Title: Research Landscape of Exercise-Related Extracellular Vesicles: A Bibliometric Analysis (2010–2024)

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Abstract

Background: Extracellular vesicles (EVs) are key mediators of interorgan communication during exercise, with growing research interest in their role in exercise physiology and health. This study aims to map the research landscape of exercise-related EVs from 2010 to 2024 using bibliometric analysis.

Methods: We analyzed 398 publications (252 articles and 146 reviews) from the Web of Science Core Collection, employing the Bibliometrix R package, VOSviewer, and Microsoft Excel to evaluate publication trends, key contributors, and research foci.

Results: The field exhibits a robust annual growth rate of 30.38%, with a peak of 85 publications and 2411 citations in 2023. China and the United States lead publication output, together contributing over 36% of total publications, with key institutions including the University of Pittsburgh and Harvard University. Core journals, such as Frontiers in Physiology and International Journal of Molecular Sciences, dominate the field. Keyword analysis highlights "extracellular vesicles," "exosomes," "exercise," and "skeletal muscle" as central themes, alongside emerging topics like microRNAs, oxidative stress, and insulin resistance.

Conclusion: These findings underscore the increasing recognition of EVs as critical mediators of exercise-induced interorgan crosstalk and their potential as biomarkers for health and disease, providing a foundation for future interdisciplinary research in exercise physiology and EV biology.

Keywords: Bibliometric Analysis, Exercise Training, Extracellular Vesicles

Highlights

Robust Growth: The field of exercise-related extracellular vesicles (EVs) has experienced a significant annual growth rate of 30.38%, with a peak of 85 articles and 2,411 citations in 2023.

Global Leadership: China and the United States are the leading contributors, accounting for over 36% of total publications, with prominent institutions like the University of Pittsburgh and Harvard University driving research.

Key Themes: Dominant keywords include "extracellular vesicles," "exosomes," "exercise," and "skeletal muscle," highlighting the focus on EVs as mediators of interorgan communication.

Emerging Trends: Research is increasingly exploring the roles of microRNAs, oxidative stress, and insulin resistance in exercise-induced EV signaling.

Interdisciplinary Potential: The study underscores the promise of EVs as biomarkers for health and disease, bridging exercise physiology and EV biology.

Plain Language Summary

This study provides a comprehensive overview of research on extracellular vesicles (EVs) released during exercise, analyzing 398 publications from 2010 to 2024. EVs are tiny particles that cells release to communicate with each other, and they play a key role in how exercise benefits the body. The findings show a rapid increase in research interest, with China and the United States leading in publications. Key topics include EVs' roles in muscle function, their potential as health biomarkers, and their connection to conditions like oxidative stress and insulin resistance. The study also identifies top journals, institutions, and authors in the field, offering valuable insights for future research. By mapping these trends, the analysis helps scientists understand the growing importance of EVs in exercise science and their potential applications in medicine.

Introduction

The investigation of variables that may mediate interorgan crosstalk during and after exercise is an exciting area of study in exercise physiology. Exercise stimulates many different metabolic pathways in several tissues, organs, and systems; therefore, it is critical to investigate the underlying molecular mechanisms promoting the metabolic benefits of exercise. During exercise, skeletal muscles release humoral factors into the bloodstream, which were termed myokines (1). These myokines are now widely recognized and extensively researched in the field of exercise science (2). Exercise triggers the release of signaling molecules from multiple tissues, including the nervous system, white and brown adipose tissue, liver, and heart, collectively termed 'exerkines,' which encompass cytokines, lipids, metabolites, and nucleic acids (3). These exerkines mediate interorgan crosstalk during exercise, with myokines representing a subset derived from skeletal muscle. Complementing exerkines, extracellular vesicles (EVs) serve as critical carriers of these signaling molecules, protecting and delivering complex cargos, such as microRNAs and proteins, to distant tissues, thereby enhancing exercise-induced interorgan communication (3, 4). Unlike myokines, which are primarily secreted proteins, EVs encapsulate a diverse array of biomolecules, offering a unique mechanism for stable, long-distance signaling (4). Notably, exercise modalities such as aerobic training and yoga have been shown to reduce inflammatory markers such as IL-6, CRP, and TNF-α in older adults and patients with multiple sclerosis, respectively, highlighting the potential of exercise-induced EVs in modulating chronic inflammation across diverse clinical populations (5, 6).

Exerkines and extracellular vesicles (EVs) have garnered significant interest due to their function as carriers of molecular signals, as EVs are recognized as key mediators in exercise-triggered communication between organs (4). EVs are membranous vesicles released by all cell types during both physiological and pathophysiological conditions. According to their biogenesis, size and biophysical properties, they can roughly be divided into two main categories: exosomes and microvesicles (7). EVs also include vesicles generated through different cell death processes, including apoptosis, necrosis, and focal cell death (8). The prospect of EVs is mainly related to their cargo. The "vesicular package" protects signals from damage and enables the transmission of multiple messages over long distances. Moreover, EVs are thought to be potential biomarkers for a number of disorders since their content may reflect the original cell status (9).

Bibliometrics analysis was initially presented by Alan Prichard in 1969 (10). Bibliometrics is a widely used method for quantitatively and statistically visualizing evidence based on information in published studies in a given research field, including authors, Countries and their cooperation, institutions, journals, analysis of keywords, references, and co-citations (11). Bibliometric analysis offers researchers a distinctive perspective on the present landscape and emerging directions in a given field, providing insights that conventional methods such as systematic reviews, meta-analyses, and evidence mapping cannot deliver (12). Unlike systematic reviews or meta-analyses, which focus on synthesizing study findings, bibliometric analysis quantitatively maps publication trends, collaborations, and research foci across a field, using tools such as CiteSpace, VOSviewer, and the Bibliometrix R-package, which are widely applied in medicine, biology, and immunology (13). This approach is particularly suited for studying exercise-related extracellular vesicles due to its ability to identify emerging trends and key research themes in this rapidly evolving interdisciplinary field (13).

To date, no bibliometric study has quantitatively examined the impact of exercise on extracellular vesicles (EVs) from 2010 to 2024, a period marked by rapid growth in EV research due to their emerging role in exercise physiology (4). This study addresses this gap by employing bibliometric methods to comprehensively evaluate existing research, driven by the interdisciplinary nature of EV studies and the need to map evolving trends and collaborations in this dynamic field (13). Using scientific visualization tools, we identify and assess current research hotspots and emerging trends to guide future investigations in exercise-related EV biology.

Materials and methods

Search strategies and data sources

Among major academic databases such as Scopus and PubMed, the Web of Science Core Collection (WoSCC) is widely recognized as the most authoritative and comprehensive source for bibliometric research. For this study, we retrieved all scientific publications on exercise-related extracellular vesicles from WoSCC, spanning the years 2010 to 2024. The search query combined the terms: TS=((exercise) OR (exercise training) OR (physical activity)) AND TS=(extracellular vesicles), limited to articles and reviews published between January 1, 2010, and July 19, 2024. The term "extracellular vesicles" was chosen because it is a widely accepted umbrella term encompassing related concepts, such as exosomes and microvesicles, ensuring comprehensive coverage of the relevant literature while minimizing redundancy. Similarly, the terms "exercise," "exercise training," and "physical activity" were selected to capture studies related to physical exertion broadly. The initial search yielded 438 records, which were subsequently refined by excluding non-relevant document types, including meeting abstracts (22), editorials (7), early access publications (5) due to potential incomplete metadata or unfinished peer-review processes, book chapters (3), corrections (2), and letters (1), as these often lack comprehensive scientific content or robust citation data required for quantitative mapping (12). After this rigorous screening process, 398 qualified records remained for analysis, comprising 252 research articles and 146 review papers. All selected publications were exported as complete records with cited references in plain text format for bibliometric mapping. Figure 1 presents a detailed flowchart of the document selection procedure.
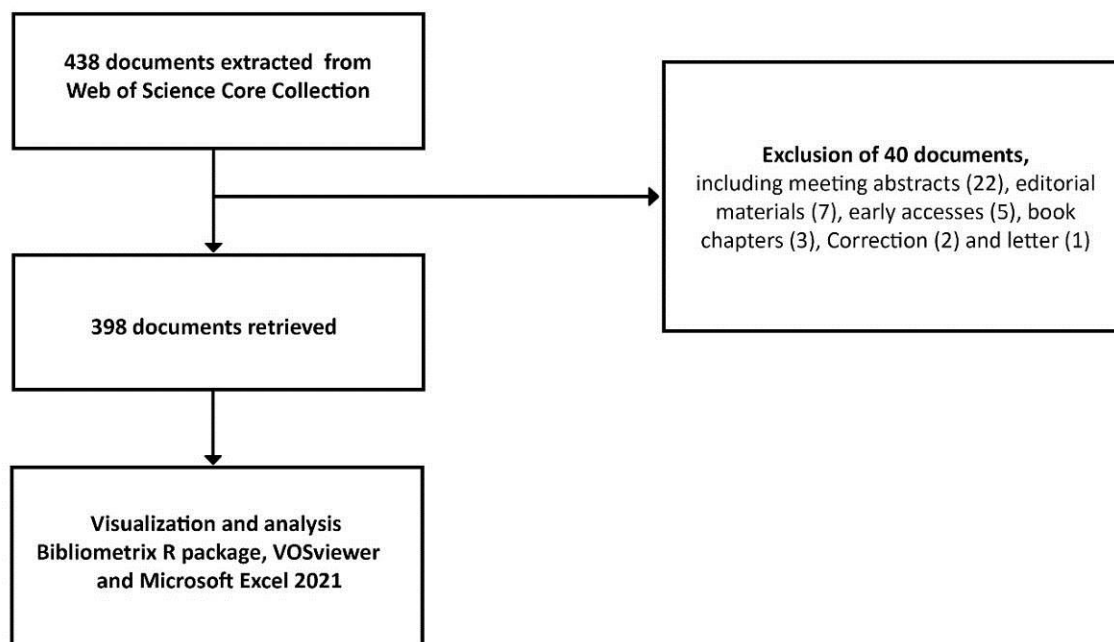
Figure 1. Flowchart of document selection

Data analysis and visualization

For this bibliometric analysis, we employed two primary software tools: the Bibliometrix R package (v4.4.1) and VOSviewer (v1.6.20). The Bibliometrix R package, run through R-Studio, facilitated quantitative analysis by extracting key publication metrics, including annual output, leading countries/institutions, prominent journals, and author h-indices, as well as co-word analysis to identify keyword relationships (14). Bibliographic coupling and thematic evolution analyses were not conducted, as the study focused on publication trends and keyword co-occurrence networks. VOSviewer generated co-occurrence network maps for keywords, where node size represented keyword frequency, node color indicated thematic clusters, and line thickness reflected the strength of co-occurrence relationships (15). This multi-tool approach ensured rigorous data synthesis and intuitive visualization of research trends.

Results

Publication Output Analysis

The 398 documents retrieved in this study were cited 9944 times, with an average of 24.98 citations per article and an H-index of 51, as summarized in Table 1, which presents key bibliometric metrics including total documents, citations, and citation impact. A total of 398 publications were identified between January 1, 2010, and July 20, 2024, including 252 articles and 146 reviews. Figure 2 demonstrates that, in recent years, the number of articles and citations in this field has generally been increasing with a

30.38% annual growth rate. Specifically, the number of citations (2411) and articles (85) peaked in 2023. The continuous increase in publications likely reflects the growing recognition of the role of extracellular vesicles (EVs) and their responsiveness to physiological and metabolic adaptations during exercise.

Table 1. Bibliographic statistics of publications extracted from WoS.

Publications	Sum of the Times Cited	Citing Articles	Average Citations per Item	H-index
398	9944	7456	24.98	51
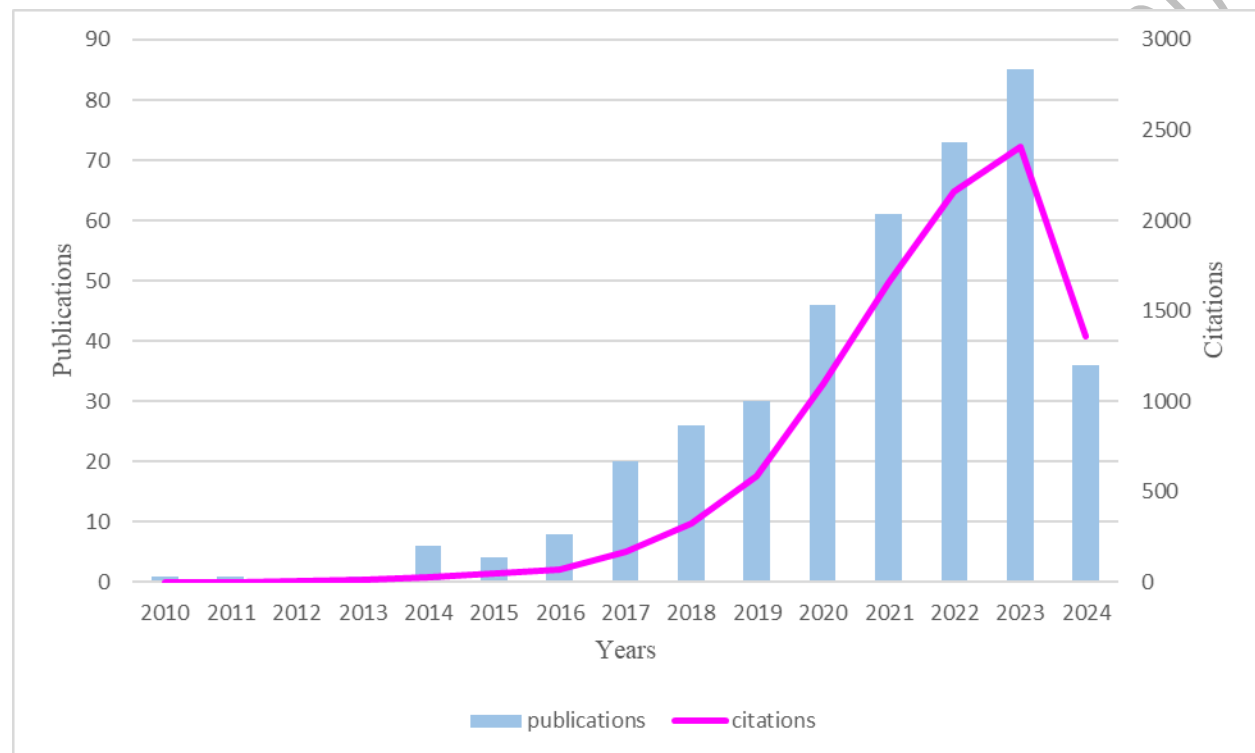
Figure 2. The annual number of publications and citations from 2010 to 2024.

Analysis of countries and institutions

A total of 36 corresponding authors' countries and 639 institutions contributed to the 398 filtered studies on exercise-related extracellular vesicles from January 1, 2010, to July 19, 2024. China and the United States led publication output, each contributing 73 articles (together accounting for over 36% of total publications), followed by Italy (n = 45), Canada (n = 25), and Brazil (n = 21), as shown in Figure 3. The details of the top 10 countries, their publications, and single-country publication (SCP) and multiple-country publication (MCP) collaborations are reported in Table 2. Regarding citations, the United States leads with 1620 total citations and an average of 22.20 citations per article, followed by China with 1579 total citations and 21.60 average citations, Italy with 1138 total citations and 25.30 average citations, Australia with 948 total citations and 55.80 average citations, and Canada with 848 total citations and 33.90 average citations.

Table 2. Top 10 corresponding author's countries, 2010-2024

Rank	Country	Publications	Publications %	SCP	MCP	MCP %
1	China	73	18.3	53	20	27.4
2	USA	73	18.3	56	17	23.3
3	Italy	45	11.3	30	15	33.3
4	Canada	25	6.3	21	4	16
5	Brazil	21	5.3	11	10	47.6
6	Germany	19	4.8	12	7	36.8
7	United Kingdom	18	4.5	11	7	38.9
8	Australia	17	4.3	11	6	35.3
9	Japan	13	3.3	11	2	15.4
10	Spain	11	2.8	7	4	36.4
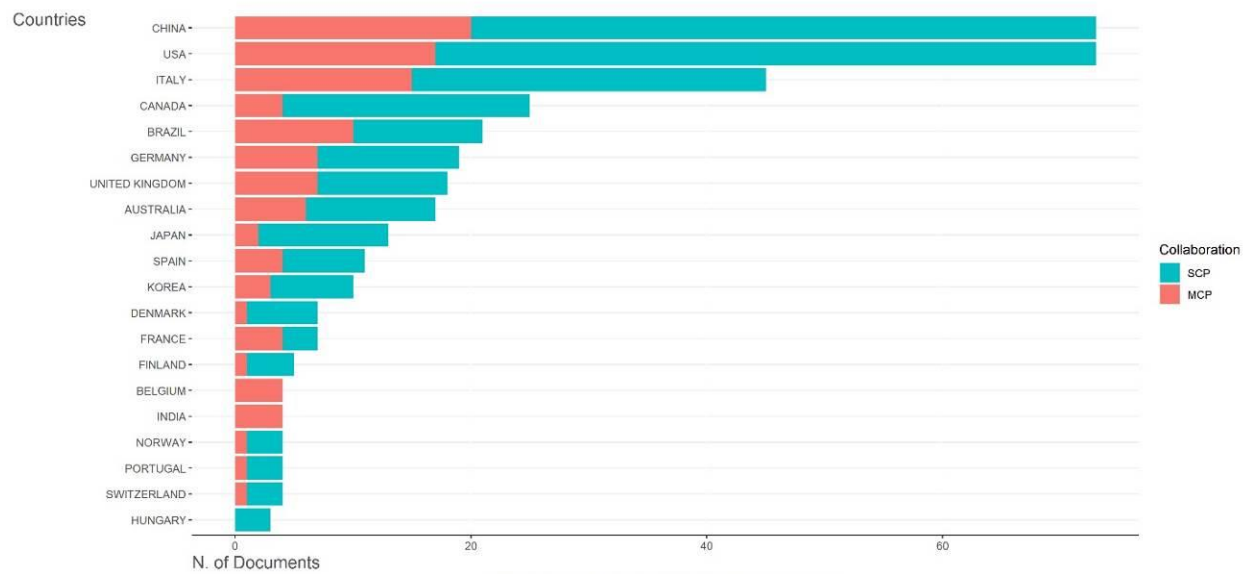
Figure 3. Number of publications in the Top 10 corresponding author's country.

The most productive institution is the Pennsylvania Commonwealth System of Higher Education (Pcshe)(36 publications), followed by the University of Pittsburgh (36 publications), Harvard University (28 publications), the University of California (25 publications), and National University of Singapore (21 publications). Lists of the top 10 institutions with the highest number of publications are shown in Table 3.

Table 3. Top 10 author's institutions

Rank	Institution	Country	Publications
1	Pennsylvania Commonwealth System of Higher Education (Pcshe)	USA	36
2	University of Pittsburgh	USA	36
3	Harvard University	USA	28
4	University of California	USA	25
5	National University of Singapore	Singapore	21
6	G D'Annunzio University of Chieti-Pescara	Italy	20
7	University of Kentucky	USA	20
8	Aarhus University	Denmark	19
9	Air Force Military Medical University	China	17
10	Harvard Medical School	USA	16

Analysis of journals

All the publications were found in a total of 231 different journals. Bradford's Law, also known as Bradford's Law of Dispersion, states that a core group of journals will contain a large proportion of relevant articles, while the remaining articles will be dispersed among a larger number of less cited journals (16). Based on this law, the number of core sources with the largest number of publications in this field is 20 (Figure 4), accounting for 8.65% (20/231) of the whole publication source sample.
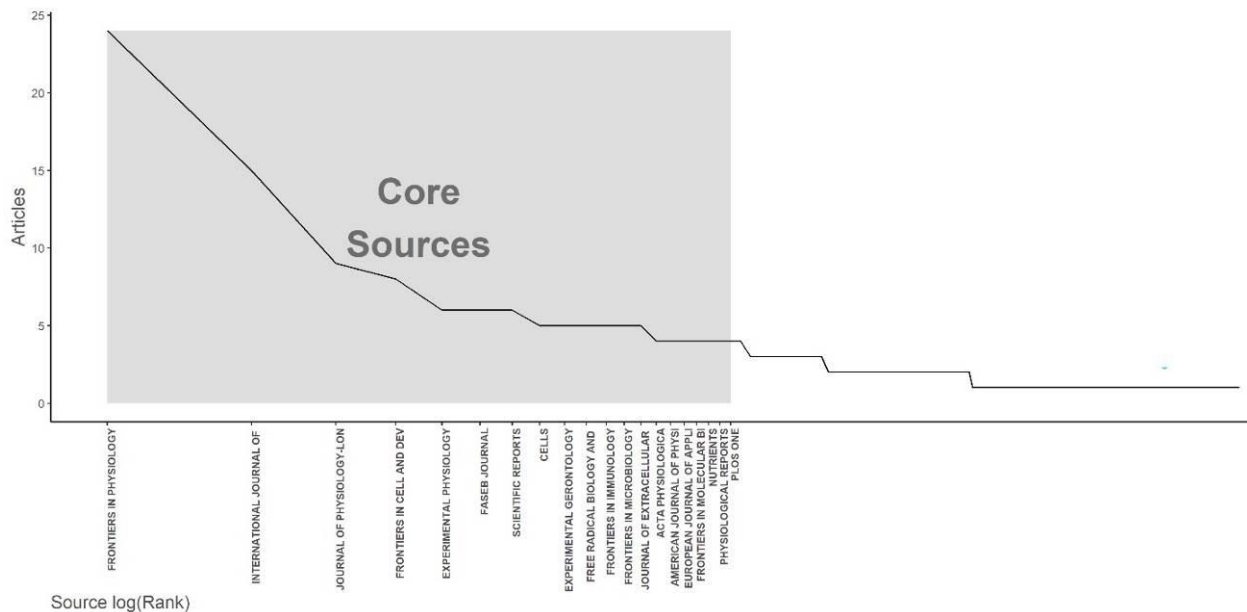

Figure 4. The core journals in the exercise-related EVs field based on Bradford's law.

Table 4 presents the basic information of the top 10 most productive journals. "Frontiers in Psychology" tops the list with 24 publications, followed by "International Journal of Molecular Sciences" with 15 publications, "Journal of Physiology-London" with 9 publications, "Frontiers in cell and developmental biology" with 8 publications, and , "Experimental Physiology" with 6 publications.

Table 4. Top 10 Relevant journals

Rank	Journal	publications	IF (2023)	JCR Category
1	Frontiers in Physiology	24	4.0	Physiology
2	International Journal of Molecular Sciences	15	5.6	Biochemistry & Molecular Biology
3	Journal of Physiology-London	9	4.7	Physiology
4	Frontiers in cell and developmental biology	8	5.5	Cell and Developmental Biology
5	Experimental Physiology	6	2.6	Physiology
6	FASEB Journal	6	4.8	Biology
7	Scientific reports	6	4.6	Multidisciplinary Sciences
8	Cells	5	6	Cell biology
9	Experimental Gerontology	5	3.9	Experimental Gerontology
10	Free Radical Biology and Medicine	5	7.4	Endocrinology & Metabolism

Analysis of Authors

The papers were contributed by 2451 authors. In terms of the number of publications in this field, Sahu A was the most productive author, with 7 publications. followed by Tarnopolsky MA (7publications), Ambrosio F (6 publications), Cechinel LR (6 publications), and Gavin TP (6 publications). The top 10 authors are presented in Table 5. Figure 5 shows the activity of these authors in the period from 2010 to 2024. Most of the top authors are still actively publishing articles in the field.

Table 5. Top 10 the most productive authors distributed by publications

Rank	Authors	Publications	Citations	Publications Fractionalized
1	Sahu A	7	19	0.671
2	Tarnopolsky MA	7	534	1.598
3	Ambrosio F	6	19	0.546
4	Cechinel LR	6	115	1.211
5	Gavin TP	6	118	0.828
6	Kargl CK	6	17	0.686
7	Whitham M	6	444	1.502
8	Adamo kb	5	11	0.744
9	Conkright WR	5	16	0.403
10	Kuang SH	5	106	0.628
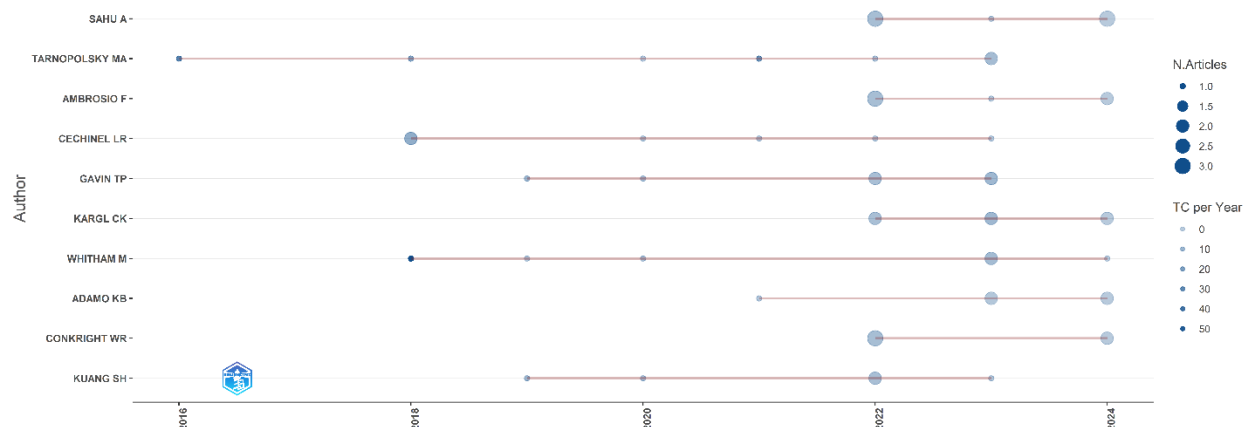
Figure 5. Authors' production overtime.

Analysis of keywords

Keywords are author summaries of the article's content, reflecting the main points and research frontiers of the study. Figure 6A illustrates the most frequently used keywords in this publication, with the size of each box representing the frequency of usage and the percentage of each keyword's usage in the total texts reviewed displayed within each box. Figure 6B shows a cloud map of the top 50 keywords used in these articles, with bolder fonts indicating more frequent occurrences. High-frequency keywords included 'extracellular vesicles', 'exosomes', 'exercise', 'skeletal muscle', 'expression', 'physical activity', 'cells', 'microRNAs', 'microvesicles', 'oxidative stress', 'biogenesis', 'gene expression', 'insulin resistance', 'release', and 'biomarkers', all occurring more than 20 times. Notably, 'oxidative stress' and 'insulin resistance' are emerging as key research foci due to their biological and clinical relevance: oxidative stress is linked to exercise-induced cellular responses and tissue repair, while insulin resistance reflects the role of exercise-related EVs in metabolic regulation, with potential implications for diseases like diabetes (4, 17).

Figure 6. The keyword analysis in exercise-related extracellular vesicles publications (2010-2024) **(A)** The treemap based on keywords plus **(B)** The wordcloud based on keywords plus.

After conducting a VOSviewer analysis, we identified a total of 2438 keywords. Following a keyword filtering process with a minimum occurrence threshold of 10, we identified a total of 65 keywords. After that, a keyword co-occurrence network map was created (Figure 7), showing important associations between terms like extracellular vesicles, exercise, exosomes, and oxidative stress. The 65 keywords are categorized into four clusters. Cluster one (red) Includes terms such as extracellular vesicles, exosome, cells, inflammation, proliferation, cancer, stem cells, regeneration, aging, primarily focusing on cell-related aspects. Cluster two (green) includes exosomes, exercise, skeletal muscle, microRNAs, plasma, microvesicles, and primarily focusing on aspects related to the release of exosomes and vesicles. Cluster

three (blue) involves physical activity, skeletal muscle, endurance exercise, aerobic exercise, insulin-resistance, obesity, adipose tissue, focusing on some influential aspects of physical activity. Finally, cluster four (yellow) which includes the keywords oxidative stress, angiogenesis, heart, mechanisms, nitric oxide, progenitor cells, and responses.

Figure 7. Co-occurrence analysis of keywords in exercise-related extracellular vesicles publications (2010–2024). **(A)** Network visualization, showing relationships between keywords as nodes connected by edges, with node size and edge thickness indicating frequency and co-occurrence strength, respectively. **(B)** Overlay visualization, highlighting temporal trends by mapping keyword frequencies over time using color gradients.

The node size shown in Figure 7A.B is positively correlated with the frequency of node content, and the thickness of the connection line is positively correlated with the co-occurrence times of node content at both ends. Different color clustering reflects the cooperative relationship between keywords (Figure 7A). The colors in the overlay visualization shown in Figure 5B represent the average publication year of the identified keywords. Most keywords were published after 2020, with greener colors (Figure 7B).

Discussion

Extracellular vesicles (EVs) represent a critical mechanism for intercellular communication across biological systems. Structurally, they are categorized into three subtypes based on size and morphology: exosomes, microvesicles, and apoptotic bodies, all featuring characteristic lipid bilayer membranes (18, 19). Functionally, these vesicles transport diverse biomolecules - particularly microRNAs (miRNAs) and mRNAs - that mediate the physiological effects of their parent cells, including intercellular signaling (20).

Notably, EVs exhibit remarkable sensitivity to physiological stress, as evidenced by their dynamic proteomic profiles (21, 22). In this context, exercise training emerges as a potent physiological stimulus with systemic health implications. Regular physical activity is associated with reduced all-cause mortality and decreased risk of various chronic, age-related pathologies (23). Significantly, many of these

conditions - including cardiovascular disease (24), metabolic disorders (17), malignancies (25), and neurodegenerative diseases (26), demonstrating substantial involvement of EVs in their pathogenesis and progression.

Bibliometric records from WoSCC indicate that exercise-related EVs have garnered increasing scholarly attention since 2001 (27)(26). Our research indicates a notable rise in the number of publications between 2010 and 2024, possibly indicating growing interest from active authors in this area. This increased attention may be due to the role of exercise in regulating extracellular vesicles and their impact on both physiological and pathological processes.

Bibliometric analysis, as applied in this study, has enabled the identification of key research trends and interdisciplinary connections in the field of exercise-related EVs. By mapping publication outputs, keyword co-occurrence networks, and international collaborations, this approach highlights critical areas such as the role of EVs in skeletal muscle signaling, microRNA transport, and their potential as biomarkers for conditions like insulin resistance and oxidative stress. These insights facilitate the prediction of future research directions, such as exploring multi-organ interactions and EV-based therapeutic applications, fostering interdisciplinary advancements in exercise physiology and molecular biology.

This study represents the inaugural bibliometric assessment of research on *Exercise-related Extracellular Vesicles*, systematically evaluating current knowledge landscapes and emerging trends through quantitative data analysis. The annual publication output demonstrates a consistent upward trajectory, reflecting both growing scholarly interest and the field's developmental potential. Our analysis of contributions according to country revealed that China and the USA dominate this field. These countries were the most productive, contributing >36% of all publications. Also, Of the top 10 institutions, five were in the USA. This could be linked to the economic progress and financial backing for scientific research in these major contributing countries.

The 398 analyzed studies on exercise-related extracellular vesicles appeared in 231 distinct journals. Applying Bradford's Law of Scattering, which divides journals into three zones where the core zone contains approximately one-third of all articles, we identified 20 core journals that collectively published a significant proportion of articles in this field. Frontiers in Physiology emerged as the most prominent journal, leading in three key metrics (Publication volume (n=24), H-index (140),Total citations (53,422)). Other high-impact journals included International Journal of Molecular Sciences, Journal of Physiology-London. Notably, among the top 10 journals by publication count, only Journal of Physiology-London and Cell and Developmental Biology maintained impact factors exceeding 5.0, highlighting the competitive nature of publishing in high-impact journals within this research domain. Amrita Sahu, affiliated with the University of Pittsburgh in the United States, has emerged as the most prolific author in the selected research field with 7 publications (Table 5). Her work is influential due to its focus on key topics such as aging, skeletal muscle, brain health, extracellular vesicles, and regenerative medicine, which align with the dominant research themes identified in this study.

Keyword co-occurrence analysis reveals that a significant portion of exercise-related extracellular vesicles originates from skeletal muscles, as evidenced by the prominence of "skeletal muscle" (appearing 54 times) alongside main keywords such as "extracellular vesicles" (96 times), "exosomes" (80 times), and "exercise" (74 times) in the co-occurrence networks. A comprehensive understanding of this phenomenon requires further examination of multi-organ interactions, which could bridge exercise

science with other fields such as oncology, where EVs may serve as biomarkers or therapeutic mediators in cancer metabolism, and neurology, where EVs may contribute to neuroprotective effects in neurodegenerative diseases (4, 17). Notably, aerobic exercise has been shown to reduce inflammatory markers such as IL-6, CRP, and TNF-α in older adults, supporting the potential role of exercise-induced EVs in modulating chronic inflammation, a key factor in both cancer and neurodegenerative diseases (5, 6).

Limitations

Several limitations should be acknowledged in this study. First, our analysis exclusively utilized the Web of Science Core Collection, excluding other major databases (PubMed, Scopus, Embase, Cochrane Library). This approach may have led to incomplete data coverage. Second, while bibliometric analysis provides valuable insights, it serves as a supplementary research tool and may not fully reflect actual research dynamics. Third, to optimize visualization clarity, we established a minimum threshold of 10 occurrences for keyword analysis. This criterion potentially excluded emerging or less frequent (but potentially significant) terms from our evaluation.

Conclusion

In summary, this research utilized literature from the Web of Science database, employing visualization tools such as VOSviewer and the Bibliometrix R package to analyze trends and focal areas in exercise-related extracellular vesicles. Statistical analyses of publication volume, countries, institutions, authors, journals, references, and keywords provided comprehensive insights into the evolutionary path and research priorities of this field. These findings highlight the critical role of EVs in exercise physiology by facilitating interorgan crosstalk and supporting physiological adaptations, such as improved muscle function and metabolic regulation. In EV biology, the analysis emphasizes EVs' capacity to deliver biomolecules for long-distance signaling. Clinically, the prominence of keywords like 'biomarkers,' 'oxidative stress,' and 'insulin resistance' suggests that exercise-induced EVs hold promise as diagnostic or therapeutic tools for chronic conditions, including cancer and neurodegenerative diseases. These insights pave the way for future interdisciplinary research to advance health and disease management.

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Authors' contributions

All sections of this article was prepared by Rasoul Eslami.

Conflict of interest

The author declared no conflict of interest.

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