artery disease, and cardiomyopathies, despite significant strides in cardiovascular research over the past-century, these diseases continue to be the foremost health burden and the primary cause of death globally, with projections indicating a rise to over 23.6 million deaths per year by 2030 [1,2].

The human gut, a complex ecosystem teeming with microorganisms, contains an estimated 1014 bacteria, nearly ten times the number of human cells. This microbial community plays a pivotal role in maintaining health and has been considered as a special "microbial organ" and "second genome" [3]. In recent years, the gut microbiota has been implicated in a variety of diseases, including frailty, cognitive dysfunction, cardiovascular diseases etc. [4] Over the past decade, a surge of clinical and basic research has underscored the critical role of the "gut-heart-axis" in cardiovascular health [5–8].

Knowledge mapping, a bibliometric analytical technique, analyzes the systematic and quantitative features of literature to offer a graphical depiction of scientific knowledge. It serves as a pivotal tool for identifying seminal research, monitoring disease progression, bolstering evidence-based medical practices, and evaluating the efficacy of medical education [9]. It offers a means to identify influential research, track the progress of diseases, support evidence-based medicine, and assess the impact of medical education, and consequently, it is an essential asset for medical professionals and has been widely adopted both domestically and globally [10,11]. Previous bibliometric studies have concentrated their efforts on elucidating the role of gut microbiota in the context of obesity, cognitive function, and depressive disorders. However, the intricate relationship between gut microbiota and cardiovascular diseases has yet to be thoroughly explored [11–13].

The study applied the commonly used bibliometric software (Citespace and VOSviewer) to analyze a thorough synthesis of the characteristics, evolutionary patterns, research hotspots and prospective directions into the gut microbiota's influence on cardiovascular diseases. The objective is to stimulate more diverse, insightful, and globally collaborative research data in this field.

2. Material and methods

2.1. Data collection

Data for this study were extracted and downloaded from the Web of Science Core Collection (WoSCC) on December 28th, 2024. Our search criteria were defined using the following formula: TS = (cardiac disease OR heart condition OR cardiovascular disorder OR heart ailment OR cardiac illness) AND TS = (gut microbiota OR intestinal flora OR intestinal microbiome OR gastrointestinal microbiota OR gut flora OR gut microbiome). The search spanned from 2006 to September 28th, 2024, and was confined to English-language publications. The study restricted the search to articles and reviews, yielding a total of 1,343 documents, averaging a yearly output of 68 publications.

2.2. Data analysis

This study employed a series of tools to manage, analyze, and visually represent data, including CiteSpace, VOSviewer, and Microsoft Office Excel 2010. CiteSpace, a leading visual analysis software in the field of bibliometrics, was utilized to dissect the literature from various perspectives. This software is adept at identifying research hotspots and trends within a defined academic sphere, presenting them in a visually engaging manner.

VOSviewer, a complimentary JAVA-based bibliometric mapping software, was also incorporated into our analytical framework. This tool excels in the visualization of scientific knowledge, offering a user-friendly interface for constructing and interpreting complex map. Its robust capacity to manage extensive datasets allows for the creation of large-scale, easily interpretable bibliometric maps, which are invaluable for uncovering the broader landscape of scholarly communication.

In addition, Microsoft Office Excel 2010 was employed for data management and to perform quantitative analyses of annual publication trends, complementing the visual insights provided by CiteSpace and VOSviewer. This comprehensive approach ensures a thorough and multifaceted exploration of the research topic.

3. Results

3.1. Global trend in publication output

There are 1680 papers adhered to our predefined inclusion and exclusion criteria, comprising 50.42% articles, 48.75% reviews, and a minor fraction of 0.83% classified as other (**Figure 1**). **Figure 1**A delineates a pronounced upward trajectory in the annual publication count, with the peak annual publication volume reached 276 articles in 2022. With the fastest growth rate in 2020–2021, indicating that research in this field has developed rapidly and is in a phase of rapid ascent. Significantly, the global scholarly community's interest in the microbiota's role in cardiac diseases peaked in 2021–2024, with a total of 1,025 publications over this 4-year period, which accounted for more than 61.01% of the total publications.

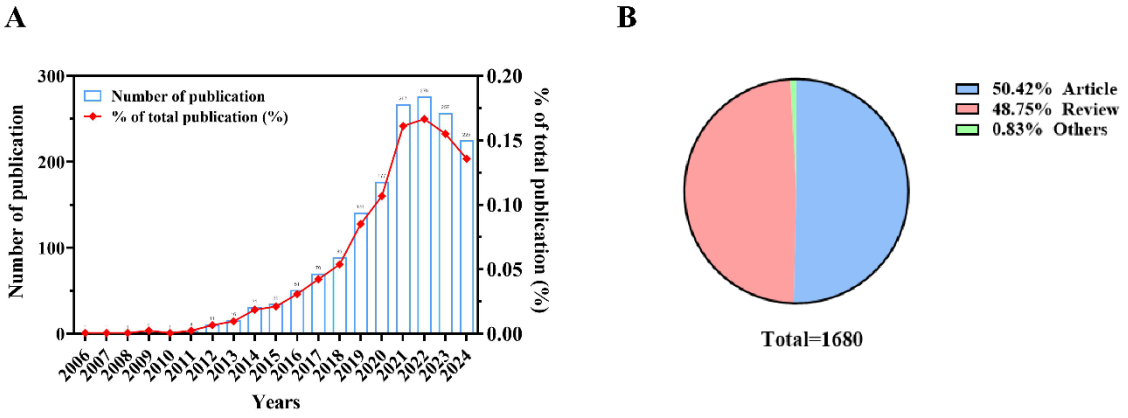


Figure 1. The trend of publication outputs.(A) The number of overall publications between 2006–2024; (B) The proportions of different article types.

3.2. Distribution of country, region, and institution

A total of 103 countries/regions and 277 institutions contributed to these scholarly publications. As detailed in **Table 1** and **Figure 2**, China emerged as the leading contributor (476, 28.3%), trailed by the United States (392, 23.3%), Italy (155, 9.2%) and India (80, 4.8%). Enhanced collaboration frequency is indicative of a nation's centrality within a collaborative network, as evidenced by Figures 2B and 2C, which map the cooperation networks across these countries/regions. The United States, China, Italy, and India were identified as the top five countries/regions based on their centrality, thereby establishing the United States and China as the most influential players in this field, as gauged by both publication volume and network centrality.

Table 1 and **Figure 2**D present the top 20 most prolific institutions. The University of California System published 52 papers and marking it as the foremost contributor to this area of research, succeeded by Institut National de la Sante et de la Recherche Medicale (Inserm), Chinese Academy of Medical Sciences-Peking Union Medical College, and Southern Medical University-China. The cooperation network among institutions, as shown in **Figure 2**E, reveals a vibrant landscape of collaborative efforts, with institutions such as the University of California System, Harvard University, and the Chinese Academy of Medical Sciences-Peking Union Medical College standing out for their active engagement in joint research endeavors.

Table 1. Top ten authors related to the research of gut microbiota on cardiovascular diseases

Authors	Country	Institution	Counts
W.H.Wilson Tang	Cleveland	Human Health, and Heart and Vascular Institute, Cleveland Clinic	11
Stanley L. Hazen	Cleveland	Department of Cellular and Molecular Medicine, Lerner Research Institute, Cleveland Clinic	10
Zeneng Wang	Cleveland	Department of Cardiovascular and Metabolic Sciences, Lerner Research Institute, Cleveland Clinic	5
Hamdi Jama	Australia	Hypertension Research Laboratory, School of Biological Sciences, Faculty of Science, Monash University Heart Failure Research Group, Baker Heart and Diabetes Institute	4
Bryan J. Neth	United States	Department of Internal Medicine- Gerontology and Geriatric Medicine, Wake Forest School of Medicine, Winston-Salem	4
Lars Gullestad	Norway	Department of Cardiology, Oslo University Hospital Rikshospitalet	4
Suzanne Craft	United States	Department of Internal Medicine, Section on Gerontology and Geriatric Medicine, Wake Forest School of Medicine	4
Asbjørn Svardal	Norway	Department of Clinical Science, University of Bergen Department of Heart Disease, Haukeland University Hospital	4
Amar B. Singh	United States	Department of Biochemistry and Molecular Biology, University of Nebraska Medical Center, Omaha	4
Marius Trøseid	Norway	Institute of Clinical Medicine, University of Oslo Research Institute of Internal Medicine, Sognsvannsveien 20, 0027 Oslo	4
Jeffrey Salomon	United States	Department of Pediatrics, University of Nebraska Medical Center	4

3.3. Distribution of authors

A total of 9,865 authors have made significant contributions to this field of study. **Table 1** highlights the top 10 most productive scholars. W.H. Wilson Tang stands out as the most prolific author, having contributed 11 publications, followed closely by Stanley L. Hazen and Zeneng Wang, both affiliated with the Cleveland Clinic. When considering the metric of total citations, W.H. Wilson Tang also secured the top position with an impressive 431 citations. Trailing behind Tang are Wang ZN and Cani PD, who have also made notable impacts in terms of citation counts (**Figure 3**).

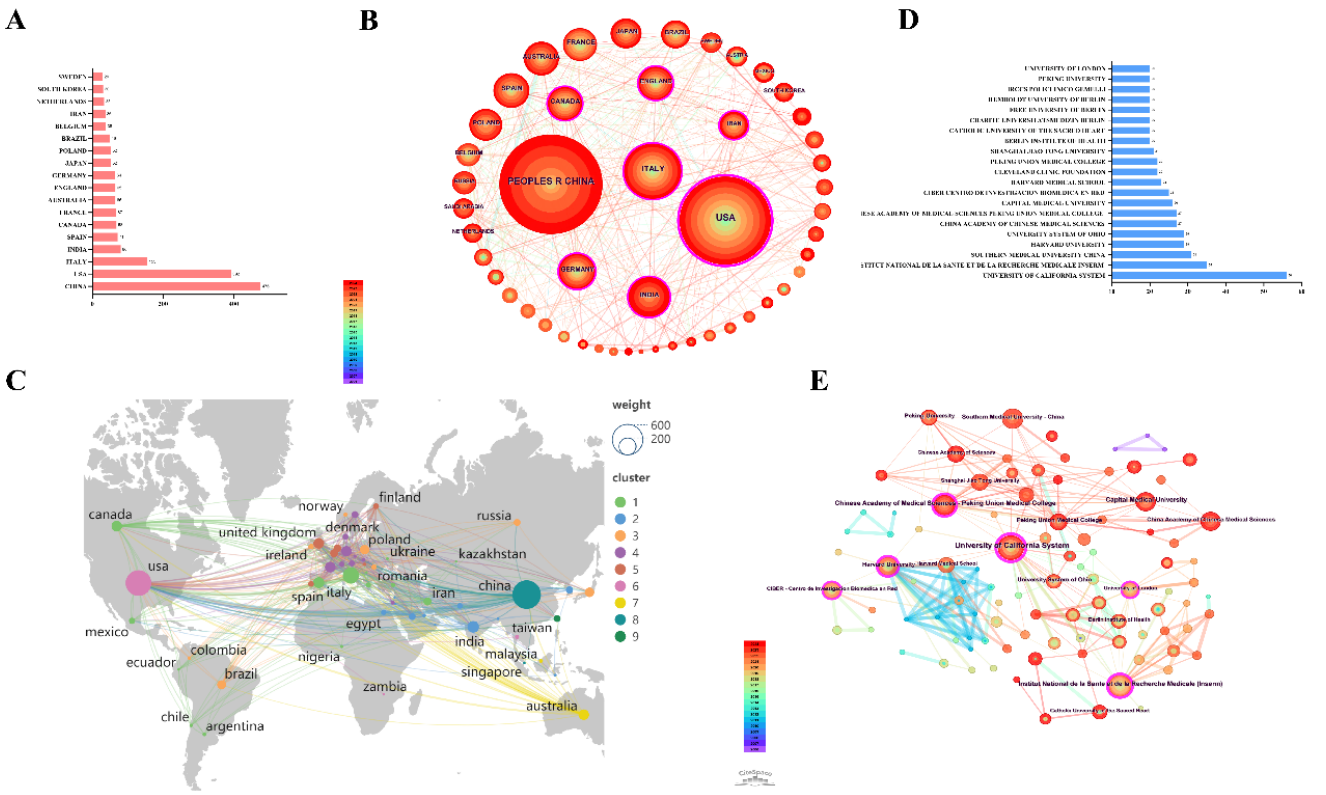


Figure 2. The co-occurrence map of countries/regions and institutions.(A, B, C: The co-occurrence map of countries/regions; D, E: The co-occurrence map of institutions).

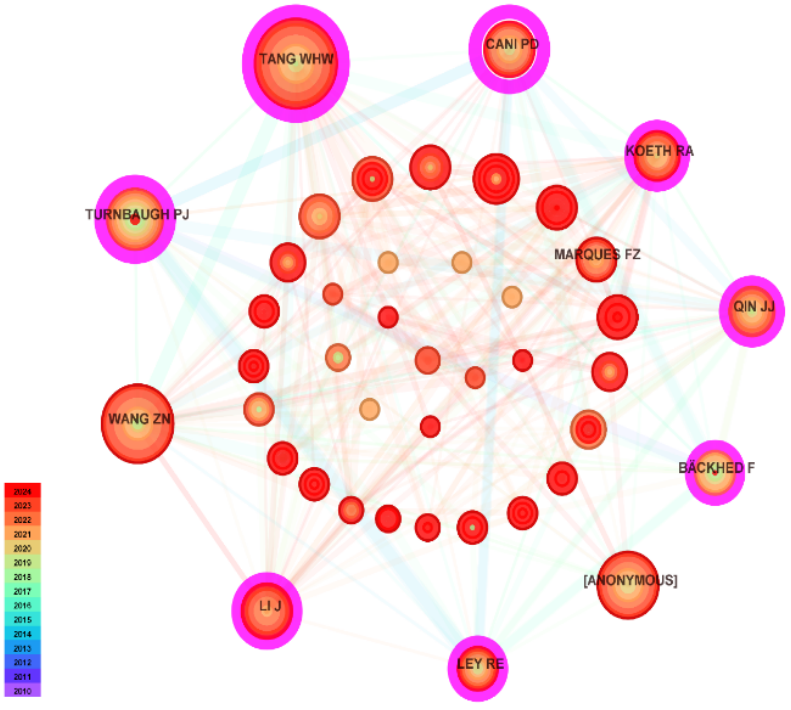


Figure 3. Co-citation author map for gut microbiota research in the cardiovascular diseases.

3.4. Distributions of journals and co-cited journals

Academic journals are pivotal platforms for disseminating the findings of scientific research. The publications under review were disseminated across 289 scholarly journals. **Table 2** delineates the attributes of the top 10 most productive journals in this context. These leading journals featured a total of 295 publications, representing 17.6% of the overall articles published in the field. When examining publication volume, the journal Nature emerged as the most influential, trailed by the American Journal of Clinical Nutrition and Gut. Notably, all of the top 10 journals are positioned within the first quartile, indicating their high impact and quality. Among them, six journals boasted an Impact Factor exceeding 20, underscoring their significance and prestige within the scientific community.

Table 2. Ranking of the top 10 journals and co-cited journals for gut microbiota research in the cardiovascular disease field

Journal	Count	IF	JCR	Co-cited journal	Co-citation	IF	JCR
Nutrients	67	4.8	Q1	Plos One	1159	2.9	Q1
International Journal of Molecular Sciences	51	4.9	Q1	Nature	1118	50.5	Q1
Scientific Reports	27	3.8	Q1	Scientific Reports	913	3.8	Q1
Frontiers in Cellular and Infection Microbiology	25	4.6	Q1	Proceedings of the National Academy of Sciences of The United States of America	906	9.4	Q1
Frontiers in Microbiology	25	4	Q2	Nutrients	833	4.8	Q1
Biomedicines	22	3.9	Q2	Circulation	781	35.5	Q1
Frontiers in Pharmacology	21	4.3	Q1	Gut	761	23	Q1
Frontiers in Cardiovascular Medicine	20	2.8	Q2	Science	743	44.7	Q1
Frontiers in Nutrition	20	4	Q2	Cell	741	45.5	Q1
Frontiers in Physiology	17	3.2	Q2	The New England Journal of Medicine	669	96.2	Q1

3.5. Co-cited references

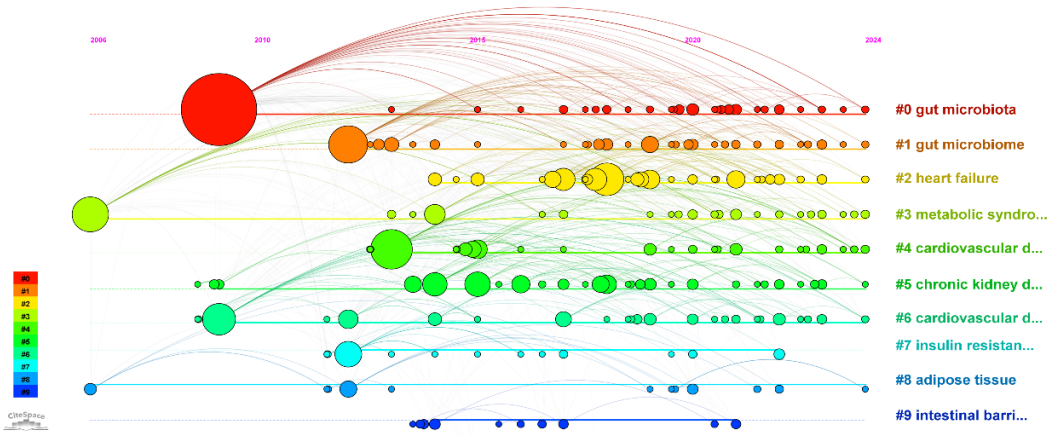
The analysis of co-cited references sheds light on the authoritative works that have shaped the field and the substantial contributions made by leading researchers. **Figure 5**A presents the largest nine clusters of references in a chronological view, highlighting the historical scientific significance of these co-cited references. The study identified 248 co-cited references pertaining to cardiovascular diseases and microbiota from the past decade. Each reference in the top twenty co-cited references garnered a minimum of 37 co-citations. Notably, Tang WHW's work from 2013 received the highest citation count, with a total of 64 citations, underscoring its seminal influence in this area of research (**Figure 5**B).

Top 20 Cited Journals with the Strongest Citation Bursts

Cited Journals	Year	Strength	Begin	End	2006 - 2024
NATURE	2006	56.47	**2009**	2018	
AM J CLIN NUTR	2006	36.98	**2009**	2018	
GUT	2006	34.09	**2009**	2017	
GASTROENTEROLOGY	2006	40.39	**2011**	2018	
P NATL ACAD SCI USA	2006	59.11	**2012**	2019	
SCIENCE	2006	40.57	**2012**	2018	
NEW ENGL J MED	2006	28.73	**2012**	2017	
DIABETES	2006	38.61	**2013**	2018	
PLOS ONE	2013	31.62	**2013**	2017	
J CLIN INVEST	2006	27.75	**2014**	2019	
J NUTR	2006	25.2	**2014**	2018	
BRIT J NUTR	2009	22.13	**2015**	2017	
APPL ENVIRON MICROB	2006	25.73	**2017**	2020	
ISME J	2018	41.96	**2018**	2021	
J LIPID RES	2006	27.15	**2018**	2021	
INT J OBESITY	2006	28.84	**2020**	2021	
FRONT CELL INFECT MI	2022	32.25	**2022**	2024	
EBIOMEDICINE	2022	31.48	**2022**	2024	
FRONT ENDOCRINOL	2022	24.52	**2022**	2024	
MICROORGANISMS	2022	24.38	**2022**	2024	

Figure 4. Top 20 cited journals with the strongest citation bursts.

A



B

Top 20 References with the Strongest Citation Bursts

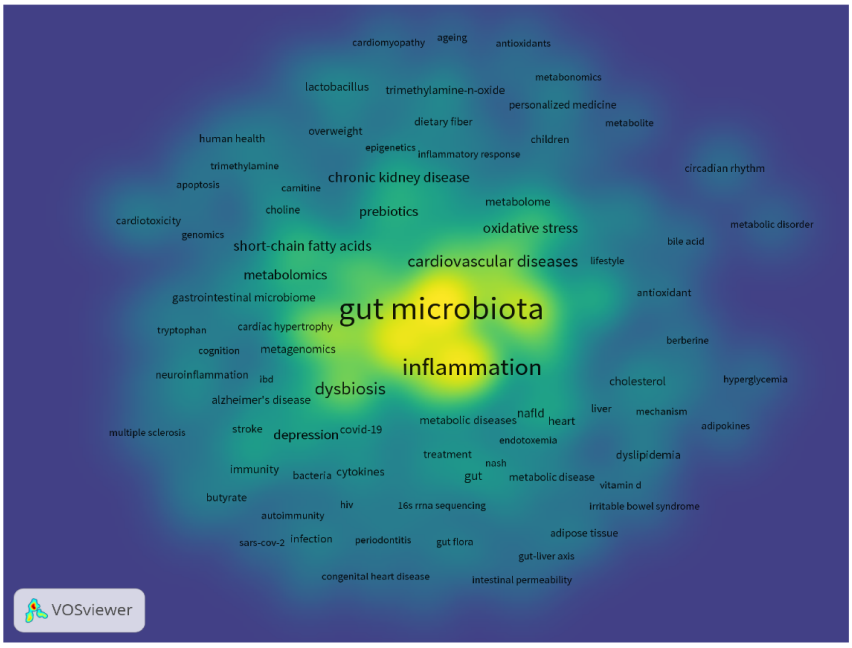
References	Year	Strength	Begin	End	2006 - 2024
Tang WHW, 2013, NEW ENGL J MED, V368, P1575, DOI 10.1056/NEJMoa1109400, DOI	2013	27.08	**2014**	2018	
Koeth RA, 2013, NAT MED, V19, P576, DOI 10.1038/nm.3145, DOI	2013	23.84	**2014**	2018	
Wang ZN, 2011, NATURE, V472, P57, DOI 10.1038/nature09922, DOI	2011	17.15	**2014**	2016	
Tremaroli V, 2012, NATURE, V489, P242, DOI 10.1038/nature11552, DOI	2012	14.66	**2014**	2016	
David LA, 2014, NATURE, V505, P559, DOI 10.1038/nature12820, DOI	2014	12.47	**2015**	2019	
Wang ZN, 2015, CELL, V163, P1585, DOI 10.1016/j.cell.2015.11.055, DOI	2015	16.33	**2017**	2020	
Tang WHW, 2015, CIRC RES, V116, P448, DOI 10.1161/CIRCRESAHA.116.305360, DOI	2015	13.61	**2017**	2020	
Zhu WF, 2016, CELL, V165, P111, DOI 10.1016/j.cell.2016.02.011, DOI	2016	21.09	**2018**	2021	
Tang WHW, 2017, CIRC RES, V120, P1183, DOI 10.1161/CIRCRESAHA.117.309715, DOI	2017	20.74	**2019**	2022	
Marques FZ, 2017, CIRCULATION, V135, P964, DOI 10.1161/CIRCULATIONAHA.116.024545, DOI	2017	17.19	**2019**	2022	
Jie ZY, 2017, NAT COMMUN, V8, P0, DOI 10.1038/s41467-017-00900-1, DOI	2017	16.72	**2019**	2022	
Li J, 2017, MICROBIOME, V5, P0, DOI 10.1186/s40168-016-0222-x, DOI	2017	16.03	**2019**	2022	
Yang T, 2015, HYPERTENSION, V65, P1331, DOI 10.1161/HYPERTENSIONAHA.115.05315, DOI	2015	12.37	**2019**	2020	
Cui X, 2018, SCI REP-UK, V8, P0, DOI 10.1038/s41598-017-18756-2, DOI	2018	11.84	**2021**	2024	
Witkowski M, 2020, CIRC RES, V127, P553, DOI 10.1161/CIRCRESAHA.120.316242, DOI	2020	22.32	**2022**	2024	
Fan Y, 2021, NAT REV MICROBIOL, V19, P55, DOI 10.1038/s41579-020-0433-9, DOI	2021	15.1	**2022**	2024	
Nemet I, 2020, CELL, V180, P862, DOI 10.1016/j.cell.2020.02.016, DOI	2020	15.1	**2022**	2024	
Tang TWH, 2019, CIRCULATION, V139, P647, DOI 10.1161/CIRCULATIONAHA.118.035235, DOI	2019	14.75	**2022**	2024	
Rinninella E, 2019, MICROORGANISMS, V7, P0, DOI 10.3390/microorganisms7010014, DOI	2019	12.63	**2022**	2024	
Bartolomaeus H, 2019, CIRCULATION, V139, P1407, DOI 10.1161/CIRCULATIONAHA.118.036652, DOI	2019	11.63	**2022**	2024	

Figure 5. Reference co-citation network knowledge map for research of gut microbiota in the cardiovascular disease from 2006 to 2024.(A: Timeline visualization map of the reference co-citation; B: Top20 references with the strongest citation burst).

3.6. Keywords with citation bursts

Keywords exhibiting citation bursts are those that have received a notable influx of citations over time from scholars active in related research domains. In the analysis, CiteSpace identified 293 keywords that experienced significant citation bursts, as depicted in **Figure 6**A. **Figure 6**B graphically represents these bursts with bars corresponding to specific years. The earliest notable activity is marked by a red bar in 2006, with the trend continuing up to 2024. The term "Adipose tissue" registered the most robust citation burst (strength = 5.17), closely followed by "insulin resistance" with a strength of 7.74. The top 15 keywords in this category spanned a burst strength range from 3.91 to 9.98, indicating their pivotal role in catalyzing research interest and discourse within the field.

A



B **Top 15 Keywords with the Strongest Citation Bursts**

Keywords	Year	Strength	Begin	End	2006 - 2024
adipose tissue	2006	5.17	**2006**	2016	
insulin resistance	2009	7.74	**2009**	2018	
glucagon like peptide 1	2009	5.12	**2009**	2018	
diet induced obesity	2010	7.67	**2010**	2018	
cardiovascular disease	2009	9.98	**2013**	2017	
inflammatory bowel disease	2013	8.85	**2013**	2018	
high fat diet	2013	4.7	**2013**	2017	
intestinal microbiota	2010	8.84	**2015**	2018	
glucose	2016	4.17	**2016**	2017	
metaanalysis	2018	3.91	**2018**	2020	
trimethylamine n-oxide	2021	4.54	**2021**	2022	
contributes	2019	4.19	**2021**	2022	
receptor	2021	3.97	**2021**	2024	
protein	2022	4.88	**2022**	2024	
acid	2022	4.19	**2022**	2024	

Figure 6. Keywords with citation bursts.(A: Visualization of keyword co-occurrence analysis from 2006 to 2024 based on the VOSviewer software; B: Top 15 keywords with the strongest citation bursts).

3.7. Hotspots and frontiers

By conducting a co-occurrence analysis of targeted keywords, the study could rapidly identify potential future research hotspots within the specified field. **Table 3** presents the top 15 high-frequency keywords, extracted from abstracts and titles that met our established criteria for the intersection of gut microbiota and cardiovascular diseases. The recurring emphasis on keywords such as "gut microbiota," "cardiovascular disease," and "adipose tissue," each appearing more than 300 times, underscores the predominant research trajectory in this area of study.

Table 3. Ranking of the top 15 keywords for gut microbiota research in the cardiovascular disease in terms of frequency

Frequency	Keywords
816	gut microbiota
327	cardiovascular disease
219	adipose tissue
186	inflammation
176	intestinal microbiota
171	insulin resistance
167	diet induced obesity
166	atherosclerosis
160	heart failure
155	chain fatty acids
143	metabolic syndrome
135	body mass index
129	blood pressure
123	gut microbiome
122	oxidative stress

The study summarized the top 10 research directions and found that in the field of research related to the gut microbiome and cardiovascular diseases, and found that biochemistry molecular biology-related research ranks first with a total of 232 papers, followed by pharmacology pharmacy-related research with a total of 214 papers, and nutrition diabetics-related research with a total of 192 papers (Figure7A). **Figure 7**B illustrates the top 10 diseases with the highest number of published papers, with heart failure dominating the list, followed by cardiometabolic disorders, infarction, and hypertension. This distribution suggests that there is a substantial and ongoing demand for research into the diverse spectrum of cardiovascular diseases.

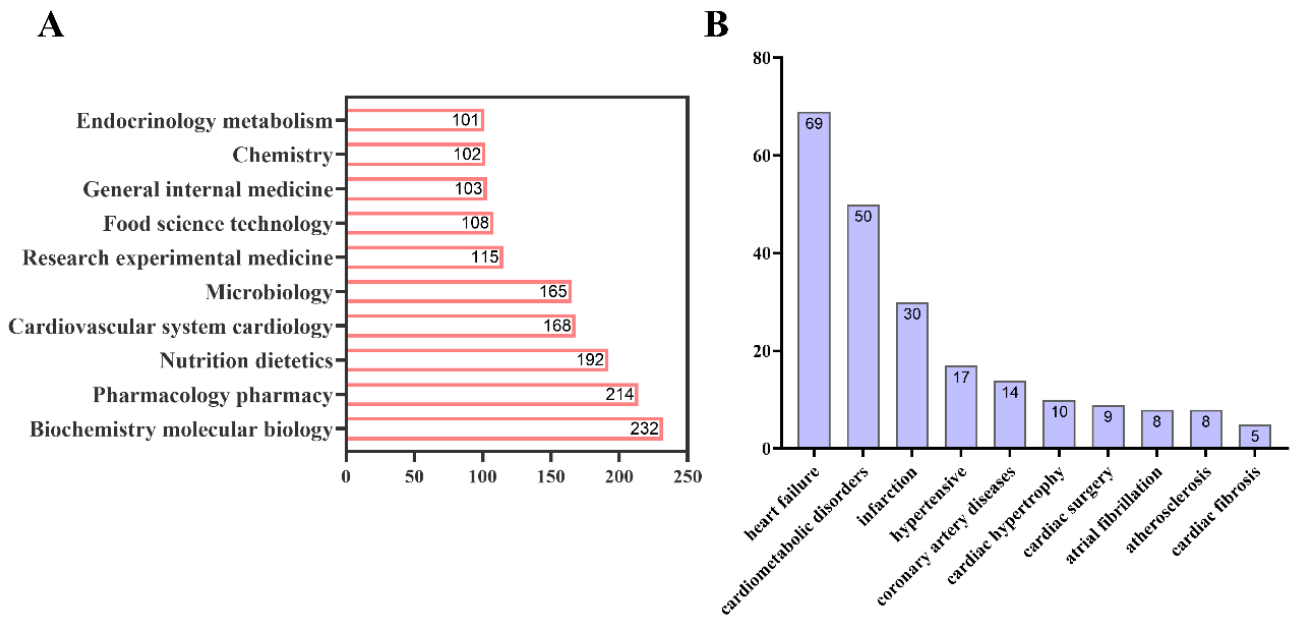


Figure 7. The top 10 research directions and diseases with the most papers.(A: The top 10 research directions; B: The top 10 diseases with the most papers).

3.8. Key gene cluster analysis

3.8.1. GO analysis

The study searched the targets for further analysis, and 135 potential targets were obtained. The 30 biological processes were mainly involved in biological process (BP), molecular function (MF), and cellular component (CC). The details are shown in **Figure 8**A–C. The process were, in the aspect of BP: regulation of inflammatory response (GO: 0050727), protein secretion (GO: 0009306), positive regulation of cytokine production (GO: 0001819), establishment of protein localization to extracellular region (GO: 0035592), and cellular response to lipopolysaccharide (GO: 0071222); in the aspect of MF: receptor ligand activity (GO: 0048018), signaling receptor activator activity (GO: 0030546), cytokine activity (GO: 0005125), cytokine receptor binding (GO: 0005126), and insulin-like growth factor receptor binding (GO: 0005159); and in the aspect of CC: endoplasmic reticulum lumen (GO: 0005788), phagocytic cup (GO: 0001891), blood microparticle (GO: 0072562), low density lipoprotein particle (GO: 0034362), and chylomicron (GO: 0042627).

3.8.2. KEGG pathway enrichment analysis

The study conducted KEGG pathway enrichment analysis on 136 targets and screened 21 signaling pathways: Malaria (hsa05144), Chagas disease (hsa05142), Pertussis (hsa05133), Yersinia infection (hsa05135), and Amoebiasis (hsa05146). The details are shown in **Figure 8**D.

3.8.3. PPI network analysis

As shown in **Figure 8**E, the study screened 136 targets and the top 20 targets were selected as the key targets. The main predicted targets were IFNG, IL10, TLR4, INS, TNF, IL6, IL1β, APOE, and AGT.

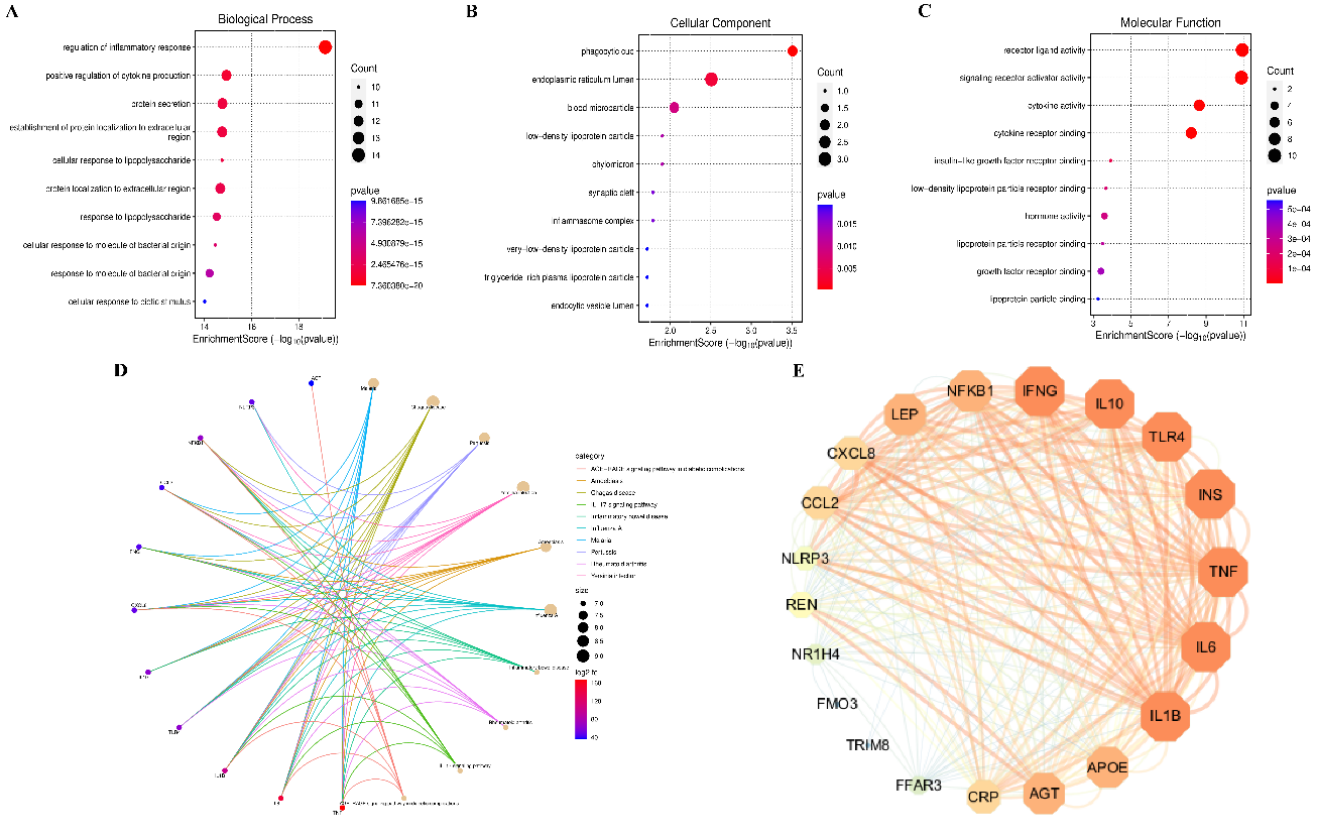


Figure 8. Key gene cluster analysis.(A–C: GO analysis; D: KEGG pathway enrichment analysis; E: PPI network analysis).

4. Discussion

4.1. Summary of the main findings

In this analysis, the study constructed a comprehensive landscape of global research on the interplay between cardiovascular diseases and gut microbiota over the past 2 decades, the study's focus has been on evaluating the current state of research, major key trends, and predicting forecasting emerging areas of interest and innovation.

The findings reveal a steady and significant rise in the annual publication count since the early 2000s, indicating a robust and promising field that is expected to continue expanding in the coming years. The United States, China, and Italy emerged as the most influential nations in terms of citation impact, while China also stands out as the most prolific contributor to the literature. The University of California System, Institut National de la Santé et de la Recherche Médicale (Inserm), and the Chinese Academy of Medical Sciences-Peking Union Medical College were identified as the top three most productive institutions, underscoring their pivotal roles in shaping the discourse in this domain. Among the leading researchers, W.H. Wilson Tang, Stanley L. Hazen, and Zeneng Wang from the Cleveland Clinic have made notable contributions, their work exemplifies the cutting-edge research that is driving the field forward. Regarding the most influential research themes, biochemistry and molecular biology, pharmacology and pharmacy, and nutrition and diabetes were the top 3 directions. These disciplines are at the forefront of uncovering the complex mechanisms linking epigenetics, gut microbiota, and cardiovascular health [5–7]. Furthermore, heart failure, cardiometabolic disorders, and myocardial infarction were identified as the cardiovascular conditions most closely associated with gut microbiota, highlighting the critical importance of these areas in future research endeavors [8]. The insights gained from this analysis not only chart

the current landscape but also provide a road for future investigations, potentially leading to breakthroughs in understanding and treating cardiovascular diseases through the lens of epigenetics and gut microbiota.

4.2. Identification of research trends

Keyword co-occurrence analysis functions as a reflective mirror, capturing the focal points and trends within academic disciplines. The analysis of keyword clusters delineates the underlying structure of knowledge, while the timeline view provides a dynamic visualization of the evolution of these research hotspots over time. As depicted in **Table 3**, the top 15 keywords appearing more than 100 times, have been identified as pivotal in the field of cardiovascular diseases and gut microbiota. The more representative keywords include gut microbiota, cardiovascular disease, adipose tissue, inflammation, intestinal microbiota, insulin resistance, diet-induced obesity, atherosclerosis, heart failure, chain fatty acids, metabolic syndrome, body mass index, blood pressure, gut microbiome, and oxidative stress. From an analysis of these keywords, the study can distill a comprehensive overview of the prevailing landscape within the associated fields:

(1) Cardiovascular disease remains the leading cause of mortality worldwide, exerting a profound impact on both developed and developing nations. The research landscape in this field is vast and constantly evolving, with a focus on improving patient outcomes through novel treatments, risk stratification, and prevention;

(2) Adipose tissue is recognized as an active participant in the pathogenesis of cardiovascular diseases, influencing the condition through a spectrum of mechanisms, including inflammation, oxidative stress, and direct effects on cardiac function. Moreover, the gut microbiota is suspected to modulate the metabolic impact of fatty acids, which could potentially influence cardiovascular health;

(3) Inflammation is a key player in the development of atherosclerosis, and recent breakthroughs have demonstrated that targeted neutralization of IL-1β can ameliorate cardiovascular outcomes, marking a significant step in understanding the role of inflammation in atherosclerotic disease;

(4) Intestinal microbiota and gut microbiome have been linked to various metabolic diseases, and ongoing research is probing the therapeutic potential of medium-chain fatty acids in managing these conditions;

(5) Diet-induced obesity models are extensively utilized to investigate the molecular aspects of obesity and its pathophysiological effects, including insulin resistance, coronary diseases and vascular dysfunction;

(6) Atherosclerosis forms the basis of a variety of cardiovascular diseases;

(7) Heart failure affects over 64 million people worldwide, with the incidence stabilizing in industrialized countries but increasing globally due to an aging population and enhanced survival rates for ischemic heart disease [9].

By distilling the top 10 research directions, the study can understand the scope and direction of research in this field. The most productive directions are biochemistry and molecular biology, with 232 literature, and then followed closely by pharmacology and pharmacy, which have yielded 214 publications. These trends underscore an escalating interest in deciphering the intricate dynamics between gut microbiota, metabolic health, and cardiovascular diseases, with a focus on developing novel therapeutic approaches to address these global health challenges.

4.3. The molecular mechanism of gut microbiota on cardiovascular disease

Given the rapid annual rise in mortality and morbidity rates attributed to cardiovascular diseases, the research of potential risk factors and innovative therapeutic strategies has become a critical imperative. Often referred to as the “forgotten organ”, the gut microbiota has been recognized as the largest endocrine organ in the human body. A

recent study revealed that distinct shifts in the microbial community's structure and function are associated with the occurrence and progression of cardiovascular diseases. However, discerning whether microbial alterations are the initiators of disease or merely consequences of pathological processes presents a complex and formidable challenge.

In patients with heart failure, the study often observes bowel wall edema and impaired barrier function, which can lead to the translocation of bacterial products into the host's circulation. Predominantly, these bacterial products are identified by toll-like receptors (TLRs), which are strategically located on the surface of immune cells, and trigger a signaling cascade that results in the release of pro-inflammatory cytokines after binding with the bacterial ligands [9]. Furthermore, preliminary clinical intervention studies have demonstrated a correlation between increased fiber intake and a reduction in blood pressure, and short-chain fatty acids (SCFAs) exert a regulatory influence on blood pressure regulation. A multitude of subsequent studies have reinforced the idea that SCFAs, generated by gut microbiota, are instrumental in modulating the host's blood pressure. Recent studies have shed additional light on the role of SCFAs in various other cardiovascular state, including the mitigation of ischemia-reperfusion injury, facilitation of cardiac repair post-myocardial infarction, and the enhancement of arterial compliance [14]. These findings underscore the multifaceted impact of the gut microbiota on cardiovascular health and highlight the potential therapeutic implications of modulating SCFA production in the context of CVD management [15].

In 2011, the Nature reported the study from Cleveland Clinic have highlighted that TMAO (Trimethylamine N-oxide), the production of gut microbiota, could increase the risk of CVD, and have the potential of predict outcomes across a spectrum of CVD phenotypes in large-scale clinical cohorts, including peripheral artery disease, coronary artery disease, acute coronary syndrome and heart failure [16,17]. Research has indicated that plasma TMAO levels exceeding approximately 6μM are predictive of an elevated risk of adverse cardiac events. A recent meta-analysis revealed that for every 10μM increase in TMAO, there is a 7.6% rise in all-cause mortality. Furthermore, it has been demonstrated that TMAO stimulates the expression of tissue factor (TF) in endothelial cells in vitro, thereby facilitating thrombosis and vascular inflammation [18]. Seldin et al. reported that elevated TMAO activates MAPK signaling and NFκB nuclear translocation. And this effect is particularly pronounced in individuals with type 2 diabetes, who often present with elevated circulating TMAO levels [19]. In addition, another production--phenylacetylglutamine (PAG), acts as an adrenergic receptor; they are crucially involved in heart disease and platelet function [20].

4.4. Practical significance of bibliometric studies

Bibliometrics is the application of statistical methods that has become an increasingly valuable tool in the field of medical research and clinical practice. It involves the quantitative analysis of literature to identify trends, patterns, and the impact of research publications. This approach provides insights into the evolution of medical knowledge and the effectiveness of various research strategies. In medical research, bibliometrics helps to assess the productivity and citation impact of individual researchers, institutions, and countries. By analyzing the citation patterns, researchers can identify the most influential studies and the key players in a particular field. This information is crucial for funding decisions, research collaborations, and the allocation of resources. Moreover, bibliometric analysis can be used to track the progress of specific diseases or conditions over time [21]. This can help in prioritizing research efforts and identifying gaps in knowledge that need to be addressed. In clinical practice, bibliometrics can aid in evidence-based medicine by identifying the most relevant and high-quality studies. By analyzing the citation frequency of clinical trials and systematic reviews, healthcare providers can make more informed decisions about treatment options and best practices. This can lead to improved patient outcomes and more efficient use of healthcare resources. Furthermore, bibliometrics can be employed to evaluate the effectiveness of medical education and

training programs. By assessing the publication output of graduates and the impact of their research, educational institutions can refine their curricula and teaching methods to better prepare future healthcare professionals [22].

4.5. Strengths and limitations

Bibliometrics plays a significant role in both medical research and clinical practice by providing a quantitative framework for understanding and evaluating the vast amount of medical literature. However, there are still exist following shortcomings: First, since the Web of Science is the most commonly used and comprehensive literature database, our data is sourced from it, thus, data not included in the Web of Science has been overlooked. Second, due to the quality differences among the included literature, our analysis may have a small degree of bias. Nevertheless, our research has unearthed the intrinsic connections between cardiovascular diseases and a series of studies on gut microbiota, and offers a means to identify influential research, track the progress of diseases, support evidence-based medicine, and assess the impact of medical education.

The study shows a steady upward trend in global research on the interplay between gut microbiota and cardiovascular diseases from 2006 to 2024. The cardiovascular system emerged as the predominant subject category, reflecting a concentrated focus within this area of study. The United States has been identified as a pivotal driver of research, highlighting its leading role in contributing to the scientific discourse. Interestingly, the analysis reveals a relatively modest level of collaboration among the constituents and authors, suggesting an opportunity for enhanced interdisciplinary cooperation. It serves as a valuable resource for identifying key research institutions and authors, pivotal journals, evolutionary trends, frontier research hotspots, and prospective directions within this dynamic field. Future research is anticipated to yield substantial breakthroughs in the development of innovative therapeutic strategies for the metabolic modulation of cardiovascular diseases.

Author contributions

Study design – Liming H and Min B
Draft preparation – Rong J and Min B
Literature review – Liming H and Min B
Data analysis – Liming H and Min B
Manuscript edit and review – Rong J and Min B
Supervision - LMH

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Disclosure statement

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