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Original Article

Mapping intellectual structures and research hotspots of chronic wound in global perspective

Yushu Zhu [a, e, 1], Yizhen Lin [b, 1], Sujie Xie [a, e, 1], Mingxuan Yang [b], Wei Zhang [a, e], Minjuan Wu [c], Yifan Liu [d], Dayuan Xu [a, e], Shuyuan Xian [a, e], Xirui Tong [a, e], Jie Huang [a, e], Luofeng Jiang [a, e], Xinya Guo [a, e], Minyi Gu [a, e], Hengkai Yu [a, e], Xinran Ding [a, e], Yixu Li [a, e], Yiyao Du [a, e], Heng He [a, e], Jianyu Lu [a, e, ***], Runzhi Huang [a, e, **], Shizhao Ji [a, e, *]

[a] Department of Burn Surgery, The First Affiliated Hospital of Naval Medical University, Shanghai, China
[b] Naval Medical University, Shanghai, 200025, China
[c] Department of Histology and Embryology, Naval Military Medical University, Shanghai 200433, China
[d] Department of Urology, Xinhua Hospital Affiliated to Shanghai Jiao Tong University School of Medicine, Shanghai, 200092, China
[e] Research Unit of Key Techniques for Treatment of Burns and Combined Burns and Trauma Injury, Chinese Academy of Medical Sciences, China

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ABSTRACT

Background: Chronic wounds included but were not limited to diabetes foot ulcers, venous leg ulcers and pressure ulcers. The challenge of difficult healing placed a heavy burden on patients and society. Our objective was to explain the healing process of chronic wounds and the development of treatment technologies in the past few years and to provide relevant, valuable information.

Methods: Our scientific publications were retrieved from the core collection of the Web of Science (WoSCC) database collection. The bibliometric visualization and analysis were performed by the software Biblioshiny based on R-bibliometrix. VOSviewer software and Citespace software were responsible for the validation of the results.

Results: A total of 8129 articles related to wound healing in chronic wounds were retrieved. The countries, institutions, and journals with the highest number of publications were the USA, the N8 research partnership, and the Journal of Wound Care, respectively. Armstrong DG and Dumville JC were the most influential authors in this field. The keyword analysis showed two key clusters of keywords, including “dressings” and “management”. Trend topics analysis revealed frequent keywords in recent years, including “nanofibers” and “injectable hydrogels”.

Conclusion: Our research was the first to reveal the cellular and molecular mechanisms and key clinical management strategies in the healing process of chronic wounds in the future through metrological and systematic evaluation, which may have important translational value in the future.

1. Introduction

Chronic wounds, defined as wounds that fail to heal within a reasonable timeframe under normal conditions [1]. Compared to acute wounds, chronic wounds refer to wounds that had healed for over 12 weeks [2]. It was reported that chronic wounds damage 1 %–2 % of the global population, with approximately 6.5 million confirmed cases in the United States alone [3]. In addition to troubling patients, chronic wounds brought a substantial economic burden on society and the healthcare system, causing over $20 billion in annual losses to the US healthcare system [1,3]. Chronic wounds also greatly increase care costs and lower patients' quality

* Corresponding author. Department of Burn Surgery, The First Affiliated Hospital of Naval Medical University, Shanghai, China.
** Corresponding author. Department of Burn Surgery, The First Affiliated Hospital of Naval Medical University, Shanghai, China.
*** Corresponding author. Department of Burn Surgery, The First Affiliated Hospital of Naval Medical University, Shanghai, China.
E-mail addresses: 578198334@qq.com (J. Lu), runzhihuang2022@163.com (R. Huang), shizhaoji2022@163.com (S. Ji).

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[1] Co-first authorship: Yushu Zhu, Yizhen Lin and Sujie Xie have contributed equally to this work.

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of life, Despite clinical and molecular heterogeneity, all chronic wounds were generally classified into one of three clinical categories: leg ulcers (venous/arterial deficiencies), diabetes foot ulcers, or pressure ulcers [4]. Chronic leg and foot ulcers were seen in many adults with vascular disease or diabetes and could be attributed to chronic venous insufficiency, arterial disease, excessive pressure, or neuropathy. These ulcers lasted for 12–13 months averagely, with recurrence rate of up to 60 %–70 %, making them an important cause of the morbidity. Chronic wounds were mainly diseases of the elderly, becoming increasingly common and difficult to treat [5]. Exploring the therapeutic effects of current and future advanced wound therapies was of paramount importance for solving the problem [6].

Wound healing was a well-organized process that included four stages: coagulation, inflammation, proliferation, and wound remodeling. Chronic wounds typically stagnated in the inflammatory stage and/or underwent a damaged proliferative stage [7]. Debridement and wound cleaning are key components of wound care, proven to accelerate healing by removing necrotic tissue and reducing wound burden [8]. When chronic wounds persisted and did not heal, elevated levels of metalloproteinases hindered the body's attempts to heal due to the effects of bacteria, necrotic tissue, and foreign objects. Debridement could remove damaged tissue, foreign objects, and related bacteria, transforming the entire bottom of the wound into an acute wound so that it could pass through the normal stage of wound healing [9]. Proper wound cleaning could reduce biological burden and delay the development of biofilms [10]. In recent years, with the continuous development of science and technology, various new multifunctional dressings had been applied to the clinical treatment of chronic wounds. For instance, dressings like hydrogels, due to their excellent biochemical and mechanical property [11], could provide slow autolytic debridement of callus and dry crusts, especially in ischemic patients or patients who could not undergo surgical debridement [5]. Take diabetic foot ulcers as an example, local treatment typically begins with debridement of necrotic, infected, or hyperkeratotic tissues, followed by rinsing with saline or an antibacterial solution and applying a customized dressing [2]. However, overly frequent or extensive debridement may delay healing [5]. In clinical practice, it is currently encountered to select appropriate therapies and improve the effectiveness of therapies based on the specific molecular mechanisms of wound healing. Consequently, it was of great significance for us to summarize and analyze the currently known relationship of chronic wounds and debridement or wound cleaning or wound dressing.

Bibliometric research referred to the use of mathematical and statistical methods to quantitatively analyze all literature in a certain field during a certain period, in order to have an intuitive understanding of the history, present, and future of the field [12]. Our study employs Bibliometrix, a powerful bibliometric analysis tool, which stands out from traditional review methods due to its unique clustering algorithms and advanced data processing capabilities. Unlike traditional reviews that often rely on qualitative summaries, Bibliometrix can process a large volume of articles simultaneously and predict future development directions more accurately [13]. In recent years, it had been extensively applied by many scholars for researches in several fields, such as chronic heart failure, periodontal disease, schizophrenia and inflammation [14–16]. However, there were still no bibliometric studies on role of wound cleaning in chronic wound. Therefore, we selected publications on the role of wound cleaning in chronic wound from the Core Collection Web of Science database and performed the analysis of countries and institutions, authors, documents and keywords. The output of articles and citation counts provide insights into the influence of different regions and authors, while the analysis of keywords highlights the hotspots and trends in this field. Our selection of 8129 publications from the Web of Science Core Collection (WOSCC) database ensures a robust dataset for our analysis. We hope our work will serve as a guide for identifying key knowledge and research priorities.

2. Materials and methods

2.1. Search strategy

The data source was obtained from the Web of Science Core Collection (WOSCC) database on July 10, 2023. Web of Science was the world's most trusted and independent global citation database. Its multidisciplinary platform connected regional, professional, data, and patent indexes to the core collection of Web of Science. Their platform included over 1.7 billion cited literature and 159 million records, providing comprehensive coverage. It almost covered fields such as biomedicine, art, engineering, humanities, and natural sciences, making our assessment of impacts more thoughtful and accurate [17]. The literature retrieval strategy was as follows: ((TS= ((ulcer* OR sore* OR wound*) NEAR/2 (pressure OR bed OR decubitus OR diabetic OR chronic OR ischemic OR vascular OR radiation OR rheumatic)))) AND ((TS = debridement) OR (TS = debride) OR (TS = wound cleaning) OR (TS = wound dressing)), literature type = article or review, year = 1942–2023. After excluding literature that did not meet the article type requirement, the results (**Supplemental File 1**) were imported into Bibliometrics analysis tools for subsequent analysis. VOSviewer software and Citespace software were responsible for the validation of the results. Since no living creatures were involved in this study, no ethical support was required.

2.2. Data analysis

Bibliometrics was an open-source tool for performing bibliometric analysis, comprehensive visualization, and knowledge mapping analysis [18]. The bibliometrix package in R version 4.3.1 (Institute for Statistics and Mathematics, Vienna, Austria; www.rproject.org) was used for quantitative analysis and visual processing of all the obtained literature. The “Biblioshiny ()” function provided a simplified windowed interface for plotting graphs in this article [18]. Annual scientific production and average citations were acquired to analyze the overall trend in this field. The production and citations were generally regarded as estimated conditions for influential countries, institutions, journals, authors, and documents. Algorithms like Bradford's law [19], Lotka's law [20], and h-index [21] were applied to estimate the core journals and authors. We also analyzed and visualized the collaboration of countries to assess the global relationship between countries. To detect the hotspots, after capturing high-frequency keywords and essential documents and building a co-occurrence network and direct citations, we accessed the concrete content of some relevant articles in this field. The trend topic in this field was obtained from the trend topics map and direct citation network. Additionally, for a better understanding of the research trends and hotspots, we carefully read the related documents, subdivided the research topic into several themes, identified research dimensions, and discussed their future directions.

3. Results

3.1. Annual publication and citation

Annual publications and citations offered us a view of the field's general situation and development tendency. As the retrieval

process shown in Fig. S1, from 1942 to July 10th,2023, a total of 8129 documents were collected from WoSCC. The annual publications and the average number of annual citations were presented in Fig. S2A and S2B. Despite slight fluctuations, the overall trend in the number of publications has grown since 2006, reaching a peak in 2022. Additionally, the growth of the number of average citations per year had been rapid since 1990 and maintained a high level after 2001. All of these above indicated that wound cleaning and chronic wounds were arousing increasing attention and had clinical significance and development potential.

3.2. Distribution characteristics of countries/regions

Since 1942, 104 countries had participated in studies on wound cleaning and chronic wounds, and four countries had more than 1000 publications. The country scientific production map represented the distribution and numbers of publications by countries/regions worldwide in Fig. S3A. The top 10 high-yield countries were depicted in Table 1. Fig. 1A showed that the United States had the most publications (5899 records with 74,209 citations), followed by China (3331 records with 19,285 citations), the United Kingdom (1686 records with 20,320 citations), and Germany (1286 records with 10,064 citations). This indicated that the USA had the highest publication production and citations and was the leading prolific and influential country for wound cleaning and chronic wound research.

The country collaboration map (Fig. 1B) presented a complete picture of academic performance and country collaboration. The United States and The United Kingdom were the two most prominent central connection points, linking with almost every other influential country, such as China, Germany, and Australia.

The top 10 institutions involved in wound cleaning and chronic wound research were shown in Fig. S3B. The N8 research partnership published the maximum number of publications (n = 191), followed by Harvard University (n = 160) and White Rose University Consortium (n = 147). These three institutions were from the UK and the USA. In summary, we hypothesized that the USA, the United Kingdom and China were the three most influential and contributing countries in wound cleaning and chronic wound research.

3.3. Source analysis

Since 1942, 1535 sources had published articles on wound cleaning and chronic wound research. Based on Bradford's Law, 22 high-production journals were classified as core research sources on wound cleaning and chronic wounds based on the number of publications (Fig. 2A) [22]. The top three core sources were the Journal of Wound Care(n = 423), International Wound Journal (n = 400), and Wounds-a Compendium of Clinical Research and Practice (n = 336). The total number of articles published in the top 20 high-local-cited academic journals was 2625 (Fig. 2B). Among them, the journal Wound Repair and Regeneration had the most citations (n = 8626), followed by Plastic and Reconstructive Surgery (n = 7069) (Fig. S4). These productive and high-cited journals were essential sources of knowledge and had a significant impact on this field. Moreover, Fig. 2C showed the growth in productivity with time for the top six most productive journals, which indicated that the number of publications per period of these journals increased rapidly.

Table 1
The top 10 high-yield countries in chronic wounds-related wound management research.

Region	Freq
USA	5899
CHINA	3331
UK	1686
GERMANY	1286
ITALY	947
INDIA	919
JAPAN	840
AUSTRALIA	740
IRAN	727
FRANCE	640

3.4. Most influential authors

In the selected period, 30,239 authors had published articles about wound cleaning and chronic wound research, and according to Lotka's law [20], 24 authors had more than ten publications. Armstrong DG had the most publications (n = 53), with 1402 total citations, followed by Dissemond J (n = 44) (Figures S5A and Figures S5B). The H index was predominantly used to evaluate the total influential power of a specific author [22]. To better analyze the most influential author, the H-index was used as an indicator to rank the authors (Fig. S5C). After analysis, Armstrong DG and Dumville JC ranked highest and were identified as the most influential authors. Thus, we speculated that Armstrong DG and Dumville JC contributed outstandingly to the study of wound cleaning and chronic wounds, laying a solid foundation for subsequent research.

3.5. Keyword analysis

3.5.1. Keyword co-occurrence network

Keywords could highly condense the key content of literature, effectively identifying research hotspots and other critical points [23]. Fig. 3A represented the growth in frequency with time for the top 10 most frequent keywords. It indicated that the frequency of the keyword “management” had risen rapidly since 2011, and since then, the difference in the frequency between this word and others increased obviously. Subsequently, the top 50 high-frequency keywords of wound cleaning and chronic wound research were picked for a word cloud (Fig. 3B) and a tree map (Fig. S6). Specifically, “management” had the most frequency of occurrence (n = 1363), followed by “vacuum-assisted closure” (n = 774), “dressings” (n = 631), “therapy” (n = 539), “skin” (n = 460), “in vitro” (n = 436), “ulcers” (n = 433), “care” (n = 347), “prevention” (n = 313), and “efficacy” (n = 312). More significantly, Biblioshiny software was performed for keyword co-occurrence analysis and categorized relevant keywords into 2 clusters, thus forming a keyword clustering network map (Fig. 3C). These clusters reflected the preliminary study content and core research regions to which the keywords referred [24]. Within the keyword co-occurrence network graph, each node represented a keyword, and the size of the node represented the popularity; the line between the nodes indicated the intimacy between the keywords [23]. In our analysis, two clusters were recognized.

Clusters1 (red): In this red cluster, the most crucial keywords were “dressing,” “skin,” “in vitro,” and “delivery”. This critical cluster revealed the mechanisms of the wound-healing process and the application of dressing-related material.

Cluster 2 (blue): In this blue cluster, the crucial keywords included “management,” “vacuum-assisted closure,” “therapy,” and “ulcers.” It mainly reflected the effects and therapeutic application of wound management.

There was a high research interest in the cellular and molecular mechanisms involved in the healing process of chronic wounds, as well as the value of efficient management in translational medicine, which was an important research direction.

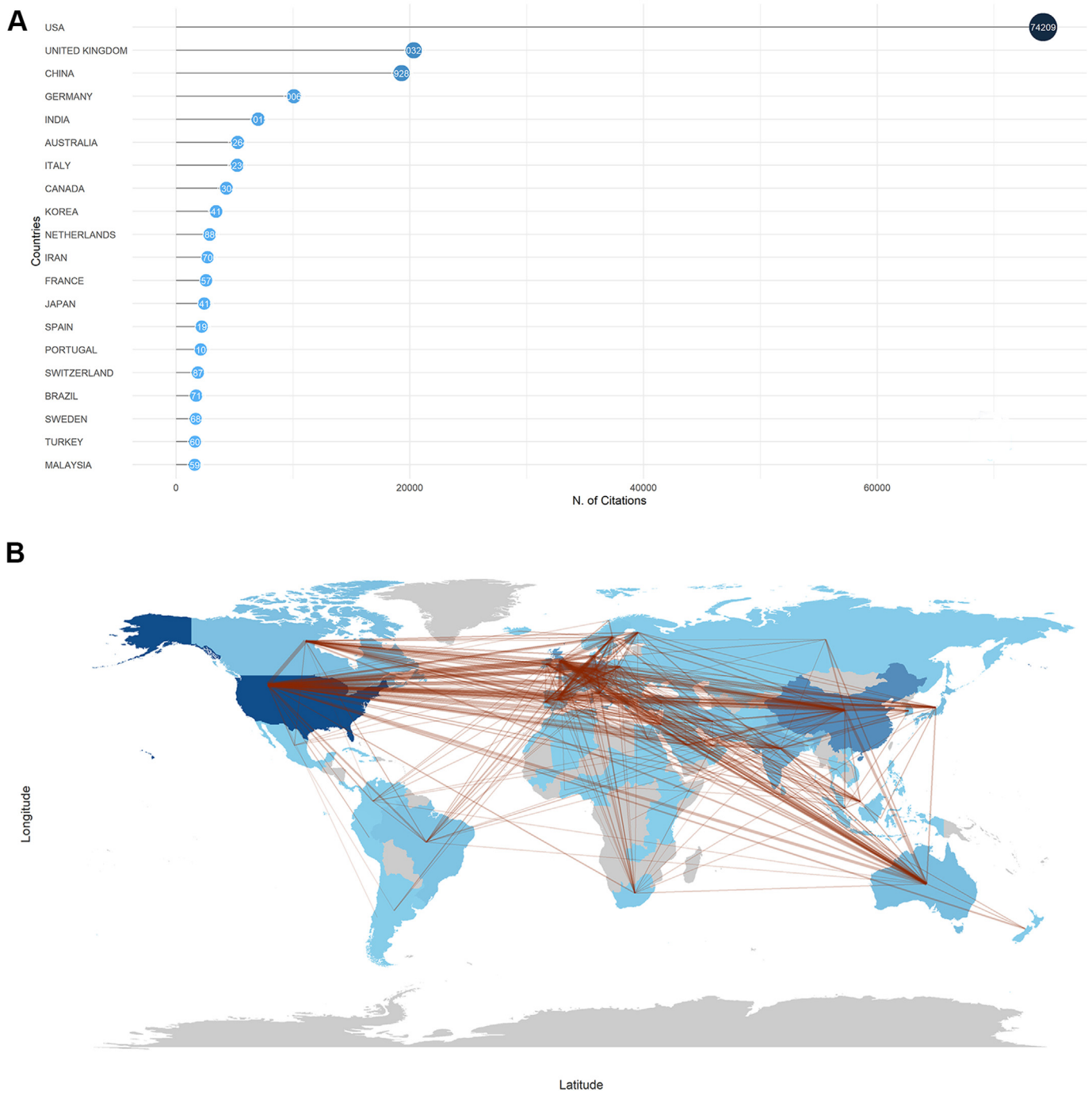

Fig. 1. Main countries/regions of chronic wounds-related wound management research production and collaboration. (A) The top 20 countries/regions of chronic wounds-related wound management research with the highest number of publications. (B) Countries/Regions production and collaboration world map of in chronic wounds-related wound management research.

3.5.2. Strategic diagram

The thematic analysis contributed to understanding the characteristics of the current research subject and provided excellent reference value for selecting future research directions. Fig. 4A presented two themes in our analysis according to their subject terms. The Y-axis of the map (Density) represented the connection intensity of basic knowledge units within a single topic. The higher the density, the higher the maturity of the theme. The X-axis of the map (Centrality) indicated the intensity of the connection between a theme and other themes. The higher the centrality, the more likely the theme would be at the core of all research topics [25].

Niche themes represented isolated themes with high maturity. The red circle was located in the second quadrant with the keywords “dressings,” “skin,” and “in-vitro,” which indicated that the mechanism of chronic wounds had been developed maturely. However, its value for the current field was limited. Basic themes represented hot themes with low maturity. The blue circle was located in the fourth quadrant, including the keywords

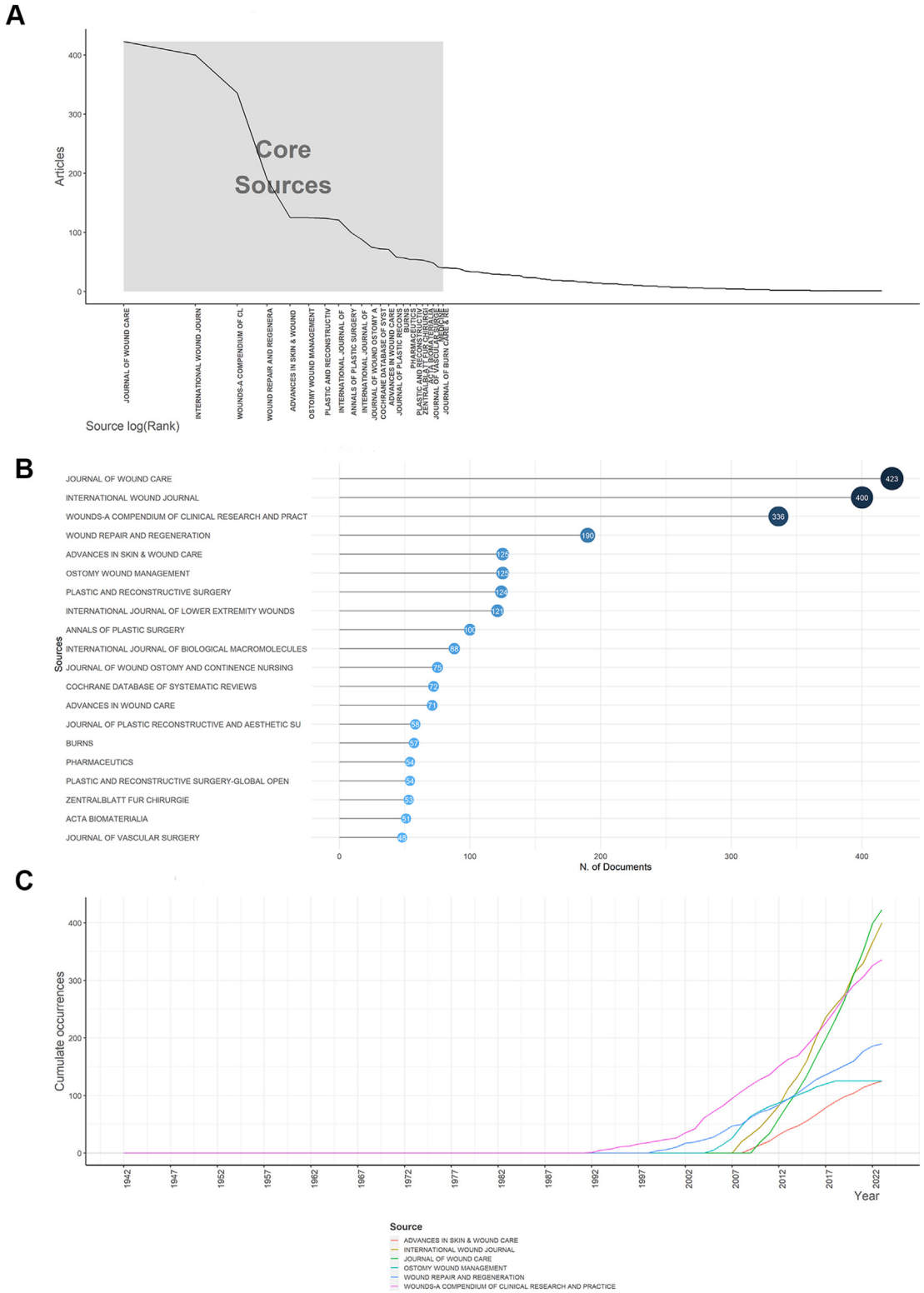

Fig. 2. Source analysis. (A) Core journals of chronic wounds-related wound management research based on Bradford's Law. (B) The top 20 journals on chronic wounds-related wound management research with the highest number of publications. (C) The six highest yielding journals growth of chronic wounds-related wound management research from 1942 to 2023.

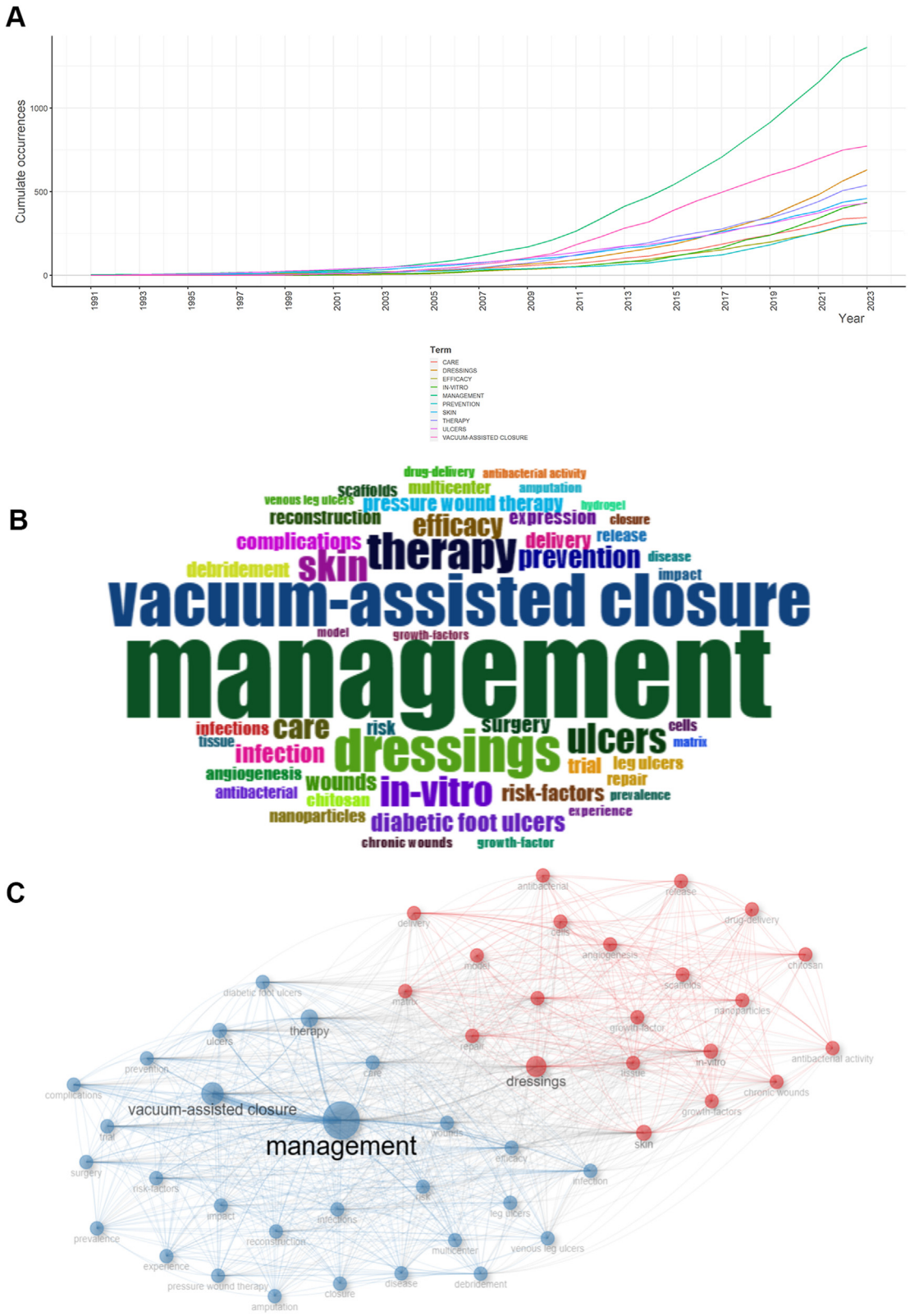

Fig. 3. Keyword analysis. (A) Top 10 most frequent keywords growth of chronic wounds-related wound management research from 1942 to 2023. (B) Visualized word cloud map based on the top 50 most frequent keywords for chronic wounds-related wound management research. (C) Visualized keywords co-occurrence network for chronic wounds-related wound management research. Each node indicated a keyword, and the connecting lines between nodes denoted the intimacy between keywords. The two clusters were red and blue.

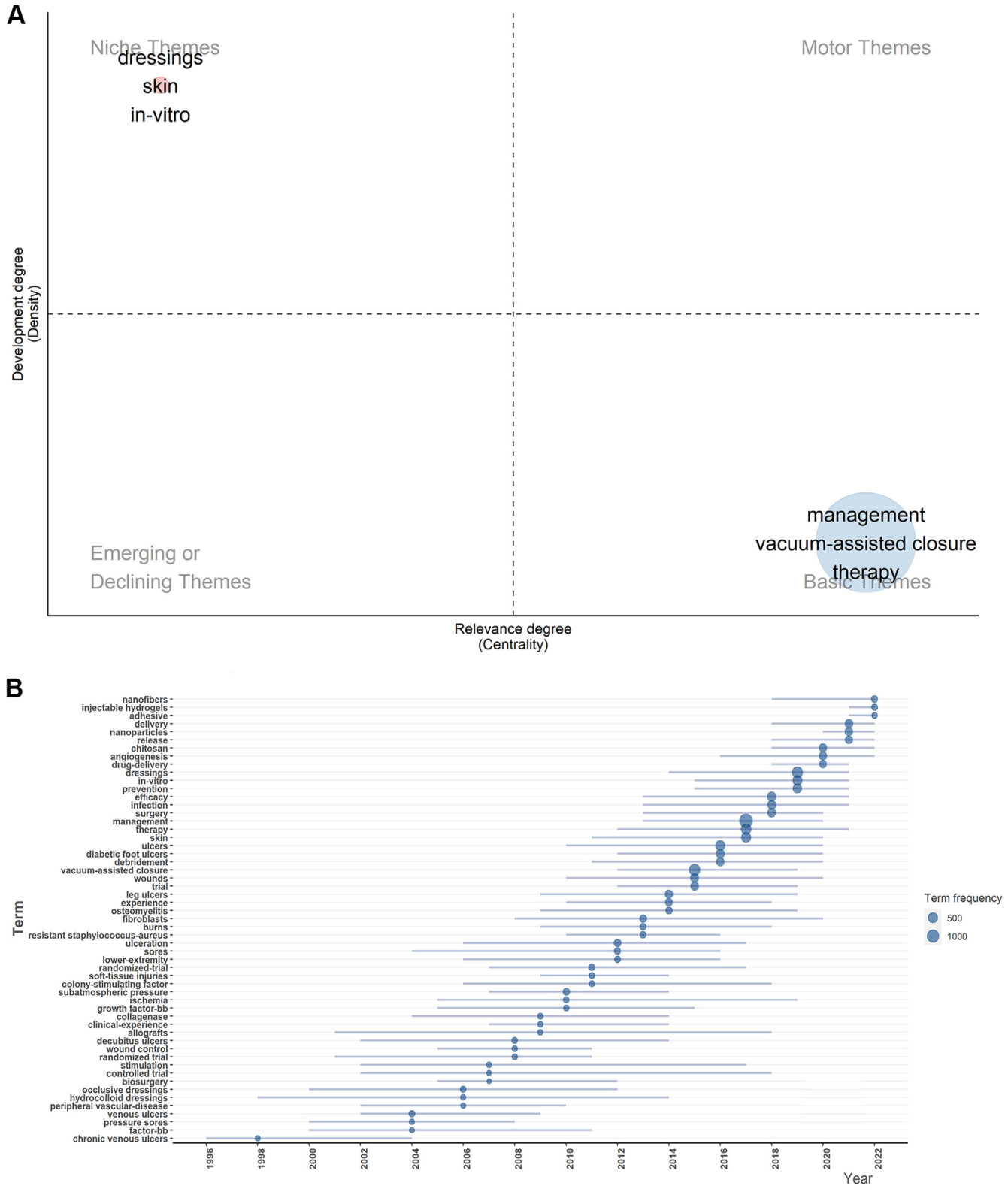

Fig. 4. Theme analysis. (A) Thematic map for chronic wounds-related wound management research. The horizontal coordinate refers to the relevance degree (centrality), and the vertical coordinate represents the development degree (density). (B) Trend topics map for chronic wounds-related wound management research. Showing trends in the occurrence of high frequency keywords for chronic wounds-related wound management research.

"management," "vacuum-assisted closure," and "therapy." Consistent with clustering 2 in the keyword co-occurrence network, these themes were recommended as the molecular mechanisms and therapeutic targets associated with chronic wounds. These themes had significant value for this field but required further development. Despite numerous advances, chronic and other difficult-to-manage wounds continued to be a treatment challenge [26]. Researchers were committed to exploring principles or methods for chronic wound healing from multiple perspectives. Enhanced understanding and correction of pathogenic factors, combined with stricter adherence to standards of care and technological breakthroughs in biological agents, was giving new hope to the problem of impaired healing [27]. Experts in wound management considered that wound bed preparation was an essential concept with significant potential as an educational tool in wound management [28]. Vacuum-assisted closure was a highly efficacious modality for treating chronic and complex wounds [26].

Subsequently, bibliophily software performed the analysis of the trend topics (Fig. 4B) from the collections since 1996, with a minimum frequency of 10 words and an annual number of 3 words. As a result, 55 keywords were presented with their frequency and popular period. From the trend topic map, we found that the topic"management" had become more and more popular since 2013 and reached its peak in 2017. "vacuum-assisted closure" became famous in 2012 and reached its peak in 2015. "dressings" came into view in 2014 and reached its peak in 2019. From 1942 to 2023, the frequency of new keywords increased while the abundance decreased, indicating an increasing concentration of research topics, with keywords centered around "management" and "dressings" (Fig. S7). Ascribed to the rapid development of sequencing techniques such as 16S-rDNA-seq, metagenomics, and single-cell RNA sequencing, research on the mechanism and effectiveness of wound management, as well as the exploration of new dressing materials, was becoming increasingly popular. According to the trend topics map, the terms "nanofibers" and "injectable hydrogels" appealed more frequently in published articles from 2018 to 2022. We predicted that the material nanofibers and injectable hydrogels may became the research hotspots in the next few years.

3.6. Documents analysis

Generally, the global cited documents reflected the impact of an article on the whole database, while the local cited documents reflected the impact of an article in our retrieved collection. The top 25 most locally cited documents among the 8129 publications were summarized in Table 2, along with their DOI and years of publication. Fig. 5A and Table 3 showed the top 25 most globally cited documents and 23 with more than 500 citations. The article of Argenta, Louis C (26) with the title "Vacuum-Assisted Closure: A New Method for Wound Control and Treatment," which was published in 1997 in Annals of Plastic Surgery, was the most locally cited article (546 citations). It was followed by the article with the title "Negative pressure wound therapy after partial diabetic foot amputation: a multicentre, randomized controlled trial" by David G. Armstrong [29] 2005 from the Lancet journal with 261 citations. Then, the article "Challenges in the Treatment of Chronic Wound" by Robert G. Frykberg and Jaminelli Banks in 2015 from Advances in Wound Care. More importantly, these articles revealed the pathophysiology of complex chronic wounds and the means and modalities available to achieve healing. The safety and efficacy of vacuum-assisted closure in promoting chronic wound healing were demonstrated. A solid foundation has been laid to guide the clinical healing of chronic wounds. Subsequently, to acquire the interrelationships between this literature and the historical evolution and hotspots of the field, the bibliophily software performed the historical direct citation network analysis and a visual map (Fig. 5B). Each node represented a piece of literature, and the lines between the nodes showed the citation relationships between publications. Articles with similar subjects and keywords would be integrated into the same cluster. From 1942 to 2023, there were 25 landmark papers in the fields of wound cleaning and chronic wound research (Fig. 5A). The article by Argenta, Louis C., titled "Vacuum-Assisted Closure: A New Method for Wound Control and Treatment" in 1997, provided valuable ideas for the start of this field [26]. Since 1997, when the effectiveness of vacuum-assisted technology for wound control and treatment was first validated [26], studies of wound bed preparation [28], negative pressure wound therapy for diabetic foot [29], and the challenges in the treatment [5] have added to this network. Accordingly, we hypothesized that these research themes might indicate the evolution of research hotspots in the research field of wound cleaning and chronic wounds.

4. Discussion

4.1. General information

Bibliometrix establishes a pioneering methodological framework for bibliometric analysis, equipped with capabilities to process multi-source heterogeneous data, conduct multidimensional algorithmic analyses, and generate dynamic visualizations, broadening the scope and depth of literature review. Regarding analytical techniques, conventional reviews rely on descriptive statistics, this study employs Bibliometrix's advanced tools—keyword co-occurrence analysis, citation network analysis, and collaboration network analysis—to systematically map core themes, knowledge evolution, and disciplinary structures in chronic wound research. For result presentation, in contrast to static tables and basic charts used in traditional studies, this research utilizes dynamic visualizations (e.g., network maps, thematic landscapes, timelines) to enhance the interpretability and expressiveness of findings. By addressing limitations in literature coverage, analytical depth, and result presentation, this study offers more globally contextualized and evidence-rich insights into chronic wound research.

In this study, we analyzed publications on wound healing in chronic wounds between 1942 and 2023 using an information visualization approach. A total of 8129 articles related to wound healing in chronic wounds were retrieved. The results presented that the global tendency of published literature on wound healing in chronic wounds continued to grow over time, revealing that wound healing in chronic wounds had attracted extensive concerns from researchers and provided a solid foundation for subsequent research. The USA had the most publications, followed by China, the United Kingdom, and Germany. The USA was the country with the highest citations. The N8 research partnership published the maximum number of publications, followed by Harvard University and White Rose University Consortium. These countries and institutions had in-depth research and abundant publications in this field, so cooperation with these countries and institutions had many advantages. In the study, the Journal of Wound Care, International Wound Journal, and Wounds-a Compendium of Clinical Research and Practice are the top three journals with significant advantages in terms of several published papers and total citations. Focusing more on these journals could help us better track the cutting-edge technologies in this field. Armstrong DG and Dumville JC are notable authors in this field, with Armstrong DG's work on diabetic foot ulcers and Dumville JC's research on wound treatment and care laying a solid foundation for subsequent studies [30–34].

After analyzing high-frequency keywords, highly cited documents, and keyword co-occurrence networks, we have identified

Table 2
The top 25 most locally cited documents in chronic wounds-related wound management research.

Rank	Title	Author	Journal	Year	Local Citations	Global Citations	LC/GC Ratio (%)
1	Vacuum-assisted closure: A new method for wound control and treatment	ARGENTA LC	ANN PLAS SURG	1997	546	1523	35.85
2	Negative pressure wound therapy after partial diabetic foot amputation: a multicentre, randomised controlled trial	ARMSTRONG DG	LANCET	2005	261	602	43.36
3	Challenges in the treatment of chronic wounds	FRYKBERG RG	ADV WOUND CARE	2015	252	1032	24.42
4	Wound bed preparation: a Systematic approach to wound management	SCHULTZ GS	WOUND REPAIR REGEN	2003	251	785	31.97
5	Wound healing and its impairment in the diabetic foot	FALANGA V	LANCET	2005	217	1548	14.02
6	Preventing foot ulcers in patients with diabetes	SINGH N	JAMA-J AM MED ASSOC	2005	217	1778	12.2
7	Bacterial load in relation to vacuum-assisted closure wound therapy: A prospective randomized trial	MOUES CM	WOUND REPAIR REGEN	2004	192	379	50.66
8	Effect of extensive debridement and treatment on the healing of diabetic foot ulcers. Diabetic ulcer study group	STEED DL	J AM COLL SURGEONS	1996	191	412	46.36
9	Chronic wound healing: A review of current management and treatments	HAN G	ADV THER	2017	191	897	21.29
10	Graftskin, a human skin equivalent, is effective in the management of noninfected neuropathic diabetic foot ulcers: A prospective randomized multicenter clinical trial	VEVES a	DIABETES CARE	2001	172	521	33.01
11	Comparison of negative pressure wound therapy using vacuum-assisted closure with advanced moist wound therapy in the treatment of diabetic foot ulcers: A multicenter randomized controlled trial	BLUME PA	DIABETES CARE	2008	171	386	44.3
12	Wound microbiology and associated approaches to wound management	BOWLER PG	CLIN MICROBIOL REV	2001	170	1137	14.95
13	Recent advances on the development of wound dressings for diabetic foot ulcer treatment—A review	MOURA LIF	ACTA BIOMATER	2013	165	479	34.45
14	Incisional negative pressure wound therapy after high-risk lower extremity fractures	STANNARD JP	J ORTHOP TRAUMA	2012	124	257	48.25
15	Effects of varying levels of subatmospheric pressure on the rate of granulation tissue formation in experimental wounds in swine	MORYKWAS MJ	ANN PLAS SURG	2001	123	249	49.4
16	Efficacy and safely of a topical gel formulation of recombinant human platelet-derived growth Factor-BB (becaplermin) in patients with chronic neuropathic diabetic ulcers: A phase III randomized placebo-controlled double-blind study	WIEMAN TJ	DIABETES CARE	1998	118	466	25.32
17	Negative pressure wound therapy after severe open fractures: A prospective randomized study	STANNARD JP	J ORTHOP TRAUMA	2009	118	218	54.13
18	The clinical efficacy and cost effectiveness of the vacuum-assisted closure technique in the management of acute and chronic wounds: A randomized controlled trial	BRAAKENBURG a	PLAST RECONSTR SURG	2006	116	225	51.56
19	Negative pressure wound therapy to treat hematomas and surgical incisions following high-energy trauma	STANNARD JP	J TRAUMA	2006	116	218	53.21
20	Advanced therapeutic dressings for effective wound Healing—A review	BOATENG J	J PHARM SCI-US	2015	116	507	22.88
21	Heat exposure study in the workplace in a glass manufacturing unit in India	JOSEPH E	WOUNDS	2000	113	245	46.12
22	State-of-the-art treatment of chronic leg ulcers: A randomized controlled trial comparing vacuum-assisted closure (V.A.C.) with modern wound dressings	VUERSTAEK JDD	J VASC SURG	2006	111	244	45.49
23	A prospective randomized evaluation of negative-pressure wound dressings for diabetic foot wounds	EGINTON MT	ANN VASC SURG	2003	110	200	55
24	Mechanisms and clinical applications of the vacuum-assisted closure (VAC) device	VENTURI ML	AM J CLIN DERMATOL	2005	110	238	46.22
25	A randomized, controlled trial of promogran (a collagen/Oxidized regenerated cellulose dressing) vs standard treatment in the management of diabetic foot ulcers	VEVES a	ARCH SURG-CHICAGO	2002	106	242	43.8

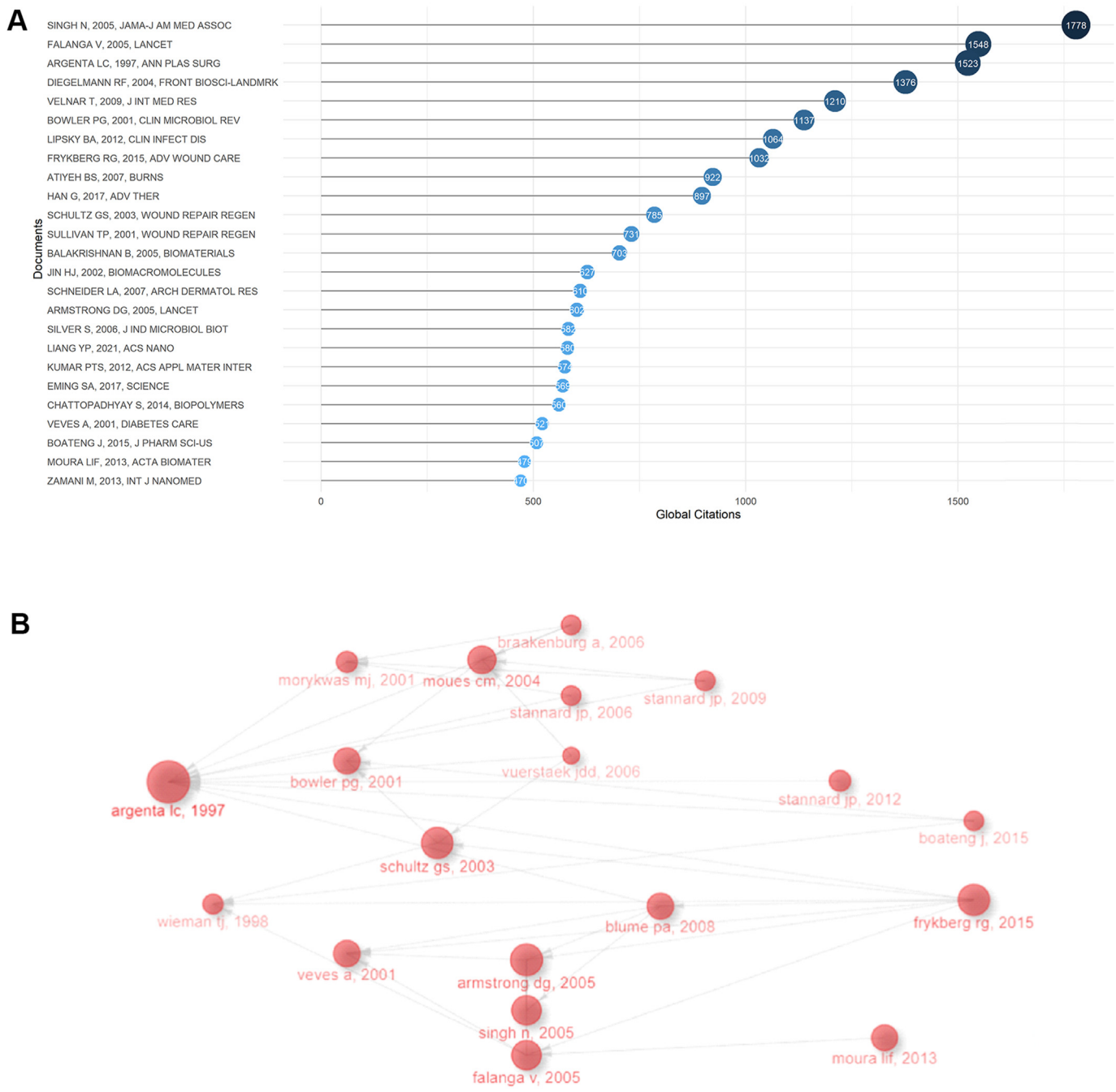

Fig. 5. Documents Analysis. (A) The top 25 most global cited documents of chronic wounds-related wound management research. (B) Visualized historical direct citation network based on the evolution trend of chronic wounds-related wound management research from 1942 to 2023.

two research hotspots related to the role of wound cleaning on chronic wound healing: cellular and molecular events in wound healing, wound management, and treatment of chronic wounds.

Subsequently, to analyze the evolution and future research trends of the field, we combined the historical direct citation network, thematic map, and trend topics map. We analyzed the evolution of research hotspots in the field and speculated that the material nanofibers and injectable hydrogels as dressings might be a future research direction. Keyword analysis was one of the most indispensable parts of bibliometric analysis, reflecting the general contents and themes of a specific article and representing research hotspots. The keywords' variation over time shows the evolution of the field. The two hotspots in research of chronic cleaning-related chronic wounds were summarized as follows.

4.2. Cellular and molecular events in chronic wound healing

Chronic wounds pose a considerable burden to patients and society and were currently an urgent problem to be solved. The healing of chronic wounds was a complex process that was divided into three overlapping phases: inflammation, migration-proliferation (including matrix deposition), and remodeling.

Table 3
The top 25 most global cited documents in chronic wounds-related wound management research.

Rank	Title	Author	Journal	Year	Total Citations	TC per Year
1	Preventing foot ulcers in patients with diabetes	SINGH N	JAMA-J AM MED ASSOC	2005	1778	93.58
2	Wound healing and its impairment in the diabetic foot	FALANGA V	LANCET	2005	1548	81.47
3	Vacuum-assisted closure: A new method for wound control and treatment	ARGENTA LC	ANN PLAS SURG	1997	1523	56.41
4	Wound healing: An overview of acute, fibrotic and delayed healing	DIEGELMANN RF	FRONT BIOSCI-LANDMRK	2004	1376	68.8
5	The wound healing process: An overview of the cellular and molecular mechanisms	VELNAR T	J INT MED RES	2009	1210	80.67
6	Wound microbiology and associated approaches to wound management	BOWLER PG	CLIN MICROBIOL REV	2001	1137	49.43
7	Executive summary: 2012 infectious diseases society of America clinical practice guideline for the diagnosis and treatment of diabetic foot infections	LIPSKY BA	CLIN INFECT DIS	2012	1064	88.67
8	Challenges in the treatment of chronic wounds	FRYKBERG RG	ADV WOUND CARE	2015	1032	114.67
9	Effect of silver on burn wound infection control and healing: Review of the literature	ATIYEH BS	BURNS	2007	922	54.24
10	Chronic wound healing: A review of current management and treatments	HAN G	ADV THER	2017	897	128.14
11	Wound bed preparation: a Systematic approach to wound management	SCHULTZ GS	WOUND REPAIR REGEN	2003	785	37.38
12	THE PIG AS a MODEL FOR HUMAN WOUND HEALING	SULLIVAN TP	WOUND REPAIR REGEN	2001	731	31.78
13	Evaluation of an in situ forming hydrogel wound dressing based on oxidized alginate and gelatin	BALAKRISHNAN B	BIOMATERIALS	2005	703	37
14	Electrospinning bombyx mori silk with Poly (ethylene oxide)	JIN HJ	BIOMACROMOLECULES	2002	627	28.5
15	Influence of pH on wound-healing: a New perspective for wound-therapy?	SCHNEIDER LA	ARCH DERMATOL RES	2007	610	35.88
16	Negative pressure wound therapy after partial diabetic foot amputation: a multicentre, randomised controlled trial	ARMSTRONG DG	LANCET	2005	602	31.68
17	Silver as biocides in burn and wound dressings and bacterial resistance to silver compounds	SILVER S	J IND MICROBIOL BIOT	2006	582	32.33
18	Functional hydrogels as wound dressing to enhance wound healing	LIANG YP	ACS NANO	2021	580	193.33
19	Flexible and microporous chitosan hydrogel/ Nano ZnO composite bandages for wound dressing: In vitro and in vivo evaluation	KUMAR PTS	ACS APPL MATER INTER	2012	574	47.83
20	Inflammation and metabolism in tissue repair and regeneration	EMING SA	SCIENCE	2017	569	81.29
21	Collagen-based biomaterials for wound healing	CHATTOPADHYAY S	BIOPOLYMERS	2014	560	56
22	Graftskin, a human skin equivalent, is effective in the management of noninfected neuropathic diabetic foot ulcers: A prospective randomized multicenter clinical trial	VEVES a	DIABETES CARE	2001	521	22.65
23	Advanced therapeutic dressings for effective wound Healing—A review	BOATENG J	J PHARM SCI-US	2015	507	56.33
24	Recent advances on the development of wound dressings for diabetic foot ulcer treatment—A review	MOURA LIF	ACTA BIOMATER	2013	479	43.55
25	Advances in drug delivery via electrospun and electrosprayed nanomaterials	ZAMANI M	INT J NANOMED	2013	470	42.73

Failure at any of these phases would disrupt the wound-healing process and led to the development of chronic wounds. In the current study, research on cellular and molecular events in chronic wound healing could be found in highly cited literature and the extensive related literature; we speculated that the study of cellular and molecular events in chronic wound healing was a hotspot of academic attention and potentially a research trend for the coming period significant for improving the treatment method and promoting chronic wounds cure rate. The healing process required the joint efforts of many tissues and cell lineages, including fibroblasts, keratocytes, and macrophages (Fig. 6). Shortly after the injury, fibrin thrombi formed, and inflammatory cells were rapidly recruited to the wound. Hemostasis and wound protection required coagulation. Platelets promoted the formation of hemostatic suppositories and also secreted mediators that could attract and activate macrophages and fibroblasts, such as platelet-derived growth factors [35]. However, if neutrophils migrated uncontrollably, the inflammatory process would be prolonged, leading to the excessive production of ROS and protease. Toxic proteinases and increased ROS levels degraded ECM and destroyed cell membranes, thereby prolonging wound healing and forming chronic wounds [37]. As the inflammatory phase subsided, accompanied by apoptosis of immune cells, the main characteristics of the subsequent proliferative phase were tissue granulation, neovascularization (angiogenesis), and epithelialization. The last phase occurred after the wound was closed and may last 1–2 years or longer, during which the temporary matrix was remodeled into organized collagen bundles.

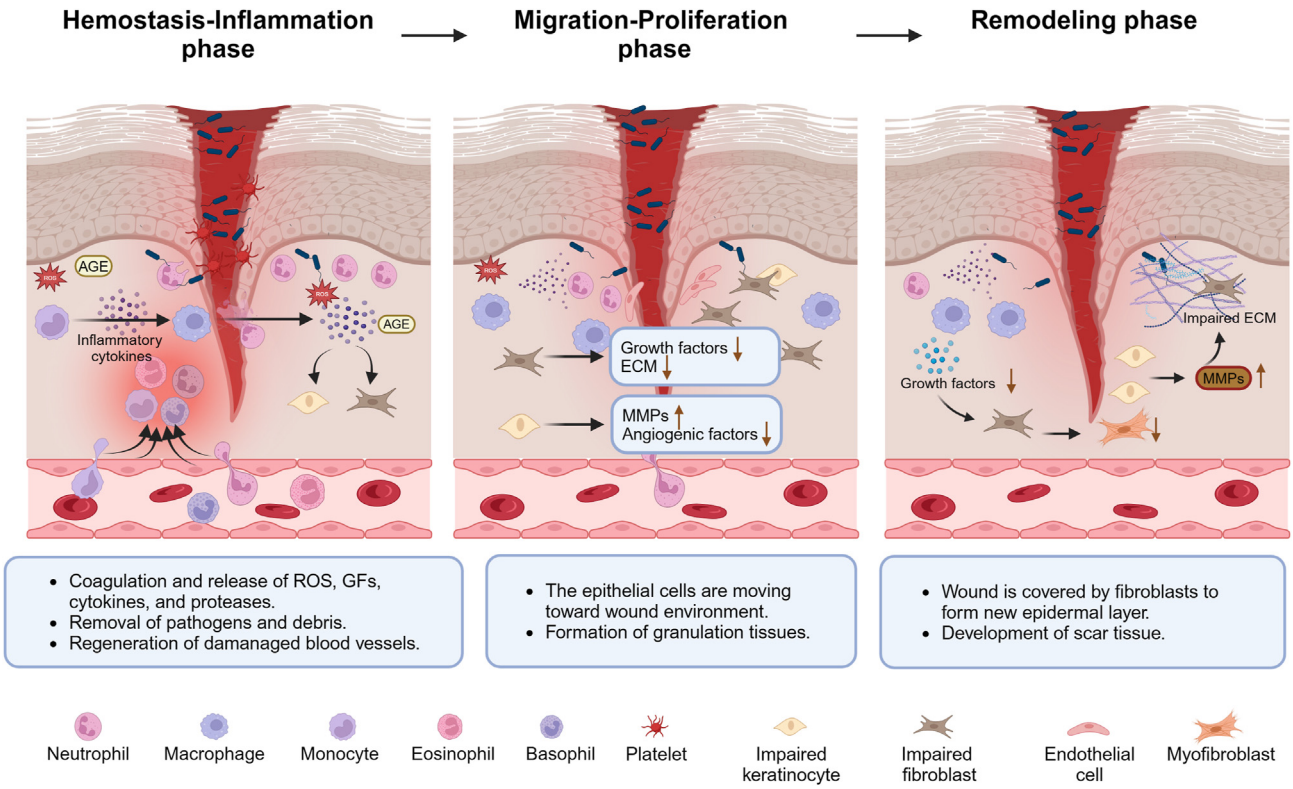

Fig. 6. Cellular and molecular events in chronic wound healing. The persistence of chronic wound is the result of a combination of factors that cause a excessive and constant chronic inflammatory response. Take diabetic wounds for an example, perturbations are closely associated with advanced glycation end (AGE) products, oxidative stress and impaired angiogenesis. These factors, such as impairment of fibroblasts and keratinocytes, lead to reduced proliferation and migration, as well as disruption of extracellular matrix (ECM) secretion and differentiation of fibroblasts into myofibroblasts. In addition, it also leads to reduced angiogenesis, chronic inflammation, and abnormal expression of matrix metalloproteinases (MMPs). Resulting in a excessive and constant chronic inflammatory response, disrupting epithelial cell formation and eventual wound closure. Ultimately, leading to the development of chronic non-healing wounds.

In previous research, with information mainly derived from experimental animal wounds, we speculated on the fundamental biological and molecular events after chronic wounds. Many experiments have confirmed that mouse models lacking inflammation related factors, plasminogen and its activators, or fibroblast growth factor-2 have prolonged wound healing time, while mouse models overexpressing certain tissue metalloproteinases (e.g., matrix metalloproteinase [MMP]1), or Smad-3 or skn-1a gene knockout (which are involved in wound healing pathways) have accelerated wound healing [36,38–40]. These findings provided ideas for improving human wound healing by manipulating growth factors, extracellular matrix (ECM), and signaling pathways. It was suggested that the combination of one or more compounds for the treatment of wounds, or the combination therapy of different compounds for wounds according to the wound healing stage, maybe the potential research direction of our effective treatment of chronic wounds [41], resulting in faster application times and higher patient satisfaction.

4.3. Wound management and treatment of chronic wounds

With the in-depth exploration of the pathophysiology of chronic wound healing in previous studies, established management principles and advanced treatments for chronic wounds were gradually being explored. Overcoming factors that cause delayed healing was a key challenge in chronic wound treatment. A high-cited document showed that all currently published guidelines and consensus reviews on chronic DFU, VLU, and PU management advocated initial treatment using standard wound care principles [5]. Common wound care technologies currently used internationally include negative pressure wound therapy, hyperbaric oxygen therapy, biophysical models, and biological and bioengineering therapies [5]. According to the analysis of the most frequent keywords, high-cited documents, thematic map, and trend topics, we found that vacuum-assisted closure and advanced dressings had been research topics.

4.3.1. Vacuum-assisted closure

Negative pressure wound therapy (NPWT) using vacuum-assisted closure (VAC) was one of the most important modes of treatment used in modern wound management [29,42–45]. Since its launch in the mid-1990s, negative pressure therapy had played a major role in the management of traumatic, acute, and chronic wounds, as well as in stabilizing skin grafts, flaps, and surgical incisions [46–50]. VAC therapy is effective generally via four dominant mechanisms of action: perfusion changes, microdeformation, exudate control and macrodeformation (Fig. 7). Hyperperfusion at the distal end and hypoperfusion near the wound caused by NPWT stimulate the delivery of nutrients and angiogenesis, respectively, promoting the wound healing process [51]. The suction applied by the VAC system helps to remove exudate and infectious materials and then decreases edema [52]. Microdeformation increases activation of transforming growth factors and increases cellular proliferation and granulation tissue, while macrodeformation appears to stimulate wound contraction [51]. So far, most clinical studies on animals and humans have reported that the use of VAC was comparable to traditional wound closure techniques and sometimes even better [53]. Argenta and Morykwa reported their research results on 300 human subjects in 1997, of which 296 patients responded well to VAC(26). Over the years, clinical trials have

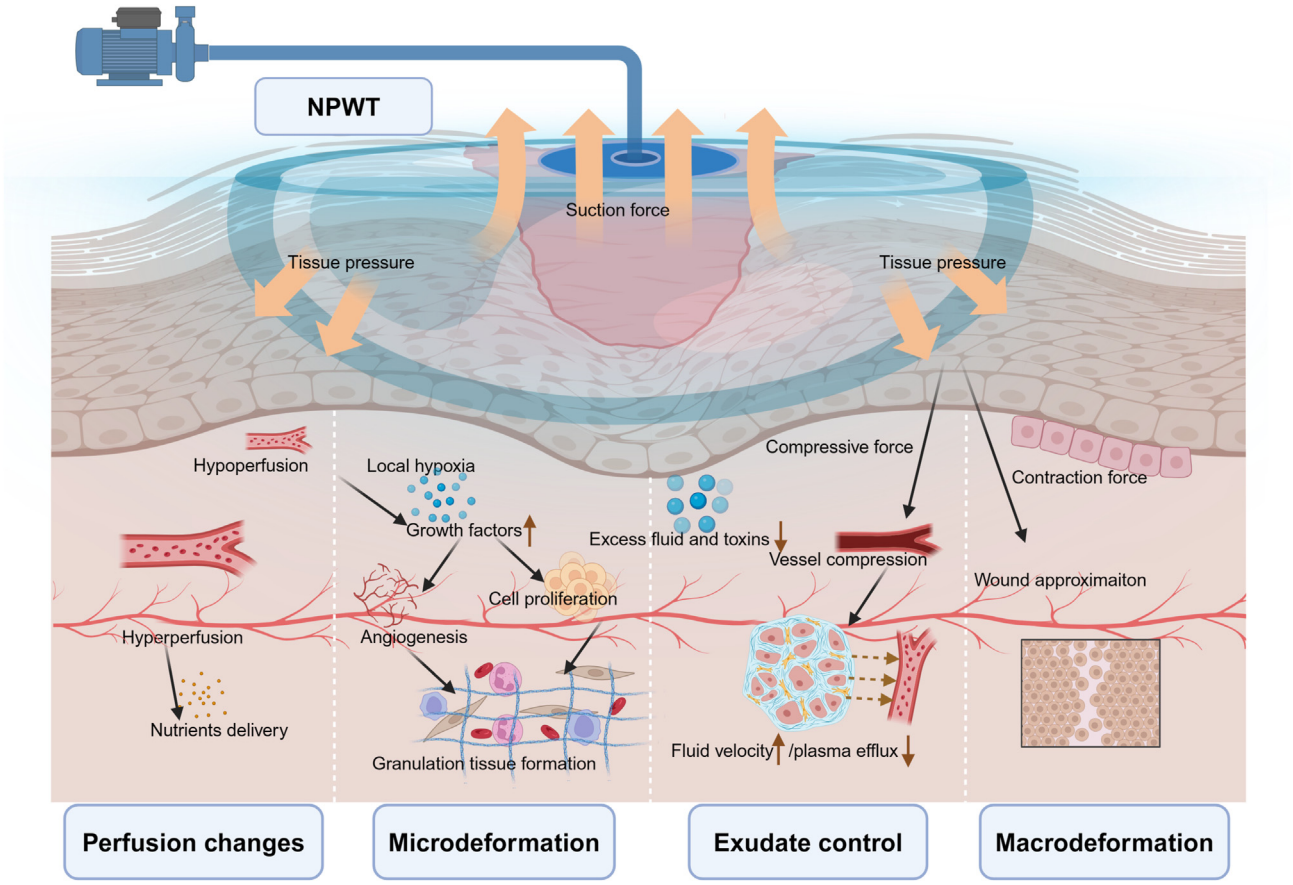

Fig. 7. Mechanisms of action involved in negative pressure wound therapy.

demonstrated that NPWT outperforms standard therapy in treating various wounds, leading to higher healing rates, faster healing speed, and potentially fewer re-amputations [26,29,54–58]. As an auxiliary means of standard chronic wound care, NPWT could effectively manage wound drainage and provide preparation for accelerating granulation tissue development, wound area contraction/reduction, delayed closure or transplantation, or primary healing [44,59]. However, application technology was crucial, and in recent years, mechanical power, ultralight, and portable NPWT devices had also been introduced [60,61], resulting in faster application time and higher patient satisfaction. Even NPWT is used by clinical doctors to combine with other advanced therapies such as cell-free and cell–matrix therapy, which may became a trend in future research on NPWT therapy [62].

4.3.2. Therapeutic dressings

In humid wound environments, modern wound dressings have demonstrated significant advantages in promoting tissue regeneration and reducing infections, scars, and pain compared with traditional dry dressings. Meanwhile, wound dressings could be used to create, maintain, and control an ideal moist environment for healing [63]. These dressings created and maintained an optimal moist environment for healing, provided a protective barrier against bacterial contamination, and promoted granulation, angiogenesis, autolysis, and rapid epidermal cell migration to accelerate wound healing [64].

Currently, with the development of biotechnology, advanced dressings had been developed, and dressing materials could include natural, modified, and synthetic polymers, as well as their mixtures or combinations, processed in the form of films, foam, hydrocolloids, and hydrogels [65]. Different from traditional dressings such as gauze and cotton wool, these modern dressings could also serve as drug delivery systems, delivering therapeutic substances like drugs, growth factors, peptides, and stem cells to the wound surface [66]. These substances could act directly as cleaning agents or debridements to remove necrotic tissue, or indirectly as antibacterial drugs to prevent infections or growth factors to aid tissue regeneration [67]. Recent studies highlighted that modern dressings, such as anti-inflammatory hydrogel dressings, held bioactive molecules and novel biomaterials that chelated chemokines, cleared excess ROS, and promoted the M1-to-M2 polarization of macrophages, so that help promote angiogenesis, collagen deposition, and epithelial cell migration, minimize fibrosis and remodel the extracellular matrix (Fig. 8) [68].

Patients typically underwent long-term treatment and frequent dressing changes in chronic wound management. A system that delivers drugs to the wound site in a controlled manner could improve patient compliance and treatment outcomes. Recently, an RCT study involving 160 patients provided evidence that the combination of recombinant epidermal growth factor and nanosilver dressings could effectively promote wound healing and prevent infection in chronic wounds [69]. Among these developed compound dressings, there was still a lack of practicality due to high costs or complex production processes [65]. Therefore, soon, research would probably focus on developing more effective, cheaper, biocompatible, and biodegradable drug dressings that could provide essential healing factors for wound sites to improve patient care and quality of life.

Nevertheless, there were still certain limitations in our study. Firstly, we retrieved articles that were collected in the Web of Science Core Collection (WoSCC) from January 1, 1942, to July 10, 2023, which

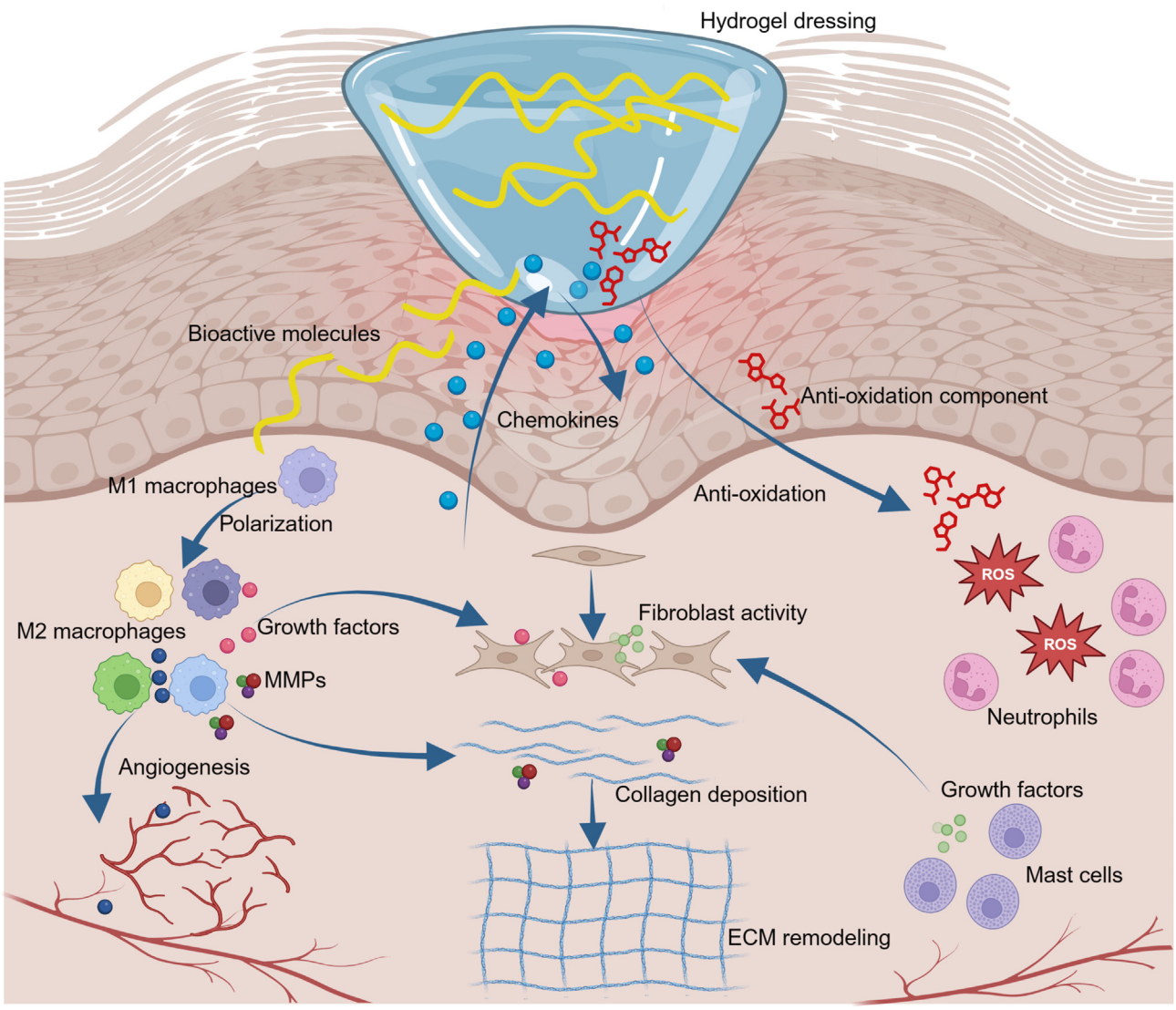

Fig. 8. The combined anti-inflammatory hydrogel dressing can promote angiogenesis, collagen deposition and epithelial cell migration, reduce fibrosis, reshape extracellular matrix (ECM) and promote wound healing by integrating drugs, bioactive small molecules and new biomaterials into the hydrogel matrix.

would cause the exclusion of some of the most recent findings as this data was continuously updated. Due to the restriction of retrieval and analysis technology, WoSCC was the only database we retrieved publications, which may contribute to an imperfect collection of relevant publications. Secondly, Bibliometrics could not evaluate the analyzed articles' quality, rationality, and limitations. Therefore, this study could not replace other types of reviews, such as systematic reviews and meta-analyses. Thirdly, due to our tendency to analyze highly cited works of literature, some cutting-edge works of literature with low cited works of literature may need to be noticed, leading to some hysteresis quality of the study. Last but not least, some recent critical publications may not had yet received sufficient attention and, therefore, may not had received in-depth exploration. Despite the limitations, this study comprehensively reviewed the global status and research trends of chronic wound healing.

5. Conclusion

In this article, we performed a visualization analysis across annual publications and citations, countries, institutions, sources, authors of publication counts, keywords, and research trends to summarize the previous research and predict potential future research hotspots on the role of wound cleaning in chronic wound healing. Through relevant analysis, we had identified two research hotspots related to the role of wound cleaning on chronic wound healing: cellular and molecular events in wound healing, wound management, and treatment of chronic wounds. Among the numerous studies on the continuous improvement and development of treatment methods, research on vacuum-assisted closure technology for negative pressure wound treatment and advanced dressings were gradually gaining more attention from scholars. A better understanding of the differences between various types of chronic wounds at the molecular and cellular levels, and further research on these topics could help improve our treatment methods, thereby increasing healing rates and promoting the development of new and more effective treatment methods. The effectiveness of current and future advanced wound treatment required more evidence to ensure its appropriate use.

Consent for publication

Not applicable.

Ethics approval and consent to participate

The study was approved by the Ethics Committee of the First Affiliated Hospital of Naval Medical University.

Data availability statement

The original contributions presented in the study are included in the article/Supplementary Material, further inquiries can be directed to the corresponding authors.

Code availability statement

The code during the current study are available in the supplementary materials.

Author contributions

Conception/design: Yushu Zhu, Yizhen Lin, Sujie Xie, Mingxuan Yang, Wei Zhang, Yifan Liu, Minjuan Wu, Dayuan Xu, Shuyuan Xian, Xirui Tong, Jie Huang, Luofeng Jiang, Xinya Guo, Minyi Gu, Hengkai Yu, Xinran Ding, Yixu Li, Yiyao Du, Heng He, Jianyu Lu, Runzhi Huang, Shizhao Ji.

Collection and/or assembly of data: Yushu Zhu, Yizhen Lin, Sujie Xie, Mingxuan Yang, Wei Zhang, Yifan Liu, Minjuan Wu, Dayuan Xu, Shuyuan Xian, Xirui Tong, Jie Huang, Luofeng Jiang, Xinya Guo, Minyi Gu, Hengkai Yu, Xinran Ding, Yixu Li, Yiyao Du, Heng He, Jianyu Lu, Runzhi Huang, Shizhao Ji.

Data analysis and interpretation: Yushu Zhu, Yizhen Lin, Sujie Xie, Mingxuan Yang, Wei Zhang, Yifan Liu, Minjuan Wu, Dayuan Xu, Shuyuan Xian, Xirui Tong, Jie Huang, Luofeng Jiang, Xinya Guo, Minyi Gu, Hengkai Yu, Xinran Ding, Yixu Li, Yiyao Du, Heng He, Jianyu Lu, Runzhi Huang, Shizhao Ji,

Manuscript writing: Yushu Zhu, Yizhen Lin, Sujie Xie, Mingxuan Yang, Wei Zhang, Yifan Liu, Minjuan Wu, Dayuan Xu, Shuyuan Xian, Xirui Tong, Jie Huang, Luofeng Jiang, Xinya Guo, Minyi Gu, Hengkai Yu, Xinran Ding, Yixu Li, Yiyao Du, Heng He, Jianyu Lu, Runzhi Huang, Shizhao Ji,

Final approval of manuscript: Yushu Zhu, Yizhen Lin, Sujie Xie, Mingxuan Yang, Wei Zhang, Yifan Liu, Minjuan Wu, Dayuan Xu, Shuyuan Xian, Xirui Tong, Jie Huang, Luofeng Jiang, Xinya Guo, Minyi Gu, Hengkai Yu, Xinran Ding, Yixu Li, Yiyao Du, Heng He, Jianyu Lu, Runzhi Huang, Shizhao Ji.

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Declaration of competing interest

The authors declare no competing interests. We all confirm that there isn't any conflict of interest between all authors.

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Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.reth.2025.05.002.

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