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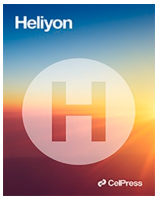

Research article

Bibliometric analysis of skeletal muscle ischemia/reperfusion (I/R) research from 1986 to 2022

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ABSTRACT

Introduction: Tissue damage due to ischemia and reperfusion is a critical medical problem worldwide. Studies in this field have made remarkable advances in understanding the pathogenesis of ischemia/reperfusion (I/R) injury and its treatment with new and known drugs. However, no bibliometric analysis exists in this area of research.

Methods: Research articles and reviews related to skeletal muscle I/R from 1986 to 2022 were retrieved from the Web of Science Core Collection. Bibliometric analysis was performed using Microsoft Excel 2019, VOSviewer (version 1.6.19), Bibliometrix (R-Tool for R-Studio), and CiteSpace (version 6.1.R5).

Results: A total of 3682 research articles and reviews from 2846 institutions in 83 countries were considered in this study. Most studies were conducted in the USA. Hobson RW (UMDNJ-New Jersey Medical School) had the highest publication, and Korthuis RJ (Louisiana State University) had the highest co-citations. Our analysis showed that, though the Journal of Surgical Research was most favored, the Journal of Biological Chemistry had the highest number of co-citations. The pathophysiology, interventions, and molecular mechanisms of skeletal muscle I/R injury emerged as the primary research areas, with "apoptosis," "signaling pathway," and "oxidative stress" as the main keywords of research hotspots.

Conclusions: This study provides a thorough overview of research trends and focal points in skeletal muscle I/R injury by applying bibliometric and visualization techniques. The insights gained from our findings offer a profound understanding of the evolving landscape of skeletal muscle I/R injury research, thereby functioning as a valuable reference and roadmap for future investigations.

1. Introduction

Ischemia/reperfusion (I/R) injury is the functional and structural changes that occur in the tissue during the restoration of the blood flow after a period of ischemia. Restoring blood flow often results in harmful effects such as necrosis of irreversibly damaged cells, marked cell swelling, and non-uniform blood flow to the tissue, leading to the deterioration of organ function [1]. This type of

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injury is often secondary to hemodialysis after severe limb ischemia, bone and soft tissue injury, vascular injury, osteofascial compartment syndrome, hemorrhagic or traumatic shock, and prolonged tourniquet use [2–4]. Skeletal muscles have high metabolic activity and are prone to ischemia-reperfusion injury [5]. Even with rapid restoration of blood flow after severe ischemia, I/R injury can lead to permanent skeletal muscle damage and necrosis or even amputation and multi-organ failure. Since its discovery [2,6], I/R has been studied extensively. Most literature provides a basic understanding of the pathophysiology of I/R injury and many prevention and treatment methods [4,7,8], some of which have successfully protected against the deleterious effects of I/R [9,10]. A systematic analysis of the scientific results and the current status of the field from a global perspective [6] will further help reveal future trends and hot spots of skeletal muscle I/R injury research.

A Bibliometric analysis helps to understand trends and frontiers in various research areas through qualitative and quantitative analysis of relevant scientific publications [11]. It compares scientific output and the impact of different countries, institutions, journals, and scholars [12] on salient research topics and provides valuable references and/or guidance for further scientific research. In recent years, bibliometric studies have been conducted on prime research topics such as stroke [13], autoimmune diseases [14], pulmonary arterial hypertension [15], periodontology [16], orthopedics [17], plastic [18], nursing [19], and other medical fields using software such as CiteSpace, VOSviewer, and the R package "bibliometrix" [20,21]. However, a bibliometric study on skeletal muscle I/R injury commonly encountered in surgical practice is lacking. This extensive analysis of the literature on skeletal muscle ischemia-reperfusion injury uses a bibliometric strategy to assess the current status and hot spots in I/R injury research and predict future research directions.

2. Materials and methods

2.1. Data sources and search strategies

Research articles and reviews on ischemia-reperfusion injury were collected from the Web of Science Core Collection (WoSCC) database of Clarivate, one of the most authoritative and comprehensive database platforms, containing more than 12,000 international academic journals [22,23]. Therefore, we chose it to access global scholarly information for bibliometric analysis [24]. The literature search was performed from the date of creation to March 16, 2023, using the search terms: ((TS=(Reperfusion) OR TS=(Reperfusion Injury)) AND ((TS=(muscle, skeletal)) OR TS=(Hindlimb))) AND (LA= ("ENGLISH") AND DT=("ARTICLE" OR "REVIEW")).

Inclusion criteria: (1) articles and reviews in the English language; (2) keywords related to reperfusion and its associated injuries in the context of skeletal muscle and hindlimb.

Exclusion criteria: (1) proceedings papers, which were not considered appropriate for the study's scope; (2) meeting abstracts, which typically lack the depth required for a thorough analysis; (3) book chapters, as they often present a broader overview rather than focused research findings; (4) editorial material, early access publications, notes, letters, and corrections, which do not contribute to the empirical body of knowledge; (5) retracted and non-English publications.

All valid data of the literature, including the year of publication, title, author's name, nationality, affiliation, abstract, keywords, and journal name, were saved in download.txt file format (refer to Appendix 1) from the WoSCC database and imported into Excel 2019 on the same day (March 16, 2023), to mitigate any potential bias arising from frequent database updates. The co-authors (Ming Zhou and Xueyuan Jia) independently searched and extracted all information from these documents. Any disagreement was resolved by consultation with experts to reach a final consensus. Finally, all co-authors used Excel 2019 to clean and analyze the data.

2.2. Data analysis

Visual analysis was performed using Microsoft Excel 2019, VOSviewer (version 1.6.19), Bibliometrix (R-Tool for R-Studio), and CiteSpace (version 6.1.R5). VOSviewer is a bibliometric analysis software that can extract vital information from numerous publications and is commonly used to build collaborative, co-citation, and co-occurrence networks [25]. We used the VOSviewer for country and institution analysis, journal and co-cited journal, author and co-cited author, and keyword co-occurrence analysis. In the VOSviewer map, a node represents an element such as country, institution, journal, and author. The size and color of the nodes indicate the number and classification of these items. The line thickness between two nodes reflects the level of collaboration or co-citation. CiteSpace, a bibliometric analysis and visualization software developed by Professor Chen [26,27], was used for dual-map overlay of journals, keyword, timeline, and citation burst analysis. The R package "bibliometrix" (https://www. bibliometrix.org) was used for thematic evolution analysis and to construct a global distribution network and three-field plot analysis of skeletal muscle ischemia-reperfusion injury publications [28]. For VOSviewer, the parameters were set as follows: Method (Linlog/modularity), with minimum document counts of 3 for a Country/region, 5 for an institution, 3 for an author, 30 for a co-cited author, 20 for a journal, 100 for co-cited journals, 30 for co-cited references, and 20 for keywords. For CiteSpace, the parameters were configured as follows: a time span from 1986 to 2023, with one year per slice and a selection criterion of the Top 50. The remaining parameters were set to default values. For bibliometrix, the "Source by Bradford Law Zones" was selected as "All Sources". In the three-field plot, the number of items for authors, keywords, and journals were set to 10, 9, and 8, respectively. The other parameters were set to default values.

Journal Citations Reports (JCR) quartile and impact factor (IF) were obtained from Citation Reports 2023. The Hirsch index (H-index, https://www.scimagojr.com) was used to measure the impact and productivity of scientific research [29]. The 2022 gross domestic product (GDP) data for different countries has been sourced from the official website of the World Bank, which can be accessed at https://data.worldbank.org.cn. Quantitative analysis and visual graphs of publications were performed using Microsoft Office Excel 2019.

Acknowledging the potential ambiguity among Chinese authors with similar names, such as Zhang Shan and Zhang Song, we implemented a meticulous disambiguation process to ensure accurate authorship analysis. We cross-checked full names, including middle names or second initials, and utilized institutional affiliations to distinguish authors. In cases where these methods were insufficient, we manually verified authorship using original articles, acknowledgments, or contact details, thus ensuring correct identification and attribution of each author's works.

No ethical review was required since all raw data used here were obtained from public databases.

2.3. Statistical analysis

We compared the Impact Factor (2022), JCR quartile (2022), and H-index (2022) of the top 20 journals in terms of the number of articles with the top 20 co-cited journals using *t*-test (parametric continuous variable) and Mann-Whitney U (categorical variable). Statistical analysis was performed with SPSS 26.0 (IBM, Armonk, NY, USA), and the significance was set at 2-tailed $p < 0.05$.

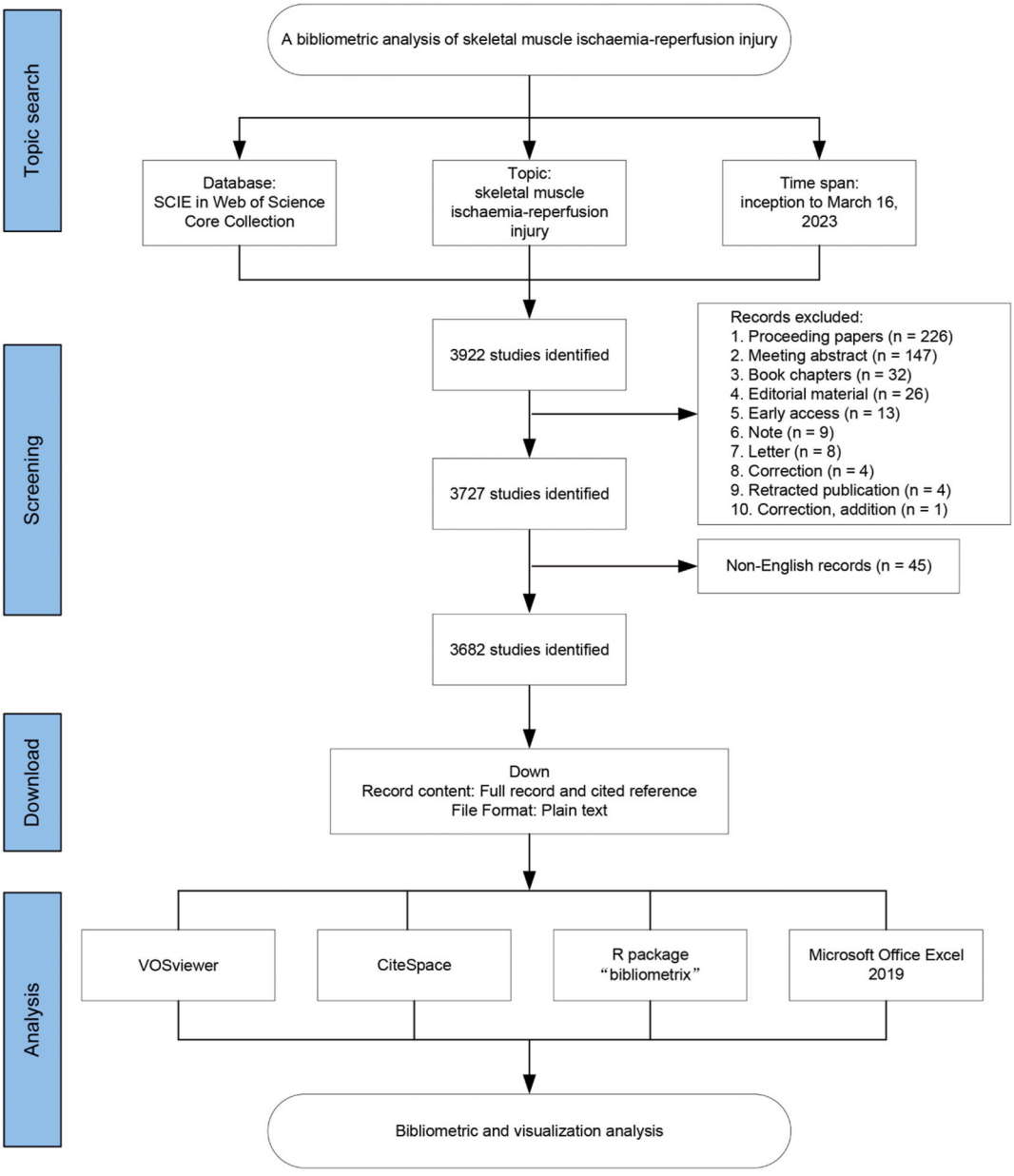


Fig. 1. Flow chart of scientometric analysis.

3. Results

3.1. Quantitative analysis of publication

A literature search on March 16, 2023, yielded 3922 documents. After excluding proceeding papers (n = 226), meeting abstracts (n = 147), book chapters (n = 32), editorial material (n = 26), early access (n = 13), notes (n = 9), letter (n = 8), correction (n = 4), the retracted publications (n = 4), corrections, additions (n = 1), and 45 non-English publications, a total of 3682 works of literature were included in the study (Fig. 1).

We observed a steady annual growth trend in the global volume of literature published on ischemia-reperfusion injury (Fig. 2). The number of documents increased annually from 1 (1986) to 161 (2018). Most studies were published in 2021 (161, 4.37 %). The year 2000 showed a clear demarcation point. From 1986 to 1999, this field was developed, with 824 papers published in 14 years. From 2000 to 2013, there was a qualitative leap, with 1,622 articles published in 14 years, almost twice as many as in the previous period. These results show that skeletal muscle ischemia-reperfusion injury is a hot research topic.

3.2. Country/region and institutional analysis

Eighty-three countries or regions have published studies on skeletal muscle I/R injury. The bulk of publications came from countries mainly in the northern hemisphere. Only eight countries (10.8 %) from the southern hemisphere, namely Australia, Brazil, New Zealand, Chile, South Africa, Argentina, Peru, and Uruguay (Fig. 3A), contributed to the I/R injury literature. The top ten countries in terms of the number of papers published are shown in Table 1. The United States of America was the most significant contributor, with more than one-third of the total publications (1334, 36.2 %). It was followed by China (327 papers, 8.9 %), Canada (265 papers, 7.2 %), and Germany (249 papers, 6.7 %). A collaborative network was constructed with 74 countries having annual publications ≥3, based on the number of publications and relationships between countries or regions (Fig. 3B). We observed that links between countries were concentrated in the northern hemisphere. The United States of America showed strong collaborations with European countries, while China showed relatively fewer collaborations with other countries.

Our study showed that 2846 institutions are involved in skeletal muscle I/R injury research, with seven out of the top ten institutions in the USA (Table 2). The four institutions with the most publications were Harvard University (n = 118, 3.2 %), University of Toronto (n = 58, 1.6 %), University of California San Diego (n = 51, 1.4 %), and University of Western Ontario (n = 41, 1.1 %). The collaborative network based on the number of publications and relationships between institutions having at least five annual publications (Fig. 4) showed that Harvard University, Brigham and Women's Hospital, Boston University, and Massachusetts General Hospital collaborated very closely.

3.3. Authors and co-cited authors

We observed that 16,132 authors are involved in studying skeletal muscle I/R injury. Among the top 10 authors, 3 published at least 20 papers each (Table 3). Our collaborative network based on authors having ≥3 publications (Fig. 5A) revealed that Hobson RW, Hechtman HB, Korthuis RJ, Moore FD, and Duran WN had the most prominent nodes as they published the most related articles. Authors from the same country collaborated more often and were more closely connected. However, there was little collaboration between authors from different countries.

Five of the 73,326 co-cited authors had more than 300 co-citations (Table 3). The author with the highest number of co-citations was Korthuis RJ (n = 451), followed by Wang WZ (n = 436) and Menger MD (n = 365). Authors with at least 30 co-citations were filtered to plot the co-citation network (Fig. 5B). Fig. 5B shows active collaboration between co-cited authors, such as Korthuis RJ, Wang WZ, and Menger MD.

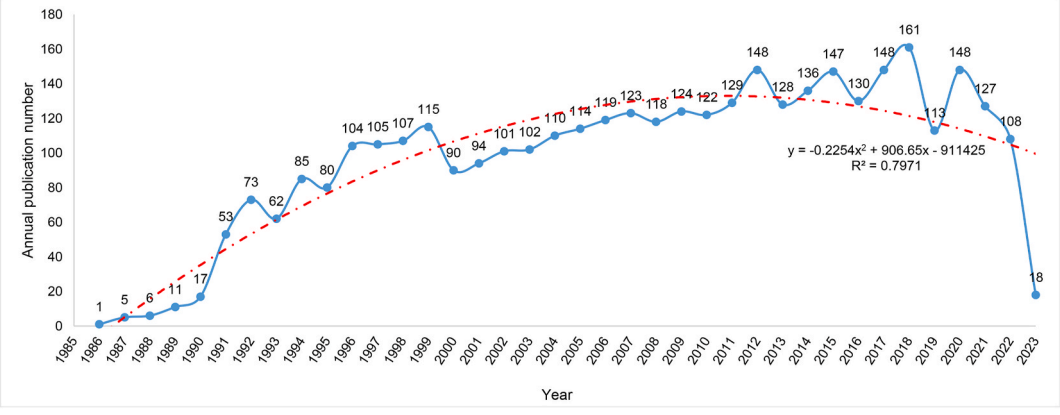


Fig. 2. Annual publications between 1986 and 2023. The data for 2023 is not complete.

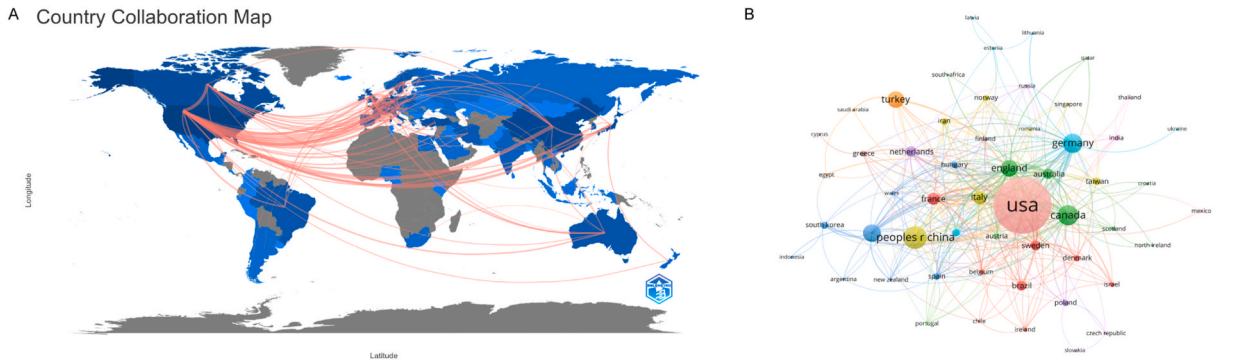


Fig. 3. Visualization analysis of country/regions. (A) The network visualization of geographical distribution. (B) Collaboration analysis of countries/regions. Node size is proportional to the number of publications by country/region, and the line thickness between nodes indicates the intensity of co-operation between countries/regions.

Table 1
Top 10 country/region on research of skeletal muscle ischemia-reperfusion injury.

Rank	Country/Region	Number of Publication	% of Total Publication	H-index	GDP ($, trillion)	Continents
1	USA	1334	36.23	2711	23.32	North America
2	China	327	8.88	1112	17.73	Asia
3	Canada	265	7.2	1381	1.99	North America
4	Germany	249	6.76	1498	4.26	Europe
5	Japan	213	5.78	1171	4.94	Asia
6	England	196	5.32	1707	3.13	Europe
7	Turkey	193	5.24	535	0.82	Asia
8	Italy	145	3.94	1189	2.11	Europe
9	France	122	3.31	1352	2.96	Europe
10	Australia	92	2.5	1193	1.55	Oceania

Table 2
Top 10 institutions on research of skeletal muscle ischemia-reperfusion injury.

Rank	Institution	Number of Publication	% of Total Publication	Global Rank	Country
1	Harvard University	118	3.2	4	USA
2	University of Toronto	58	1.58	41	Canada
3	University of California San Diego	51	1.39	301	USA
4	University of Western Ontario	41	1.11	597	Canada
5	Duke University	38	1.03	79	USA
6	University of Nevada	38	1.03	2135	USA
7	University of Florida	37	1	137	USA
8	Brigham and Women's Hospital	36	0.98	84	USA
9	Louisiana State University	35	0.95	2546	USA
10	Universidade de Sao Paulo	33	0.9	50	Brazil

3.4. Journals and co-cited journals

Studies on skeletal muscle I/R injury have been published in 962 journals. The top 20 journals publishing research articles and reviews on skeletal muscle I/R injury are listed in Table 4. The top three journals are the Journal of Surgical Research (IF 2.2), the American Journal of Physiology-Heart and Circulatory Physiology (IF 4.8), and Plastic and Reconstructive Surgery (IF 3.6). Nine of the top 20 journals showed a JCR quartile ranking of Q1, thus indicating that these journals have a high academic reputation in the field. In terms of the number of co-citations among the top 20 journals, the Journal of Biological Chemistry (Co-citation = 5319), Circulation (Co-citation = 5262), Circulation Research (Co-citation = 4572) and American Journal of Physiology (Co-citation = 4309) were cited more than 4000 times (Table 5). Nature had the highest impact factor (IF = 64.8), followed by Science (IF = 56.9). We constructed a collaborative network based on journals with published papers greater than or equal to 20 (Fig. 6A). Fig. 6A shows that the Journal of Surgical Research has active citation relationships with the Journal of Vascular Surgery, Plastic and Reconstructive Surgery, and the American Journal of Physiology-Heart and Circulatory Physiology. For better visualization of the co-citation relationship between journals, the collaborative network constructed for journals with more than 100 citations was classified into four categories (Fig. 6B). Articles from journals within the same category are more likely to have a similar research orientation or a specific internal logic [30]. For example, the Journal of Biological Chemistry and Circulation Research, Circulation, and American Journal of Physiology has a

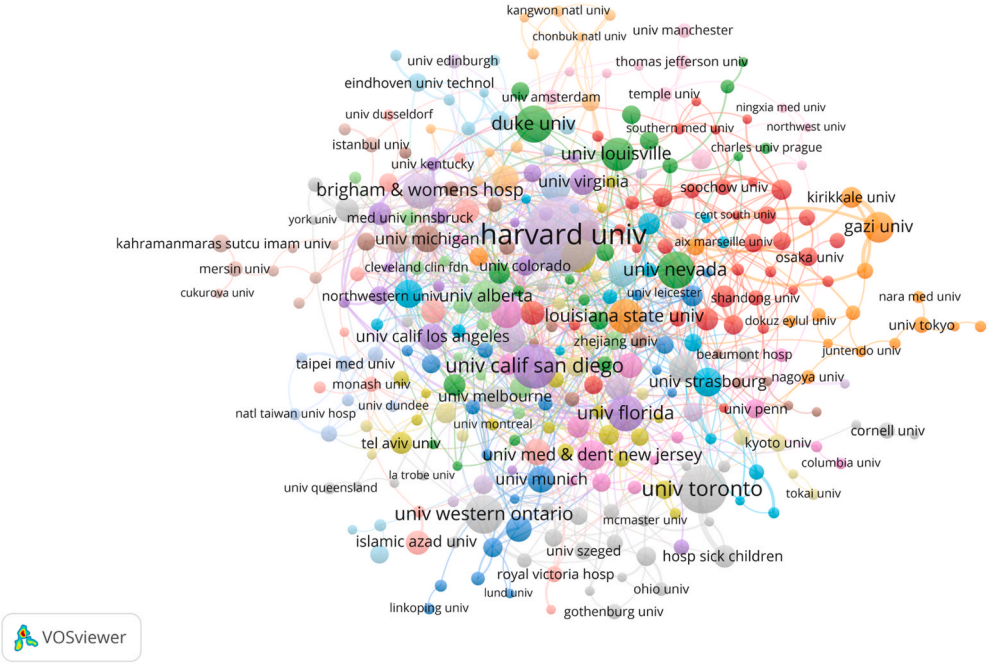


Fig. 4. Visualization analysis of institutions. Node size is proportional to the number of publications by the institution, and the thickness of the connecting line between the nodes is the strength of the institution's co-operation. Different colors represent clusters with different affinities.

Table 3
Top 10 authors and co-cited authors on research of skeletal muscle ischemia-reperfusion injury.

Rank	Author	Affiliations	Number of Publication	Co-Cited Authors	Affiliations	Citations
1	Hobson RW	UMDNJ-New Jersey Medical School	25	Korthuis RJ	Louisiana State University	451
2	Hechtman HB	Brigham and Women's Hospital	23	Wang WZ	University of Nevada School of Medicine	436
3	Korthuis RJ	Louisiana State University	20	Menger MD	University of Saarland	365
4	Moore FD	Brigham and Women's Hospital	19	Granger DN	Louisiana State University	329
5	Duran WN	UMDNJ-New Jersey Medical School	13	Pang CY	University of Toronto	313
6	Austen WG	Massachusetts General Hospital	12	Murry CE	Duke University	294
7	Freischlag JA	Medical College of Wisconsin	12	Blaisdell FW	University California Davis Medical Center	279
8	Walker PM	University of Toronto	12	Hausenloy DJ	University College London	275
9	Kobzik L	Brigham and Women's Hospital	11	Mccord JM	University of Colorado	273
10	Cambria RA	UMDNJ-New Jersey Medical School	10	Carden DL	Louisiana State University	258

strong co-citation relationship because they focus on the pathophysiological processes and molecular mechanisms of skeletal muscle ischemia-reperfusion injury.

The average IF ($p = 0.021$) and H-index ($p = 0.005$) of the top 20 co-cited journals were higher than the top 20 journals regarding the number of publications. However, the JCR quartile did not differ significantly between the two ($p = 0.623$) (Table 6).

A dual-map overlay of journals generated with CiteSpace was used to study the citation relationships between journals and cited journals. The map showed clusters of cited journals on the left, clusters of co-cited journals on the right, and sample waves from left to right showing citation associations represented by colored paths [31]. The four main citation paths are marked in orange and green, representing studies published in Molecular/Biology/Immunology and Medicine/Medical/Clinical journals primarily cited by Molecular/Biology/Genetics and Health/Nursing/Medicine journals, as shown in Fig. 6.

3.5. Co-cited references and references with citation bursts

Over the past 37 years of research, 118657 references have been made to the literature on skeletal muscle I/R injury. The top 20 co-cited references (Table 7) had a minimum citation of 75, and the top two were cited more than 200 times. We selected the literature

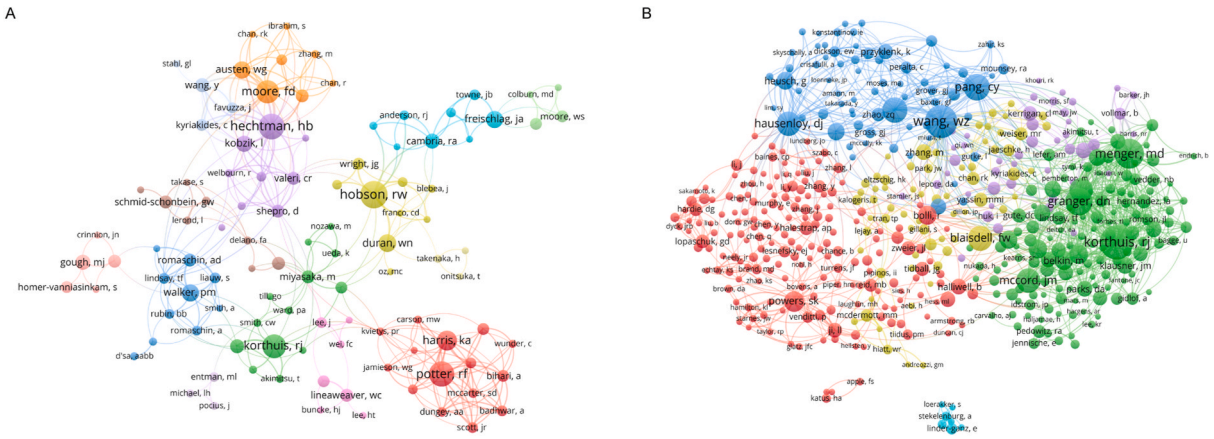


Fig. 5. Visualization analysis of authors. (A) Network visualization mapping of authors. (B) Network visualization mapping of co-cited Authors. The size of the nodes corresponds to the number of publications authored by each individual, while the thickness of the connecting lines between nodes indicates the intensity of collaboration among authors. Nodes of different colors denote authors belonging to distinct clusters.

Table 4
Top 20 journals on research of skeletal muscle ischemia-reperfusion injury.

Rank	Journal	Number of Publication	Country	Impact Factor (2022)	JCR Quartile (2022)	H-Index (2022)
1	Journal of Surgical Research	143	USA	2.2	Q2	177
2	American Journal of Physiology - Heart and Circulatory Physiology	106	USA	4.8	Q2	216
3	Plastic and Reconstructive Surgery	72	USA	3.6	Q1	198
4	Journal of Applied Physiology	71	USA	3.3	Q2	251
5	Microsurgery	62	USA	2.1	Q2	70
6	Journal of Vascular Surgery	50	USA	4.3	Q2	210
7	PLoS ONE	46	USA	3.7	Q2	404
8	Journal of Reconstructive Microsurgery	44	USA	2.1	Q2	61
9	Journal of Molecular and Cellular Cardiology	41	USA	5.0	Q2	169
10	Free Radical Biology and Medicine	39	USA	7.4	Q1	289
11	Annals of Plastic Surgery	39	USA	1.5	Q3	101
12	American Journal of Physiology - Regulatory Integrative and Comparative Physiology	36	USA	2.8	Q2	189
13	Frontiers in Physiology	34	Switzerland	4.0	Q2	140
14	Circulation Research	33	USA	20.1	Q1	369
15	International Journal of Molecular Sciences	33	Switzerland	5.6	Q1	230
16	Cardiovascular Research	32	USA	10.9	Q1	234
17	Circulation	31	USA	37.8	Q1	654
18	American Journal of Physiology	31	USA	3.0	Q1	82
19	European Journal of Vascular and Endovascular Surgery	27	England	5.7	Q1	133
20	Journal of Orthopaedic Research	25	USA	2.8	Q2	168

with more than or equal to 30 citations to construct the co-citation network graph (Fig. 7A).

Citation burst studies indicate the most active area of research frequently cited by scholars in a given field over time. It reflects emerging academic trends and new topics, predicts frontier directions, and reveals potential hotspots in a field. CiteSpace analysis identified the top 25 research articles with citation bursts (Fig. 7B). The earliest citation burst occurred in 1987, and the most recent citation burst was in 2018, as shown in Fig. 7B. The burst intensity of the top 25 references ranged from 9.99 to 24.73, and the endurance intensity was from 2 to 5 years. Our analysis indicated that the current research focuses on studying the primary sources of ROS production in skeletal muscle during ischemia-reperfusion, the mechanisms of mitochondrial dysfunction in skeletal muscle I/R, and the effects of I/R injury on different muscle phenotypes.

3.6. Analysis of keywords

Keyword analysis is used to determine the research hotspots in a particular field. We used VOSviewer to perform a co-occurrence analysis and found 11770 keywords. These keywords were further classified into six categories with the help of a collaborative network constructed with keywords having more than 20 occurrences (Fig. 8A). The most prominent keywords that emerged were Skeletal muscle (red), Ischemia-reperfusion (yellow), Mitochondrial dysfunction (green), Mechanistic studies (dark blue), Oxidative stress (purple), and Therapeutic modalities (light blue). The top 20 high-frequency keywords in skeletal muscle I/R research are listed in

Table 5
Top 20 co-cited journals on research of skeletal muscle ischemia-reperfusion injury.

Rank	Co-cited Journal	Cited Number	Country	Impact Factor (2022)	JCR Quartile (2022)	H-Index (2022)
1	Journal of Biological Chemistry	5319	USA	4.8	Q2	544
2	Circulation	5262	USA	37.8	Q1	654
3	Circulation Research	4572	USA	20.1	Q1	369
4	American Journal of Physiology	4309	USA	3.0	Q1	82
5	American Journal of Physiology - Heart and Circulatory Physiology	3833	USA	4.8	Q2	216
6	Journal of Applied Physiology	3336	USA	3.3	Q2	251
7	Proceedings of the National Academy of Sciences of the United States of America	3118	USA	11.1	Q1	838
8	Journal of Surgical Research	2674	USA	2.2	Q2	177
9	Cardiovascular Research	2628	England	10.9	Q1	234
10	Journal of Clinical Investigation	2626	USA	15.9	Q1	527
11	Journal of Molecular and Cellular Cardiology	2261	USA	5.0	Q2	169
12	Plastic and Reconstructive Surgery	2186	USA	3.6	Q1	198
13	Nature	1898	England	64.8	Q1	1331
14	Free Radical Biology and Medicine	1785	USA	7.4	Q1	289
15	Journal of Vascular Surgery	1613	USA	4.3	Q2	210
16	Journal of Physiology	1469	England	5.5	Q1	261
17	Science	1445	USA	56.9	Q1	1283
18	PLoS ONE	1383	USA	3.7	Q2	404
19	faseb j	1380	USA	4.8	Q2	297
20	Biochemical and Biophysical Research Communications	1304	USA	3.1	Q3	282

Table 8. Excluding skeletal muscle and ischemia-reperfusion-related keywords, oxidative stress, expression, rat, activation, nitric-oxide, heart, model, inflammation, microcirculation, apoptosis, and exercise appeared at least 170 times. The top 25 keywords with the highest burst intensity are shown in Fig. 8B. We found that free radical (26.58), xanthine oxidase (26.34), and neutrophil (22.73) had the highest burst intensity. The keyword with the most prolonged outbreak was free radical, which lasted 17 years from 1987 to 2004. Interestingly, the three keywords apoptosis, pathway, and oxidative stress showed a recent (2014–2023) outbreak of citations, suggesting that the studies on the mechanisms of skeletal muscle I/R injury may be a hot spot for future research.

We also mapped a timeline view of skeletal muscle I/R injury research keywords using CiteSpace (Fig. 8C) to study the emergence, prevalence, and decline of hotspots over the period and research progression of each cluster (i.e., subfield) [31]. A total of 10 clusters were identified: fatty acid oxidation, angiogenesis, monoclonal antibody, reperfusion injury, oxidative stress, near-infrared spectroscopy, injury, creatine kinase, protein synthesis, and strength training (Table 9). Except for protein synthesis and strength training (#8 and #9), the other eight clusters pointed towards the main research interest, with #0 (fatty acid oxidation) being the largest cluster, followed by #1 (angiogenesis) and #2 (monoclonal antibody).

A three-field plot that describes the relationship between the principal elements by the strength of the connecting links [28] was plotted with authors, keywords, and journals as the main elements (Fig. 8D). Our result showed that “skeletal muscle” and “mitochondria” were the most frequently used keywords. The authors, Wang WZ and Zamboni WA, had a relatively strong association with the keywords “skeletal muscle” and “muscle”. The Journal of Surgical Research and American Journal of Physiology-Heart and Circulatory Physiology covered the most high-frequency keywords.

4. Discussion

Over the past few decades, researchers have made tremendous efforts to study skeletal muscle ischemia-reperfusion injury and have made significant progress in its treatment (Fig. 9). In this study, we did a bibliometric analysis of the research publications over 37 years on skeletal muscle I/R injury to (1) assess the involvement of country, institution, author, impact, and their collaboration with each other, (2) map areas of knowledge, and (3) identify research hotspots and emerging trends. Our findings provide a solid foundation for exploring the body of knowledge in the field of skeletal muscle I/R injury.

4.1. General information

One indicator of a field’s development direction is the yearly variation in production output. According to the WoSCC database, 16132 authors from 2846 institutions in 83 countries/regions published 3682 articles or reviews on ischemia-reperfusion injury in 962 scientific journals. With the first articles being published in 1986, we observed that the general trend until 2023 is a slow but steady growth of the knowledge base. The top 10 countries contributing to research on ischemia-reperfusion injury were the developed countries except for China and Turkey. The USA contributed more than 1/3rd (36.23 %) of the total publications, with the highest H-index, and about 70 % of the top 10 research institutions, indicating the USA has a positive academic influence on skeletal muscle I/R. Our study also showed significant research collaborations between the USA and European countries, while there are relatively few collaborations in Asian countries. Despite having the second-highest number of publications, none of the Chinese institutions made it

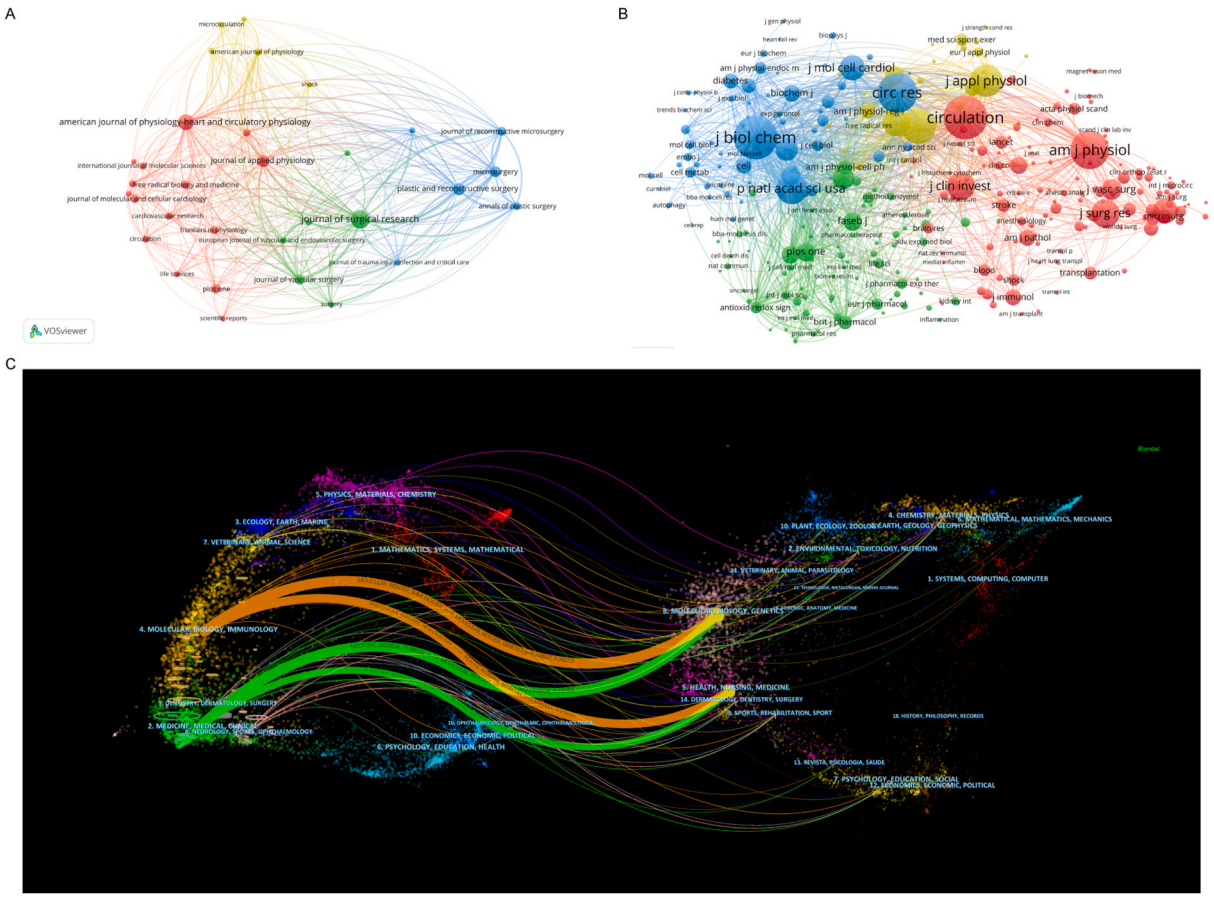


Fig. 6. Visualization analysis of journals. (A) The network visualization of journals. (B) The network visualization of co-cited journals. Node size is proportional to the number of journal publications, and the thickness of the connecting lines between nodes is the citation strength between journals. Each node's color corresponds to a cluster, with different hues representing distinct clusters. (C) Dual-map overlay of journals on research of skeletal muscle ischemia/reperfusion injury. The citing journals collection is on the left, the cited journals collection is on the right, and the colored paths indicate the citation relationships. The four main citation paths are marked in orange and green, representing studies published in Molecular/Biology/Immunology and Medicine/Medical/Clinical journals primarily cited by Molecular/Biology/Genetics and Health/Nursing/Medicine journals.

Table 6
Analysis comparing top 20 journals with top 20 co-cited journals on impact factor, JCR quartile and H-index.

	Top 20 journals	Top 20 co-cited journals	*p* Value
Impact Factor (2022)	6.64 ± 8.43	13.65 ± 18.20	0.021*
JCR Quartile (2022)			0.623
Q1	8	11	
Q2	11	8	
Q3	1	1	
H-Index (2021)	217.25 ± 136.49	430.80 ± 351.12	0.005*

to the top 10 research institutions. This indicates that there is relative fragmentation of research in China. The Harvard University of USA emerged as the most active collaborator in studying skeletal muscle ischemia-reperfusion injury. A high level of co-operation between countries and institutions is vital for high-quality research results. Therefore, researchers must strengthen their co-operation and exchanges with global institutions as research progresses to enhance their academic impact.

Our study showed that Hobson RW, Hechtman HB, and Korthuis RJ are the pioneers in this field, with at least 20 published articles each. Hobson RW and his group mainly studied the pathophysiological changes of skeletal muscle I/R injury and quantitative and qualitative assessment methods [32–35], which laid a solid foundation for skeletal muscle I/R research. Korthuis RJ and his group published 20 articles with the highest citation frequency (Citation = 451). They mainly focused on intervention strategies for skeletal muscle I/R injury and related mechanisms [36], such as ischemic preconditioning prevents [37–39], inflammatory responses [40],

Table 7
Top 20 co-cited articles on research of skeletal muscle ischemia-reperfusion injury.

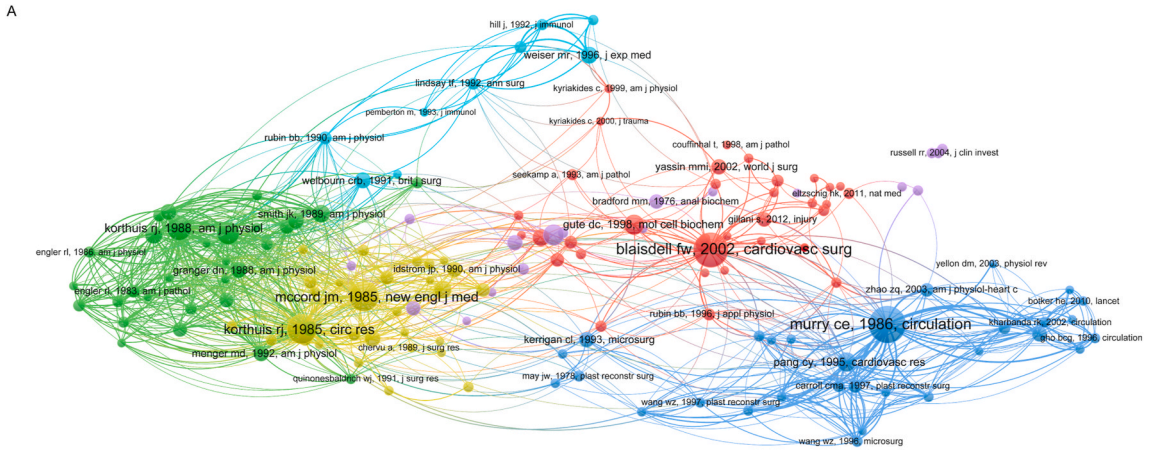
Rank	Co-cited reference	Journal						
		Citations	Year	Name	Country	Impact Factor (2022)	JCR Quartile (2022)	H-Index (2022)
1	Preconditioning with ischemia: a delay of lethal cell injury in ischemic myocardium	258	1986	Circulation	USA	37.8	Q1	654
2	The pathophysiology of skeletal muscle ischemia and the reperfusion syndrome: a review	234	2002	Cardiovascular Surgery	USA	–	–	–
3	The role of oxygen-derived free radicals in ischemia-induced increases in canine skeletal muscle vascular permeability	192	1985	Circulation Research	USA	20.1	Q1	369
4	Oxygen-derived free radicals in postischemic tissue injury	190	1985	New England Journal of Medicine	USA	158.5	Q1	1130
5	Leukocyte depletion attenuates vascular injury in postischemic skeletal muscle	139	1988	American Journal of Physiology	USA	3.0	Q1	82
6	Neutrophil-mediated microvascular dysfunction in postischemic canine skeletal muscle. Role of granulocyte adherence	124	1990	Circulation Research	USA	20.1	Q1	369
7	Protein measurement with the Folin phenol reagent	112	1951	Journal of Biological Chemistry	USA	4.8	Q2	544
8	Inflammatory responses to ischemia and reperfusion in skeletal muscle	105	1998	Molecular and Cellular Biochemistry	USA	4.2	Q2	132
9	Acute ischaemic preconditioning protects against skeletal muscle infarction in the pig	100	1995	Cardiovascular Research	England	10.9	Q1	234
10	Metabolic response of skeletal muscle to ischemia	88	1986	American Journal of Physiology	USA	3.0	Q1	82
11	Role of neutrophils in ischemia-reperfusion-induced microvascular injury	87	1987	American Journal of Physiology	USA	3.0	Q1	82
12	Free radical defense mechanisms and neutrophil infiltration in postischemic skeletal muscle	86	1989	American Journal of Physiology	USA	3.0	Q1	82
13	Reperfusion injury of ischemic skeletal muscle is mediated by natural antibody and complement	85	1996	Journal of Experimental Medicine	USA	15.3	Q1	478
14	Ischemia-reperfusion injury	83	1994	British Journal of Surgery	England	9.6	Q1	219
15	Salvage of skeletal muscle with free radical scavengers	79	1987	Journal of Vascular Surgery	USA	4.3	Q2	210
16	Pathophysiology of ischemia-reperfusion injury	78	2000	Journal of Pathology	England	7.3	Q1	297
17	Tissue destruction by neutrophils	76	1989	New England Journal of Medicine	USA	158.5	Q1	1130
18	Pathophysiology of ischemia reperfusion injury: central role of the neutrophil	76	1991	British Journal of Surgery	England	9.6	Q1	219
19	Role of xanthine oxidase and granulocytes in ischemia-reperfusion injury	75	1988	American Journal of Physiology	USA	3.0	Q1	82
20	Reduction of the extent of ischemic myocardial injury by neutrophil depletion in the dog	75	1983	Circulation	USA	37.8	Q1	654

CD18-dependent adherence [41], and adhesion molecule [42].

Journal of Surgical Research (IF = 2.2, Q2) had the highest number of published articles, indicating that it is currently the most sought-after journal in this area of research. The journal with the highest impact factor was Circulation (IF = 37.8, Q1). Most of the co-cited journals greatly impacted the Q1 JCR ranking. Comparing the IF and H-index of the top 20 journals regarding the number of publications and the top 20 co-cited journals, we found that the average IF ($p = 0.021$) and H-index ($p = 0.005$) of the top 20 co-cited journals were significantly high. Thus, the research articles published in these journals were internationally viewed, read, and referred to by researchers in this field and can be used to assess the current status and hot spots in I/R injury research. We further observed that studies on skeletal muscle I/R injury were mainly published in journals that mainly publish research papers on subjects related to Molecular, Biology, Immunology and Medicine, Medical, and Clinical, suggesting that the current research trend is mainly focused on understanding essential molecular as well as clinical aspect of I/R injury.

4.2. Knowledge base

Co-citation is literature cited by several other publications simultaneously. It is the basis of research in a particular field [31]. In this study, we selected the 20 most co-cited publications to determine the research base of skeletal muscle I/R. Murry CE et al. [43] published the most cited study in 1986, which showed that multiple brief ischemic preconditioning could ameliorate reperfusion



B

Top 25 References with the Strongest Citation Bursts

References	Year	Strength	Begin	End	1986 - 2023
KORTHUIS RJ, 1985, CIRC RES, V57, P599, DOI 10.1161/01.RES.57.4.599, DOI	1985	13.67	1987	1990	
BLEBEA J, 1987, J SURG RES, V43, P311, DOI 10.1016/0022-4804(87)90087-4, DOI	1987	13.04	1988	1992	
HARRIS K, 1986, AM J PHYSIOL, V250, PH213, DOI 10.1152/ajpheart.1986.250.2.H213, DOI	1986	11.02	1988	1991	
SUVAL WD, 1987, AM J SURG, V154, P211, DOI 10.1016/0002-9610(87)90181-4, DOI	1987	10.98	1989	1992	
KORTHUIS RJ, 1988, AM J PHYSIOL, V254, PH823, DOI 10.1152/ajpheart.1988.254.5.H823, DOI	1988	21.71	1990	1993	
SMITH JK, 1989, AM J PHYSIOL, V256, PH789, DOI 10.1152/ajpheart.1989.256.3.H789, DOI	1989	16.77	1990	1994	
CARDEN DL, 1990, CIRC RES, V66, P1436, DOI 10.1161/01.RES.66.5.1436, DOI	1990	24.36	1991	1995	
GRANGER DN, 1989, AM J PHYSIOL, V257, PG683, DOI 10.1152/ajpgi.1989.257.5.G683, DOI	1989	11.53	1991	1994	
LEHR HA, 1991, J CLIN INVEST, V87, P2036, DOI 10.1172/JCI115233, DOI	1991	12.86	1992	1995	
MENGER MD, 1992, AM J PHYSIOL, V263, PH1892, DOI 10.1152/ajpheart.1992.263.6.H1892, DOI	1992	17.75	1994	1997	
MENGER MD, 1992, AM J PHYSIOL, V263, PH1901, DOI 10.1152/ajpheart.1992.263.6.H1901, DOI	1992	15.58	1994	1997	
PANG CY, 1995, CARDIOVASC RES, V29, P782, DOI 10.1016/S0008-6363(96)88613-5, DOI	1995	13.93	1996	2000	
Weiser MR, 1996, J EXP MED, V183, P2343, DOI 10.1084/jem.183.5.2343, DOI	1996	11.13	1997	2001	
Lee HT, 1996, J SURG RES, V63, P29, DOI 10.1006/jsre.1996.0217, DOI	1996	10.67	1998	2001	
Gute DC, 1998, MOL CELL BIOCHEM, V179, P169, DOI 10.1023/A:1006832207864, DOI	1998	11.87	2001	2003	
Wang WZ, 1998, J TRAUMA, V45, P953, DOI 10.1097/00005373-199811000-00018, DOI	1998	9.99	2001	2003	
Blaisdell FW, 2002, CARDIOVASC SURG, V10, P620, DOI 10.1016/S0967-2109(02)00070-4, DOI	2002	24.73	2004	2007	
Chan RK, 2004, J SURG RES, V122, P54, DOI 10.1016/j.jss.2004.05.003, DOI	2004	10.63	2006	2009	
Murphy E, 2008, PHYSIOL REV, V88, P581, DOI 10.1152/physrev.00024.2007, DOI	2008	11.07	2010	2012	
Botker HE, 2010, LANCET, V375, P727, DOI 10.1016/S0140-6736(09)62001-8, DOI	2010	11.92	2011	2015	
Gillani S, 2012, INJURY, V43, P670, DOI 10.1016/j.injury.2011.03.008, DOI	2012	14.23	2013	2017	
Chouchani ET, 2014, NATURE, V515, P431, DOI 10.1038/nature13909, DOI	2014	11.59	2016	2019	
Lejay A, 2014, INT J BIOCHEM CELL B, V50, P101, DOI 10.1016/j.biocel.2014.02.013, DOI	2014	10.42	2017	2019	
Paradis S, 2016, AM J PHYSIOL-CELL PH, V310, PC968, DOI 10.1152/ajpcell.00356.2015, DOI	2016	12.43	2018	2021	
Charles AL, 2017, FRONT PHYSIOL, V8, P0, DOI 10.3389/fphys.2017.00052, DOI	2017	10.17	2018	2023	

Fig. 7. Visualization analysis of co-cited references. (A) The network visualization of co-cited references. Each node represents a reference, where the node's size represents the citation counts, and each link between references indicates that the two references were co-cited, with a thicker line indicating a closer relationship. (B) Top 25 references with the strongest citation bursts. The blue bars indicate references that have been published, and the red bars indicate citation bursts.

Table 8
Top 20 keywords on research of skeletal muscle ischemia-reperfusion injury.

Rank	Keywords	Occurrences	Rank	Keywords	Occurrences
1	skeletal-muscle	1576	11	expression	281
2	ischemia	692	12	rat	268
3	ischemia-reperfusion injury	669	13	activation	267
4	reperfusion injury	655	14	nitric-oxide	254
5	reperfusion	593	15	heart	221
6	injury	436	16	model	201
7	oxidative stress	431	17	inflammation	187
8	ischemia-reperfusion	360	18	microcirculation	186
9	skeletal muscle	327	19	apoptosis	182
10	ischemia/reperfusion injury	304	20	exercise	178

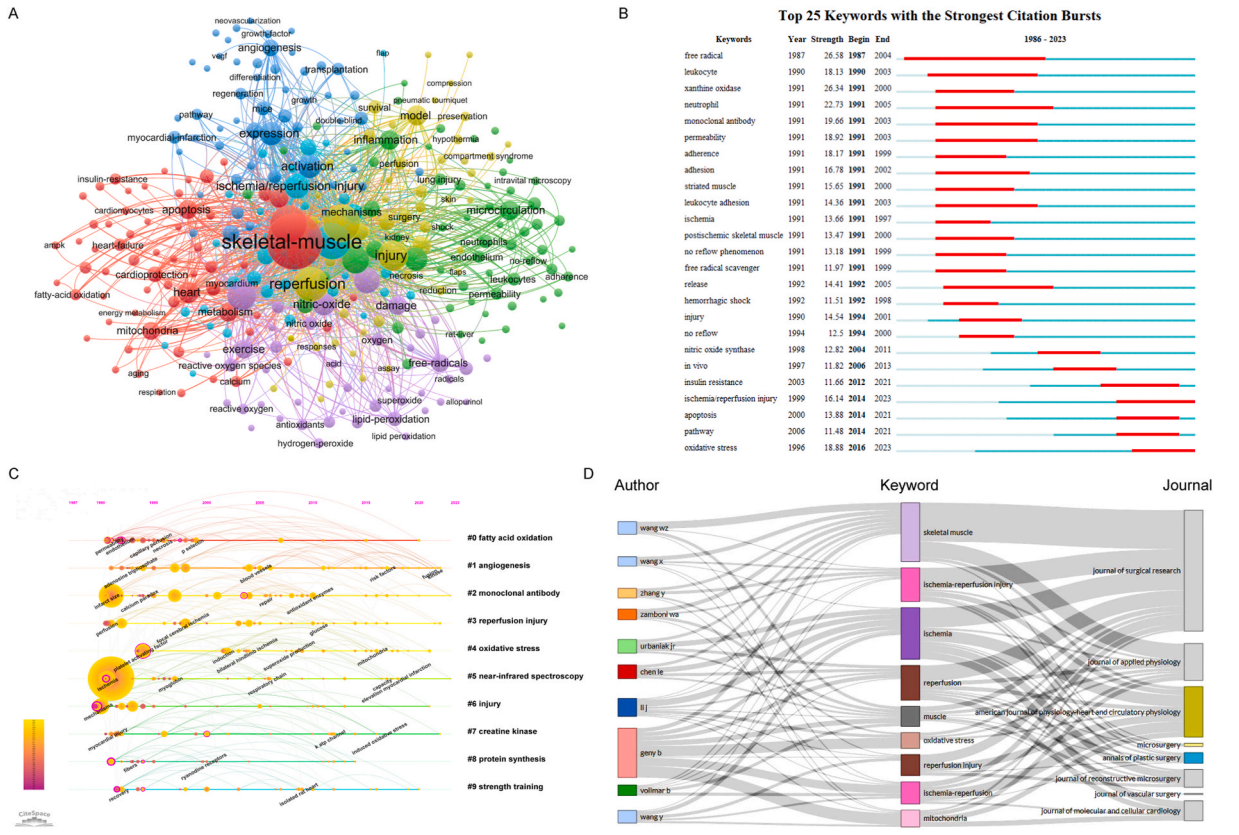


Fig. 8. Visualization analysis of keywords. (A) Network visualization mapping of the keywords. The nodes represent keywords, and their size is proportional to the frequency of the keywords. The nodes and lines of different colors symbolize diverse keyword clusters. (B) Top 25 keywords with the strongest citation bursts. Red and bold horizontal bars indicate hot spots with the strongest citation bursts. (C) Timeline view of the 10 clusters of the co-occurrence keywords. Each horizontal line indicates a cluster. The size of the circle indicates the frequency of occurrence, with the most recently established links in yellow. (D) Three-field plot of analysis authors, keywords, and journals on the research of skeletal muscle ischemia/reperfusion injury (middle field: keywords; left field: authors; right field: journals).

Table 9
Cluster summary of keywords time line view.

Cluster ID	Size	Silhouette	Mean (Year)	Cluster lable
0	175	0.568	2008	fatty acid oxidation
1	155	0.587	2009	angiogenesis
2	152	0.642	1995	monoclonal antibody
3	139	0.562	2003	reperfusion injury
4	119	0.693	2002	oxidative stress
5	116	0.677	1999	near-infrared spectroscopy
6	38	0.881	2008	injury
7	22	0.903	2001	creatine kinase
8	6	0.973	1998	protein synthesis
9	3	0.987	2016	strength training

injury. It laid the foundation for studying intervention strategies for I/R. To date, ischemic preconditioning remains a hot research topic in skeletal muscle I/R [44,45]. These top 20 most co-cited publications have focused on 1) the pathophysiology of skeletal muscle I/R, including the role of oxygen radicals, centrioles, antibody complement, inflammatory response, metabolic response, and xanthine oxidase; and 2) interventions for skeletal muscle I/R, such as ischemic preconditioning.

References with strong citation bursts are also used to characterize the research base of a field [31]. We identified the top 25 references with citation bursts using CiteSpace. The research article published by Blaisdell FW [1] in 2022 on the pathophysiology of skeletal muscle ischemia-reperfusion in Cardiovascular Surgery showed the strongest citation burst (intensity = 24.73) from 2004 to 2007. This indicates that research was mainly focused on skeletal muscle I/R pathophysiology during this period. The article with the longest duration of the citation burst was (2018–2023, intensity = 10.17), published by Charles AL et al. [46] in Frontiers in

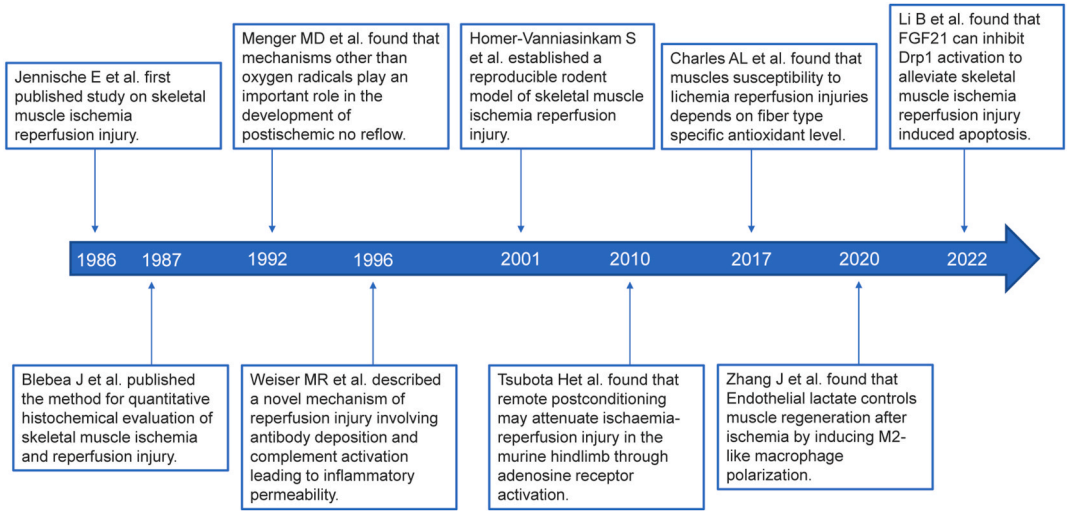


Fig. 9. Timeline of part of landmark achievements in skeletal muscle ischemia/reperfusion injury.

Physiology, 2017. They showed that glycolytic muscles are more prone to I/R than oxidation and suggested that muscle susceptibility is linked to muscle metabolic phenotypes, mainly muscle mitochondrial oxidative capacity. These results from our citation bursts study can be used by future researchers to locate studies that have made significant contributions to skeletal muscle I/R research.

4.3. Hotspots and frontiers

Keyword analysis helps to capture the core content and boundaries of a research field, and changes in keywords over time represent the evolution of the field [24]. Our bibliometric study showed that the dominant keywords were oxidative stress, expression, rat, activation, nitric oxide, model, inflammation, microcirculation, and apoptosis (Table 7). These keywords are closely related to the hot spots of research on skeletal muscle I/R mechanisms. The clustering analysis of keywords identified ten major subfields in skeletal muscle I/R research, and the timeline view showed the development of these subfields. We unfolded the analysis by highly explosive keywords, apoptosis, pathway, and oxidative stress, which had a recent (2014–2023) explosion of citations, indicating that the pathological mechanisms, molecular mechanisms, and downstream pathways of skeletal muscle I/R injury are the new research hotspots.

Apoptosis, defined as programmed cell death, was first proposed in 1972 by Kerr JF et al. [47] as distinct from necrosis. In recent decades, evidence from I/R models of the heart [48], liver [49], kidney [50], and brain [51] suggests that apoptosis is a major factor in I/R-induced cell death. However, the occurrence of apoptosis in skeletal muscle I/R injury remains controversial [52]. Knight KR et al. [53] found no indication of apoptosis in the nuclei of skeletal muscle fibers in a rat lower extremity tourniquet model. Wang WZ et al. [52] reported the presence of microscopic vascular endothelial cells in skeletal muscle of ischemia-reperfusion-induced apoptosis and concluded that necrosis was one of the major contributors. A recent study showed that FGF21 inhibited Drp1 activation and ameliorated I/R-induced apoptosis in skeletal muscle [54]. Another study showed that necrosis inhibitor-1 could ameliorate skeletal muscle I/R injury by regulating Bok-mediated apoptosis [55]. As research in this field has deepened, several types of programmed cell death have been proposed [56–59]. The potential existence of additional death modes and their mechanisms in skeletal muscle ischemia-reperfusion (I/R) injury may be a promising direction for future studies.

Signaling pathways are a series of enzymatic reactions in which molecular signals from outside the cell are transmitted across the cell membrane to exert effects inside the cell. Studies have shown that multiple signaling pathways are involved in skeletal muscle I/R injury [60,61]. A genome-wide expression profiling study on skeletal muscle I/R injury in rats showed that mitogen-activated protein kinase (MAPK) and nuclear factor kappa-B (NF-κB) signaling pathways play an essential role in skeletal muscle I/R injury [60]. MAPK is a group of serine-activated proteins that can be activated by various extracellular stimuli, such as cytokines, neurotransmitters, hormones, cellular stress, and cell adhesion [62]. Zhu N et al. [63] found that Schisandrin B could ameliorate oxidative stress and inflammation by regulating p38MAPK and extracellular signal-regulated kinase (ERK) 1/2 in a rat hindlimb ischemia-reperfusion model. NF-κB is a dimeric redox-sensitive transcription factor composed of p50 and p65 that plays an essential role in ischemia-reperfusion injury [64]. NF-κB can be activated in various ways, releasing pro-inflammatory cytokines such as interleukin 6, interleukin 1, and tumor necrosis factor-alpha (TNF-α). Several studies have shown that inhibition of NF-κB is a potential intervention for treating I/R injury [64–66].

Oxidative stress is a state in which there is an imbalance between oxidative and antioxidant actions in the body. During skeletal muscle ischemia-reperfusion, large amounts of reactive oxygen species (ROS) are generated, which exceed the scavenging capacity of antioxidants, resulting in damage to proteins, lipids, and DNA [7]. Cheng et al. [67] showed that pterostilbene could attenuate oxidative stress damage in skeletal muscle caused by ischemia-reperfusion injury by activating silent information regulator 1 (SIRT1).

Kuroda et al. [68] reported that 3-carbamoyl PROXYL-enhanced magnetic resonance imaging could effectively assess oxidative stress caused by skeletal muscle I/R, providing a basis for imaging assessment of oxidative stress.

Therefore, exploring the pathophysiological process of skeletal muscle I/R, in-depth molecular biology research, and mechanism exploration may be the hot spots and trends in the future.

5. Limitations

Utilizing three software programs: CiteSpace, VOSviewer, and R-bibliometrix, we conducted a systematic analysis of skeletal muscle I/R research trends, focal points, and advancements over the past 30 years, employing a bibliometric approach for the first time. However, there are several limitations to this study. Firstly, all literature utilized was sourced solely from the Web of Science. While the timely updates, authority, and breadth of the Web of Science facilitated the acquisition of extensive literature data to bolster our analysis, incorporating other databases could have potentially yielded additional relevant publications. Secondly, our study only encompassed research and review articles written in English, excluding non-English or non-research/review articles, which may have led to some omissions. Lastly, we would like to mention that as new studies are continuously emerging, we may have overlooked certain influential recently published works.

6. Conclusions

This study systematically reviewed more than thirty years of research in skeletal muscle I/R using bibliometric analysis to provide researchers with a holistic perspective. We found a significant increase in the number of articles published over the past two decades. Undoubtedly, the United States of America and China are the core centers of skeletal muscle I/R research. In terms of institutions, Harvard University is the leader in the field. Regarding authors, Hobson RW has the most output, while Korthuis RJ has the most impact and is widely cited. In terms of journals, the Journal of Surgical Research is the leading source of skeletal muscle I/R research, and the Journal of Biological Chemistry is the most cited. The pathophysiology, interventions, and molecular biological mechanisms of skeletal muscle I/R injury are the main research directions in this field. Apoptosis, signaling pathways, and oxidative stress are hot spots for future research. The results of this study provide a comprehensive bibliometric analysis of skeletal muscle I/R research from a global perspective, which may provide valuable clues for future research directions and scientific decisions in this field.

Ethics approval and consent to participate

Not applicable.

Consent for publication

All authors have read and approved the content and agree to submit for consideration for publication in the journal.

Data and code availability

The datasets generated and/or analysed during the current study are available in the [The Science Citation Index Expanded of Clarivate Analytics'S Web of Science Core Collection (WoSCC)] repository, https://www.webofscience.com/wos/alldb/basic-search. We have uploaded the search results in Appendix 1 of the supplementary materials.

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CRediT authorship contribution statement

Ming Zhou: Writing – original draft, Visualization, Software, Resources, Methodology, Formal analysis, Data curation, Conceptualization. **Xueyuan Jia:** Writing – original draft, Resources, Methodology, Formal analysis, Data curation. **Hao Liu:** Formal analysis, Data curation. **Yuan Xue:** Writing – review & editing, Validation. **Yapeng Wang:** Writing – review & editing, Validation. **Zeqing Li:** Writing – review & editing, Validation. **Yongwei Wu:** Writing – review & editing, Validation, Supervision, Project administration. **Yongjun Rui:** Writing – review & editing, Supervision, Project administration, Investigation, Funding acquisition, Conceptualization.

Declaration of competing interest

The authors declare the following financial interests/personal relationships which may be considered as potential competing interests:Yongjun Rui reports financial support was provided by Wuxi Health Commission.

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Abbreviations

I/R	ischemia/reperfusion
WoSCC	Web of Science Core Collection
JCR	Journal Citation Report
IF	impact factor
H-index	Hirsch index
GDP	gross domestic product
MAPK	mitogen-activated protein kinase
NF-κB	nuclear factor kappa-B
ERK	extracellular signal-regulated kinase
TNF-α	tumor necrosis factor-alpha
SIRT1	silent information regulator 1

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.heliyon.2024.e37492.

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