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A Bibliometric Analysis of Global Research Production Pertaining to Diabetic Foot Ulcers in the Past Ten Years

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ABSTRACT

The aim of this study was to demonstrate the state of diabetic foot ulcer (DFU) research in the past 10 years by bibliometric analysis, especially by performing document co-citation and co-word visualization analysis to reveal the research hotspots, frontiers, and core literature. The literature in connection with DFUs from 2007 to 2018 was retrieved from the Web of Science Core Collection database (WoSCC). We used the WoSCC and CiteSpace to analyze publication outcomes, journals, research direction, research hotspots, and frontiers. Overall, 4580 publications on DFUs were retrieved until March 22, 2018. The number of publications from the United States accounts for approximately one third of all publications from the top 10 countries. Surgery accounted for the largest proportion of the publications we retrieved from the WoSCC in terms of research areas. Results of this analysis indicated that DFU research has been in a stable, mature stage. Developed countries pay more attention to DFU research field than do developing countries, especially the United States. The complications of DFUs, such as lower extremity amputation and diabetic foot infection, are the hotspots. Diabetic foot infection, wound management, prediction studies on DFU, and diseases related to DFU are the research frontiers that should be observed closely in the future.

Diabetes mellitus is 1 of the most well-known chronic diseases in almost all countries. With the development of society and technology, people have changed their lifestyle, as characterized by decreased physical exercise and increased obesity, which are responsible for the increase in the number of people with diabetes mellitus. It was estimated that 415 million people all over the world had diabetes in 2013, and the number is expected to rise to 592 million by 2035 (1). In addition, the complication of diabetes mellitus is also an issue urgent to be solved. Diabetic foot ulcer (DFU) is 1 of the most common complications of diabetes and leads to high hospital costs. It was reported that the total additional medical cost associated with diabetes for treating diabetic foot diseases in America ranges from $9 to $13 billion (2). These chronic, nonhealing foot ulcers occur in approximately 15% of all people with diabetes and are responsible for patients' decreased quality of life (3). Unfortunately , if a DFU has developed, there is a high risk of wound progression, which may result in amputation. It was reported that > 85% of foot amputations in patients are caused by DFU (4). Therefore, the International Diabetes Foundation is paying more attention to DFUs, taking into consideration the substantial social, medical, and economic burdens (5).

Nevertheless, the rapid growth of DFU literature brought about challenges in identifying emerging trends and hotspots of DFU research. The traditional expert reviews on DFU have become insufficient for comprehensive understanding of this field. Fortunately, the development of bibliometrics is playing an important role in performing reviews in many research fields. However, there are few specific bibliometric analyses of DFU. CiteSpace software was used as an analysis tool to perform a bibliometric analysis. It was invented by Professor Chaomei Chen from Drexel University in early 2004 to create statistical visualization analysis of scientific references, and it is characterized by co-citation network maps of cited references, cited authors, and cited journals, as well as co-occurrence network maps of keywords, terms, authors, and so on (6,7). Because of the increasing number of publications about DFU, it is imperative to make valuable and evidential results using scientific methods such as bibliometric analysis via CiteSpace, which contributes to helping investigators understand this research area thoroughly. In our study, we used the Web of Science Core Collection database (WoSCC) to perform simple statistical analysis of literature related to DFU that were published from 2007 to 2018 and CiteSpace to perform bibliometric visualization analysis of related references derived from the WoSCC to demonstrate the hot spots and frontiers of research on DFUs in the past 10 years.

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Materials and Methods

All of the reference data used in our study were retrieved from the WoSCC and the data retrieval strategy was topic: diabetic foot ulcer* OR diabetic foot wound*; time span: 2007 to 2018 (retrieved data March 22, 2018); and document type: article, review, proceedings paper. A total of 4580 references were retrieved. Then we chose "Full Record and Cited References" to manually download the information of each publication in TXT format, containing the title, author names, abstract, key words, references, and more. We used the WoSCC to perform simple statistical analysis, including publication outcomes, country, and research area.

CiteSpace was used to perform bibliometric visualization analysis, including co-citation analysis in references and co-occurrence analysis of the keywords to generate visualization knowledge maps and to demonstrate the comprehensive research situation of the DFU research field in the past 10 years, especially research hotspots, fronts, and classic basal literature. Visualization knowledge maps are made up of nodes that represent elements such as a cited reference, institution, author, and keyword, and the links between nodes that represent relationships of co-authorship or co-occurrence or co-citations. The color of links between nodes represents the year of first co-citation. The Tree Ring History represents the citation history of an article. The whole size of it reflects the cited times of the reference. The color of Tree Ring History represents the time of a corresponding citation, and the thickness of it is proportional to the number of citations in a given time slicing. The purple ring represents the key document that may play an important role in the field (6,8,9).

The following were the parameters of CiteSpace: time slicing (2007 to 2018), year per slice (1), term source (Title, Abstract, Author Keywords [DE], Keywords Plus [ID]). Other parameters were chosen in accordance with specific conditions.

Results

A total of 4580 publications were indexed in the WoSCC from 2007 to 2018. The distribution of publications between 2007 and 2018 is presented in Fig. 1. As shown in this figure, the number of publications increased, with some fluctuations during this period. Because the retrieval date was March 22, 2018, the volume of publications in 2018 is unsurprisingly less than the other years. Thus, we excluded the year 2018.

The distribution of the top 10 countries publishing papers on DFU indexed in the WoSCC from 2007 to 2018 is as follows. The United States published the highest number of literature on DFU (n = 1495), followed by the United Kingdom (n = 463), the People's Republic of China (n = 336), Germany (n = 318), Italy (n = 267), the Netherlands (n = 198), India (n = 187), France (n = 162), Australia (n = 157), and Canada (n = 154).

The top 10 research areas related to DFU classified by the WoSCC are as follows. Surgery accounted for the largest proportion of the publications we retrieved from the WoSCC (n = 1259), followed by dermatology (n = 997), endocrinology metabolism (n = 792), orthopedics (n = 504), research experimental medicine (n = 410), general internal medicine (n = 340), cell biology (n = 287), engineering (n = 252), cardiovascular system cardiology (n = 241), and pharmacology pharmacy (n = 203).

The records we retrieved from the WoSCC from 2007 to 2018 were analyzed using CiteSpace to detect the core and classic basal literature.

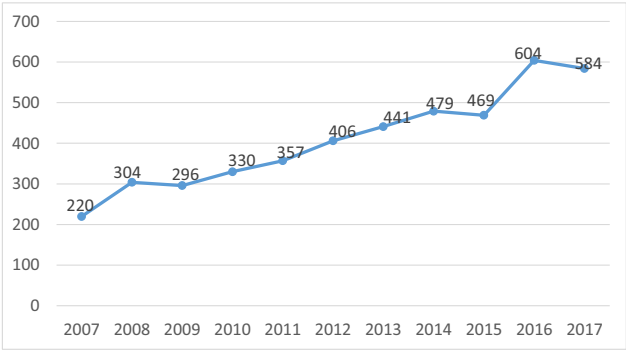

Fig. 1. The annual number of publications on diabetic foot ulcers indexed by Web of Science Core Collection from 2007 to 2017.

Here, we chose "Cited references" as the node type and "Top N per slice" as the selection criteria, then selected the top 20 most cited or occurred items from each slice. In the co-citation network maps of cited references created by CiteSpace (Fig. 2*A*), 131 nodes and 501 links were selected. In this figure, we showed the 10 top-cited documents. The details of these 10 publications, including author, title, published year, and co-cited frequency are summarized in Table 1. We also listed the top 10 publications sorted by centrality, as shown in Table 2. The centrality is a quantitative indicator of references, meaning that a reference's larger centrality implies a more important role in the cluster. When combining Table 1 with Table 2, we found 6 core references with high centrality, as well as high co-cited frequency (10–15). Furthermore, we listed the top 10 publications sorted by bursts, as shown in Table 3. These represent more important publications about this field in recent 10 years.

Furthermore, we chose "title" as the label to generate co-citation clusters of references. Co-citation cluster is a network made up of co-cited references, and it can be used to detect study frontiers. In this cluster analysis, the modularity Q was 0.4912, and the silhouette was 0.3762, which indicated that co-cited publications formed an obvious and relatively independent cluster network. In total, we got 8 co-citation clusters that were named by the number of publications in each cluster. Fig. 2*B* shows us the largest 6 co-citation clusters of references: diabetic foot infection (ID no. 0), comparative efficacy (ID no. 1), wound management (ID no. 2), removable device (ID no. 3), diabetic foot infection (ID no. 4), and endovascular revascularization (ID no. 5). These clusters were also shown in a timeline view (Fig. 2*C*). We also listed the details of these 6 clusters (Table 4).

Next, we chose "Keywords" as node type and "Top N per slice" as selection criteria, then selected the top 100 most cited or occurred items from each slice. We chose "pathfinder" and "pruning the merged network" for the network analysis. Next, we got a keyword knowledge map with 280 nodes and 374 links (Fig. 3*A*). Table 5 shows us the information of the top 20 keywords sorted by co-citation counts, top 20 keywords sorted by burst, and top 20 keywords sorted by centrality.

Furthermore, we chose the keyword as the label to generate co-occurrence clusters of keywords. In this cluster analysis, the modularity Q was 0.8104, and the silhouette was 0.757, indicating that we got an obvious and relatively independent cluster network, and the label of each cluster is relatively accurate. In total, we got 17 co-occurrence clusters that were named by the number of items in each cluster. Fig. 3*B* shows us the largest 15 co-occurrence clusters of keywords that represent hot research topics: resistant *Staphylococcus aureus* (ID no. 0), ulcer (ID no. 1), expression (ID no. 2), film (ID no. 3), revascularization (ID no. 4), peripheral neuropathy (ID no. 5), management (ID no. 6), foot ulceration (ID no. 7), amputation (ID no. 8), endothelial cell (ID no. 9), diabetic foot ulcer (ID no. 10), randomized controlled trail (ID no. 11), multicenter (ID no. 12), infection (ID no. 13), plantar ulcer (ID no. 14), and angipars (ID no. 15). We also listed the details of these 15 clusters (Table 6). Fig. 4 shows us the details of keywords with the strongest citation bursts of publications on DFU from 2007 to 2018. The red line represents the period of the burst keyword, indicating the beginning and end of the time interval of each burst (16).

Discussion

In relation to the number of publications, the studied period could be divided into the following 3 stages: from 2007 to 2014 (first stage), from 2014 to 2016 (second stage), and from 2016 to 2017. The first stage is a stable development stage, but the publications in 2009 were fewer than in 2008. However, an upward trend was maintained during this period. The second stage is a rapid development stage after a 2-year stable period (2014 to 2015). An accelerated increase occurred in 2016. The third stage decreased in 2017. As shown in Fig. 1, the

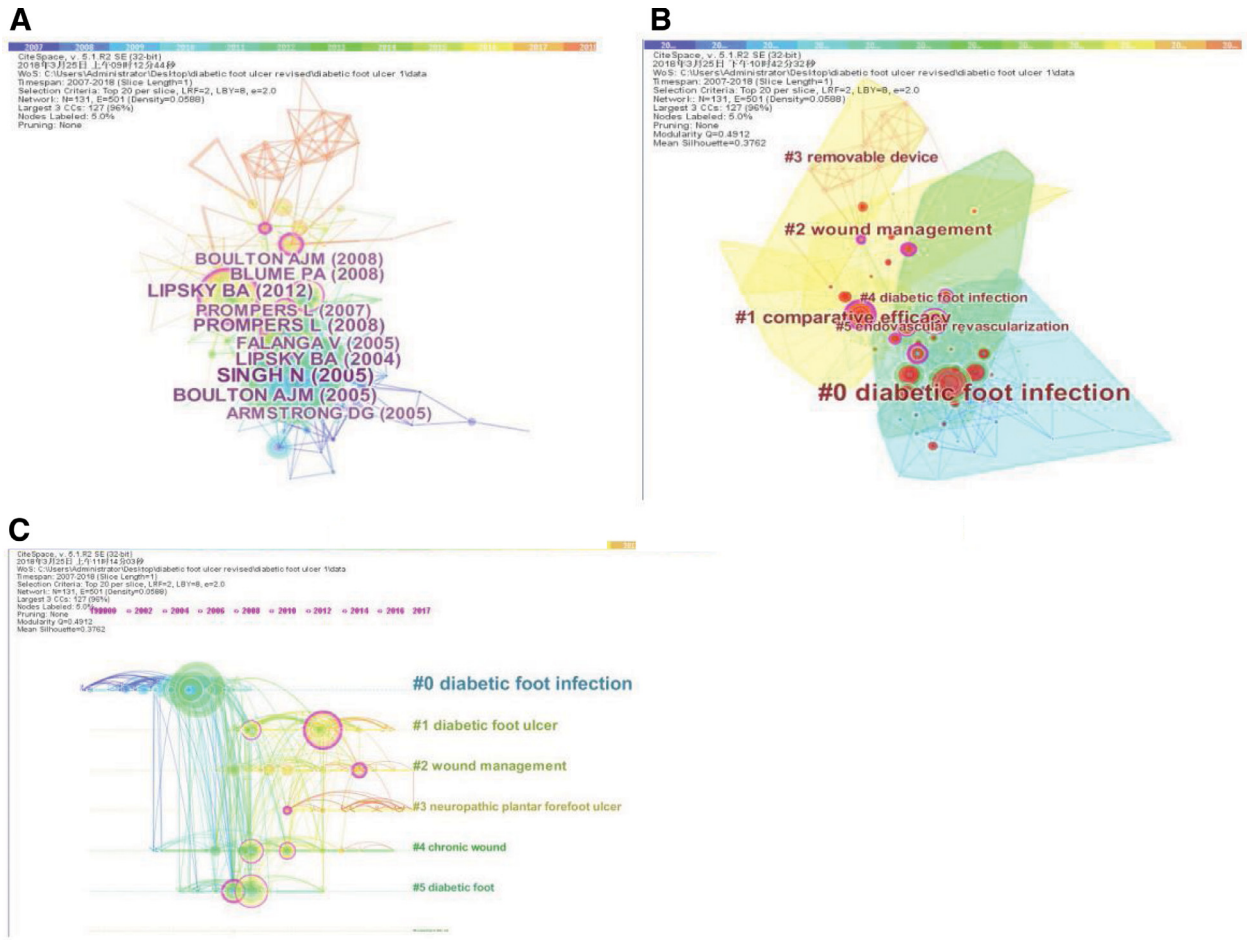

Fig. 2. (*A*) The 10 top-cited publications on diabetic foot ulcers (DFUs) indexed in Web of Science from 2007 to 2018. (*B*) Reference co-citation map of publications on DFUs from 2007 to 2018. (*C*) Reference co-citation (timeline view) map of publications on DFUs from 2007 to 2018.

number of publications has increased at a stable slope rate over the past 10 years, which indicates that DFU research has been in a stable, mature stage; that it has drawn increased attention; and that more DFU research is being performed.

According to the analysis by country, the top 10 countries (4 European countries, 2 American countries, 2 Asian countries, 1 Oceanian country) that engaged in DFU research contributed to 3737 publications, accounting for 81.59% of the total number of publications. China

Table 1
The information of the 10 top references sorted by co-cited frequency

No.	First Author	Year	Title	Co-Cited Frequency
1	Singh N	2005	Preventing Foot Ulcers in Patients With Diabetes	280
2	Boulton AJM	2005	The Global Burden of Diabetic Foot Disease	188
3	Lipsky BA	2012	2012 Infectious Diseases Society of America Clinical Practice Guideline for the Diagnosis and Treatment of Diabetic Foot Infections	171
4	Lipsky BA	2004	Diagnosis and Treatment of Diabetic Foot Infections	169
5	Prompers L	2008	Prediction of Outcome in Individuals With Diabetic Foot Ulcers: Focus on the Differences Between Individuals With and Without Peripheral Arterial Disease. The EURODIALE Study	163
6	Falanga V	2005	Wound Healing and Its Impairment in the Diabetic Foot	122
7	Blume PA	2008	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	118
8	Prompers L	2007	High Prevalence of Ischaemia, Infection and Serious Comorbidity in Patients With Diabetic Foot Disease in Europe. Baseline Results From the EURODIALE Study	113
9	Armstrong DG	2005	Negative Pressure Wound Therapy After Partial Diabetic Foot Amputation: A Multicentre, Randomised Controlled Trial	109
10	Boulton AJM	2008	Comprehensive Foot Examination and Risk Assessment: A Report of the Task Force of the Foot Care Interest Group of the American Diabetes Association, With Endorsement by the American Association of Clinical Endocrinologists	105

Table 2
The information of the 10 top references sorted by centrality

No.	First Author	Year	Title	Centrality
1	Rice JB	2014	Burden of Diabetic Foot Ulcers for Medicare and Private Insurers	0.33
2	Prompers L	2007	High Prevalence of Ischaemia, Infection and Serious Comorbidity in Patients With Diabetic Foot Disease in Europe. Baseline Results From the EURODIALE Study	0.28
3	Lipsky BA	2012	2012 Infectious Diseases Society of America Clinical Practice Guideline for the Diagnosis and Treatment of Diabetic Foot Infections	0.26
4	Driver VR	2010	The Costs of Diabetic Foot: The Economic Case for the Limb Salvage Team	0.24
5	Blume PA	2008	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	0.18
6	Prompers L	2008	Prediction of Outcome in Individuals With Diabetic Foot Ulcers: Focus on the Differences Between Individuals With and Without Peripheral Arterial Disease. The EURODIALE Study	0.17
7	Boulton AJM	2008	Comprehensive Foot Examination and Risk Assessment: A Report of the Task Force of the Foot Care Interest Group of the American Diabetes Association, With Endorsement by the American Association Of Clinical Endocrinologists	0.11
8	Londahl M	2010	Hyperbaric Oxygen Therapy Facilitates Healing of Chronic Foot Ulcers in Patients With Diabetes	0.10
9	Lipsky BA	2004	Diagnosis and Treatment of Diabetic Foot Infections	0.09
10	Steed DL	2006	Guidelines for the Treatment of Diabetic Ulcers	0.09

Table 3
The information of 10 top references sorted by bursts

Bursts	References	Cluster ID
45.75	2012 Infectious Diseases Society of America Clinical Practice Guideline for the Diagnosis and Treatment of Diabetic Foot Infections	1
30.46	Diagnosis and Treatment of Diabetic Foot Infections	0
28.19	Preventing Foot Ulcers in Patients With Diabetes	0
27.40	The Global Burden of Diabetic Foot Disease	0
26.86	Factors Affecting Wound Healing	2
25.56	Human Skin Wounds: A Major and Snowballing Threat to Public Health and the Economy	2
25.44	The North-West Diabetes Foot Care Study: Incidence of, and Risk Factors for, New Diabetic Foot Ulceration in a Community-Based Patient Cohort	0
25.02	Burden of Diabetic Foot Ulcers for Medicare and Private Insurers	2
22.81	Diabetic Foot Ulcers	0
22.53	Prediction of Outcome in Individuals With Diabetic Foot Ulcers: Focus on the Differences Between Individuals With and Without Peripheral Arterial Disease. The EURODIALE Study	5

Abbreviation: ID, identifier.

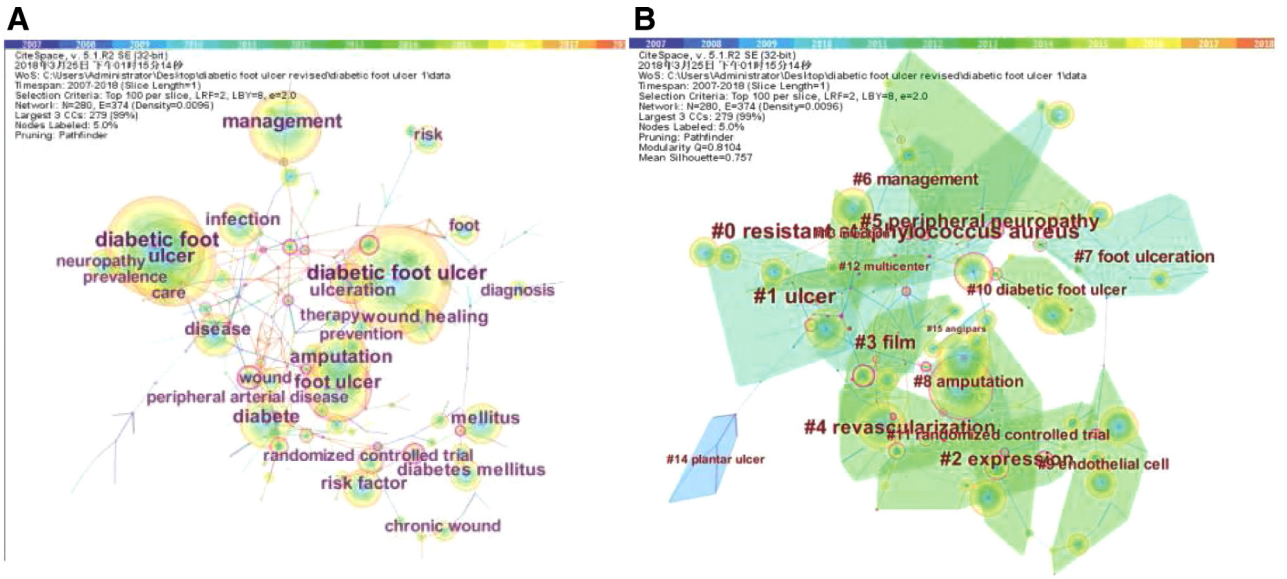

Fig. 3. (*A*) Keyword co-occurrence knowledge map of publications on diabetic foot ulcers from 2007 to 2018. (*B*) Keyword co-occurrence knowledge map of publications on diabetic foot ulcers from 2007 to 2018 (after clustering).

Table 4
The information of largest 6 co-citation clusters of publications taking title as the label

Cluster ID	Size	Silhouette	Mean (year)	Label (LLR)
0	39	0.63	2003	Diabetic foot infection
1	23	0.684	2011	Comparative efficacy
2	20	0.714	2011	Wound management
3	16	0.957	2014	Removable device
4	14	0.736	2009	Diabetic foot infection
5	13	0.794	2007	Endovascular revascularization

Abbreviation: ID, identifier.

Table 5
The information of top 20 keywords sorted by count, burst, and centrality, respectively

No.	Count	Keywords	No.	Burst	Keywords	No.	Centrality	Keywords
1	1012	Diabetic foot ulcer	1	9.68	Meta analysis	1	0.40	Survival
2	926	Diabetic foot	2	9.59	High risk	2	0.36	Endothelial growth factor
3	830	Ulcer	3	8.70	Rat	3	0.30	Scaffold
4	693	Management	4	8.57	Individual	4	0.29	Peripheral arterial disease
5	629	Foot ulcer	5	8.57	Biofilm	5	0.28	Fibroblast
6	562	Amputation	6	8.39	Graft	6	0.26	Mortality
7	504	Diabete	7	8.17	Polyneuropathy	7	0.26	Up regulation
8	426	Disease	8	7.95	Validation	8	0.25	Randomized trail
9	420	Infection	9	7.90	Antibiotics	9	0.24	Clinical trail
10	407	Wound healing	10	7.09	Lower limb amputation	10	0.24	Efficacy
11	404	Mellitus	11	7.08	Mesenchymal stem cell	11	0.24	Inflammation
12	392	Ulceration	12	6.82	Differentiation	12	0.24	Debridement
13	391	Risk factor	13	6.79	Keratinocyte	13	0.23	Surgery
14	324	Diabetes mellitus	14	6.78	Total contact cast	14	0.23	Membrane
15	312	Neuropathy	15	6.74	Vascular disease	15	0.22	People
16	300	Risk	16	6.52	Impact	16	0.21	Skin
17	289	Prevalence	17	6.47	Diabetic foot syndrome	17	0.21	Peripheral neuropathy
18	288	Care	18	6.47	Therapeutic footwear	18	0.21	Experience
19	287	Foot	19	6.41	System	19	0.20	Revascularization
20	255	Randomized controlled tria	20	6.37	Colony stimulating factor	20	0.19	Venous leg ulcer

was 1 of the 2 developing countries in the list and published more articles on DFU than the other developing country, which indicated its significant progress in life sciences in that 10-year period. The United States (n = 1495) published the highest number of literature on DFU, reflecting its dominant position in this research field.

Keywords that concentrate on the expression of current research issue or concepts can describe the research hotspots rationally, whereas burst words stand for research frontiers (6). According to the top 10 keywords of DFU, we inferred the top 3 research hotspots and listed them accordingly as follows.

Table 6
The information of the largest 15 co-occurrence clusters of keywords

Cluster ID	Size	Silhouette	Mean (year)	Label (LLR)
0	28	0.814	2008	Resistant *Staphylococcus aureus*
1	28	0.832	2008	Ulcer
2	24	0.92	2009	Expression
3	23	0.837	2012	Film
4	22	0.886	2008	Revascularization
5	22	0.856	2009	Peripheral neuropathy
6	19	0.901	2010	Management
7	18	0.942	2008	Foot ulceration
8	16	0.902	2009	Amputation
9	15	0.969	2010	Endothelial cell
10	15	0.899	2007	Diabetic foot ulcer
11	14	0.875	2011	Randomized controlled trail
12	10	0.873	2013	Multicenter
13	9	0.989	2007	Infection
14	9	0.911	2012	Plantar ulcer
15	5	0.976	2007	Angipars

Abbreviation: ID, identifier.

Diabetic foot management. Limb-or life-threatening complications in patients with diabetes, such as DFUs, can be prevented with an integrated, multidisciplinary method. If ulceration occurs, removal of pressure from the site of the ulcer and management of the wound, such as routine examination of feet, education in foot care, and close follow-up will allow healing in most cases (17). DFU complications, such as amputation or foot infection, are common, costly, and difficult to treat. Individuals with DFUs require multiple medical and surgical management interventions to prevent complications. A team including multiple medical, nursing, and especially surgical specialties are needed (18).

Lower extremity amputation. Lower extremity amputation associated with increased health care costs and an increased risk of death is a terrible surgical complication of diabetes (19). It was reported that every 20 seconds, a lower limb is lost due to diabetes, and diabetic foot infection (DFI) accounts for this high incidence of amputation (12). In the United States, >50% of patients with diabetes suffer lower extremity amputation, and 85% of those requiring lower extremity amputations have intractable DFU (20).

Diabetic foot infection. Foot infection is 1 of the most common problems in diabetic patients. Additionally, it is a risk factor for limb amputation. DFI, which includes paronychia, cellulitis, myositis, abscess, necrotizing fasciitis, septic arthritis, tendonitis, and osteomyelitis, is considered clinically as soft tissue or bone infection below the malleoli (21). Patients with diabetes have at least a 10-fold greater risk of foot infection than do subjects without diabetes (22). Thus, the study of DFI drew much attention in this DFU research field.

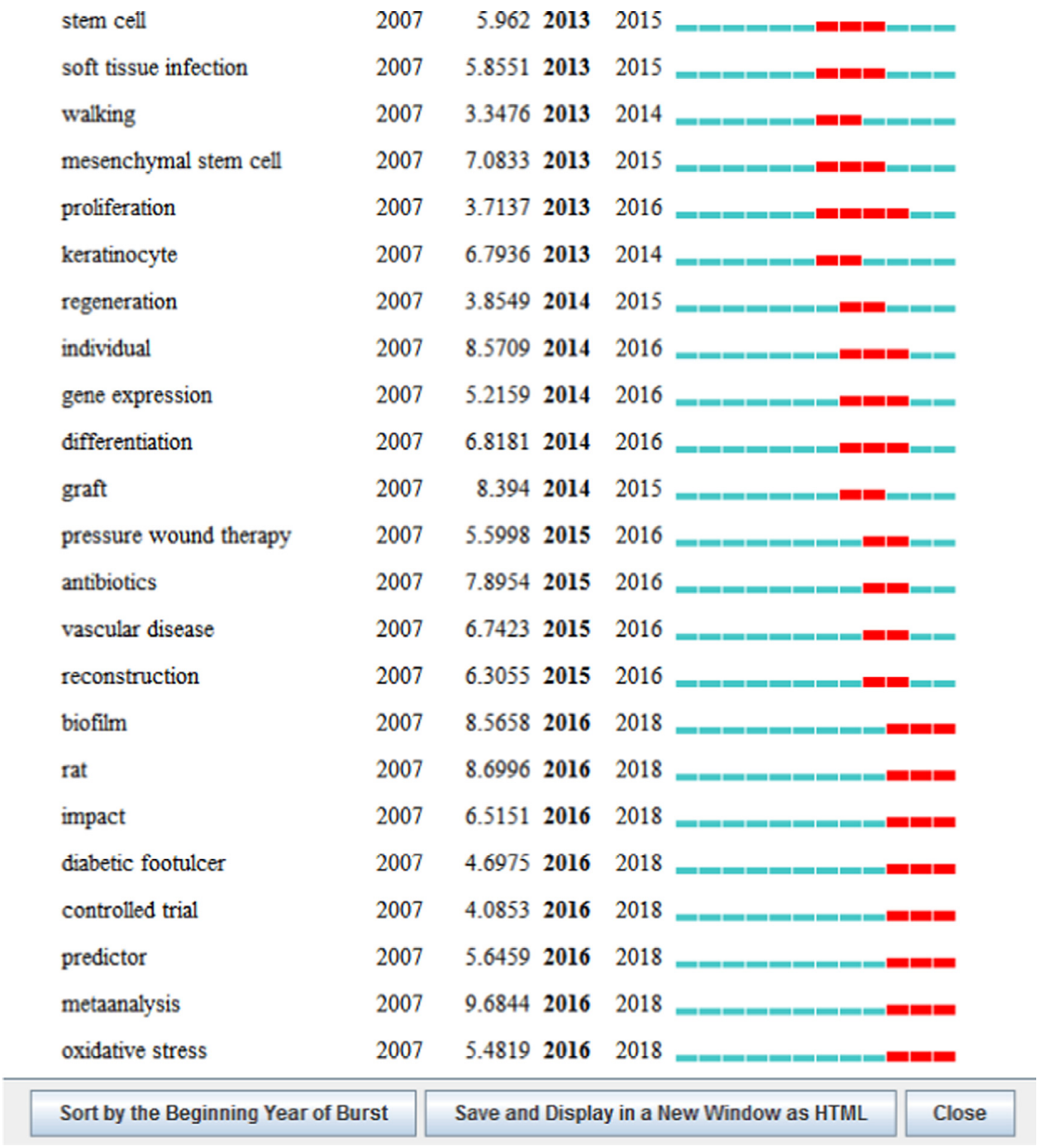

Fig. 4. Some of the keywords with the strongest citation bursts of publications on diabetic foot ulcers from 2007 to 2018.

Burst words represent emerging research directions, which are called the *research frontier*. Furthermore, co-citation clusters of references also represent the research frontiers. Thus, according to Fig. 2*B* and Fig. 4, we inferred the top 3 research frontiers and listed them accordingly as follows.

Diabetic foot infection. As introduced earlier, DFI is 1 of the most common problems in diabetic patients. It is the primary research frontier, as well as a research hotspot, which indicates that DFI is and will be a significant direction in this research area.

Wound management. Everett and Mathioudakis (23) believe that there is still room for improvement in DFU outcomes, although surgical debridement, dressings to facilitate a moist wound environment and exudate control, wound off-loading, vascular assessment, and infection and glycemic control are standard practices in DFU management. They reviewed related literature about the rationale and guidelines for current standard of care practices and reviewed the evidence for the efficacy of adjuvant agents. Then they concluded that nonsurgical debridement agents, dressings and topical agents, oxygen therapy, negative-pressure wound therapy, acellular bioproducts, human growth factors, energy-based therapy, and systemic therapy are beneficial in improving wound healing rates. In addition, some researchers believe that in addition to these traditional methods of wound care, telemedicine can be an important additional tool for patients at home. They also hold the view that the best wound care pathway for patients with DFUs depends on a combination of competence and professional skills in wound management and continuity of care (24).

Prediction studies on DFU and diseases related to DFU. Recently, many researchers focused on the prediction study on this research area, such as a study on genetic predictors associated with diabetic retinopathy in patients with diabetic foot (25), studies on amputation predictors in DFU (26,27), and a study on predictors of severity in DFIs (28).

In our study, there is a limitation. We only analyzed nearly a decade of publications. The results of our study cannot reflect changes in the research area of this field. Thus, more publications, including their references, should be retrieved to detect changes in this research field.

In conclusion, we found that the number of publications has been increasing at a stable slope rate over the past 10 years, which indicates that DFU research has been in a stable, mature stage, and it has drawn increased attention. The United States published the most literature on DFU, followed by the United Kingdom, the People's Republic of China, Germany, Italy, the Netherlands, India, France, Australia, and Canada. Surgery accounted for the largest proportion of the publications we retrieved from the WoSCC, followed by dermatology, endocrinology metabolism, orthopedics, research experimental medicine, general internal medicine, cell biology, engineering, cardiovascular system cardiology, and pharmacology pharmacy. Diabetic foot management, lower extremity amputation, and DFI are the top 3 hotspots in this field. DFI, wound management, and prediction studies on DFU and diseases related to DFU are the top 3 research frontiers in this field. The results of our study provide unique information with respect to the high volume and variety of published data within the field of DFU, and it will be helpful for researchers who focus on diabetes or DFUs to acquire useful information about DFUs, especially hotspots and frontiers of this research field.

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