



POEMS syndrome in the 21st century: A bibliometric analysis

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ARTICLE INFO

Keywords:

POEMS syndrome
Bibliometric analysis
Plasma cell neoplasm
VEGF
Diagnosis

ABSTRACT

Background: POEMS syndrome is a rare and complex plasma cell disorder characterized by polyneuropathy, organomegaly, endocrinopathy, high M protein levels, and skin changes. Understanding of POEMS syndrome has advanced rapidly since the 21st century. This study aims to summarize and evaluate the research status of POEMS syndrome in the past 23 years through a bibliometric and visualization analysis, and identify research focuses and emerging hotspots for the future.

Methods: POEMS syndrome-related articles published between January 1, 2000, and March 8, 2023, were systematically retrieved from the Web of Science Core Collection. Data processing and visualization analysis were carried out using a combination of R software, HistCite, VOSviewer, and CiteSpace.

Results: Since entering the 21st century, 3677 authors from 1125 institutions in 68 countries/regions have published 830 original and review articles on POEMS syndrome in 408 journals so far, among which the USA, Japan, and China published the most articles, and Mayo Clinic, Udice French Research Universities, and Peking Union Medical College listed the top three most prolific institutions. However, collaborative research across countries and groups in the study of POEMS syndrome remain significantly limited. Angela Dispenzieri ranked first in POEMS syndrome research from every aspect of authors, producing the most papers and contributing the most-cited article, followed by Satoshi Kuwabara and Sonoko Misawa. *Internal medicine* was the most productive journal on POEMS syndrome. "endothelial growth factor" was the keyword with the highest occurrence except for "POEMS syndrome", and "bevacizumab", "lenalidomide", "dexamethasone", and "management" were recognized as emerging topics.

Conclusion: This study utilized bibliometric and visualization analysis to systematically summarize the research of POEMS syndrome in the first two decades of the 21st century, offering a data-based and objective perspective on the field of POEMS syndrome and guiding researchers in the identification of novel research directions.

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<https://doi.org/10.1016/j.heliyon.2023.e20612>

Received 3 July 2023; Received in revised form 26 September 2023; Accepted 2 October 2023

Available online 4 October 2023

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1. Introduction

POEMS syndrome is an infrequent yet harmful paraneoplastic syndrome that arises as a result of an underlying clonal plasma cell neoplasm. Since first reported in 1938 [1], described in 1956 [2] and named in 1980 [3], POEMS syndrome has gradually gained recognition over the past forty years. estimated incidence of POEMS syndrome is around 0.3 cases per 100,000 individuals, and as a group of clinical disorders attributable to plasma cell malignancies, it has a preference for elderly and male individuals, which is consistent with multiple myeloma (MM) [4]. POEMS syndrome affects multiple organs and symptoms are diverse. In addition to the polyneuropathy, organomegaly, endocrinopathy, monoclonal plasma cell disorder, and skin changes that give rise to the acronym POEMS, other significant manifestations include papilledema, excessive extravascular fluid retention, sclerotic bone abnormalities, elevated levels of vascular endothelial growth factor (VEGF), a propensity for thrombosis, and irregular pulmonary function assessments. Contrary to MM, POEMS syndrome is characterized by a number of key features, including polyneuropathy, endocrine dysfunction, and volume overload that are more frequent; a lack of association with bone pain, severe infiltration of plasma cells into the bone marrow, or renal failure which are typical symptoms of MM; high levels of VEGF; sclerotic bone lesions in the majority of cases; generally high overall survival rate; and a predominance of lambda light chain [5]. Although the pathogenesis of POEMS syndrome remains elusive, considerable progress has been achieved. The interplay of several cytokines elicited by clonal and polyclonal plasma cells involves angiogenesis and microvascular permeability and is believed to be significant in the context of POEMS syndrome development. To date, VEGF is the cytokine that has been found to be most relevant to disease activity [6]. However, the ambiguous efficacy of anti-VEGF therapy implied that it may not be the primary underlying factor but rather only a downstream mediator in the initiation and progression of POEMS syndrome [7–11].

The diagnosis of POEMS syndrome relies on a blend of clinical and laboratory features. Three major criteria are available [12], of which polyneuropathy and monoclonal plasma cell disorder must be included, as well as at least one minor criterion. POEMS syndrome is usually underdiagnosed because of its rarity and misdiagnosed due to symptomatic similarity. It's critical to distinguish POEMS syndrome from monoclonal gammopathy of undetermined significance (MGUS), chronic inflammatory demyelinating polyneuropathy, MM, smoldering MM (SMM), and solitary plasmacytoma, as the treatment, supportive care, and potential treatment-related toxicities of POEMS syndrome are markedly different from these diseases [13]. Currently, there is neither a cure nor a standard treatment for POEMS syndrome. Treatments help manage symptoms and therapies depend on symptoms. Radiation therapy is the primary approach for POEMS syndrome patients with dominant plasmacytoma [14]. Patients with widespread sclerotic lesions or extensive bone marrow involvement, as well as those who exhibit disease progression within 3–6 months following radiation therapy, should be considered for systemic therapy. Alkylating agents remain the mainstay of treatment [15], administered in the form of low-dose in conventional therapy or high-dose paired with autologous stem cell transplantation (ASCT). Corticosteroids could provide temporary relief, and lenalidomide [16] has demonstrated efficacy despite tolerable side effects, and thalidomide [17] has also proven promising activity as well as proteasome inhibitors [18–20] such as bortezomib and carfilzomib.

Bibliometric analysis is an emerging statistical approach to analyzing large quantities of heterogeneous publications [21]. It employs citation counts as the measure of research quality and collects contribution data from various perspectives in a specific field, including authorship, institution, country, journal, keyword, and citation, to statistically and qualitatively evaluate trends in the field, and to identify research priorities and novel topics in the field [22]. Visualization can present research findings in a more intuitive manner, thereby facilitating a comprehensive understanding of the entire field and key points. Therefore, the integration of bibliometric analysis and visualization would be an efficient research method for POEMS syndrome. Although knowledge of POEMS syndrome has advanced for more than 40 years, there hasn't been any bibliometric analysis report on POEMS syndrome yet thus far.

Research on POEMS syndrome progressed slowly prior to 2000 with fewer than 250 relevant articles and mainly case reports but expanded rapidly with over 1300 publications in the first two decades of the 21st century. Within this research, we conducted a comprehensive analysis of the progress in POEMS syndrome research in the 21st century and provided a systematic depiction and visual representation of the present status and emerging trends in this area. The essence was condensed to help scholars familiarize themselves with this area quickly and the forefront was investigated to guide researchers to track novel hotspots, thereby accelerating the advancement of POEMS syndrome research.

2. Methods

2.1. Search strategy

The Web of Science Core Collection (WoSCC) comprises more than 10,000 top-tier journals and is the most widely used database for medical bibliometric analyses in the world. POEMS syndrome-relevant literature was searched in WoSCC on March 8, 2023. Entry Terms of POEMS syndrome were discovered within the Medical Subject Headings (MeSH) database (<https://www.ncbi.nlm.nih.gov/mesh>) and subsequently incorporated into the search query in the following manner: TI = (“POEMS syndrome” OR “Syndrome, POEMS” OR “Takatsuki's Syndrome” OR “Syndrome, Takatsuki's”OR “Takatsuki Syndrome”OR “Polyneuropathy Organomegaly”OR “Organomegalies, Polyneuropathy”OR “Organomegaly, Polyneuropathy”OR “Polyneuropathy Organomegalies”OR “Crow-Fukase Syndrome”OR “Crow Fukase Syndrome”OR “Syndrome, Crow-Fukase”OR “Polyneuropathy, Organomegaly, Endocrinopathy, M Protein, and Skin Changes Syndrome”). Based on our search criteria, we identified documents that included references to POEMS syndrome or its equivalent terms in their titles, abstracts, or keywords. These documents were limited to those published on or after January 1, 2000, and were constrained to original articles and review articles. We excluded meeting abstracts, case reports, editorial

materials, and other document types from the search results. Additionally, we did not impose any language restrictions during the search process.

2.2. Data collection

Information on the literature was downloaded from the WoSCC after identified through search strategy above, which includes author, title, source, citation, accession number, document type, abstract, address, and cited references. The documents were downloaded in both txt and BibTeX formats to facilitate further analysis. In addition, the H-index of the top 10 most prolific authors was gathered from the Web of Science database on March 8, 2023. The 2021 Journal Citation Report (JCR) category quartile and 2021 impact factor (IF) of the top 10 core journals on POEMS syndrome were obtained from Web of Science as well.

2.3. Statistical analyses and visualization

Bibliometric data were analyzed and visualized through CiteSpace (version 6.2.R1), HistCite (version 12.03.17), VOSviewer (version 1.6.19), and bibliometrix package (version 4.1.2) based on R language platform. HistCite was employed not only to determine the count of publications and citations associated with prolific countries/regions, institutions, and authors, but also to identify the 10 publications that had accrued the most citations in the realm of POEMS syndrome. The annual counts of citations and publications were determined using HistCite and visualized using the ggplot2 package (version 3.3.6) within the R programming language platform. VOSviewer was utilized to identify both the top 10 keywords with the greatest frequency of occurrences and the clustering of the top 85 keywords. CiteSpace was utilized for several purposes in the analysis of POEMS syndrome research. It was employed to create a dual-map overlay of journals about the subject and to identify the top 25 keywords with the largest emerging influence. Additionally, CiteSpace was employed to assess the collaborative involvement among countries, institutions, and authors. The specific configuration settings for CiteSpace included a scale factor of $k = 25$, measuring link strength through cosine similarity, determining link scope within slices, and applying pruning with pathfinder and sliced network algorithms. Furthermore, the bibliometrix package was applied to visualize the collaborations and distribution of publications among countries/regions, as well as to display the yearly publications of the top 10 most prolific authors. It was also utilized for visualizing the clustering of collaborative efforts among authors, institutions, and countries. Additionally, the package was used to calculate the ratios of original articles to review articles for each year.

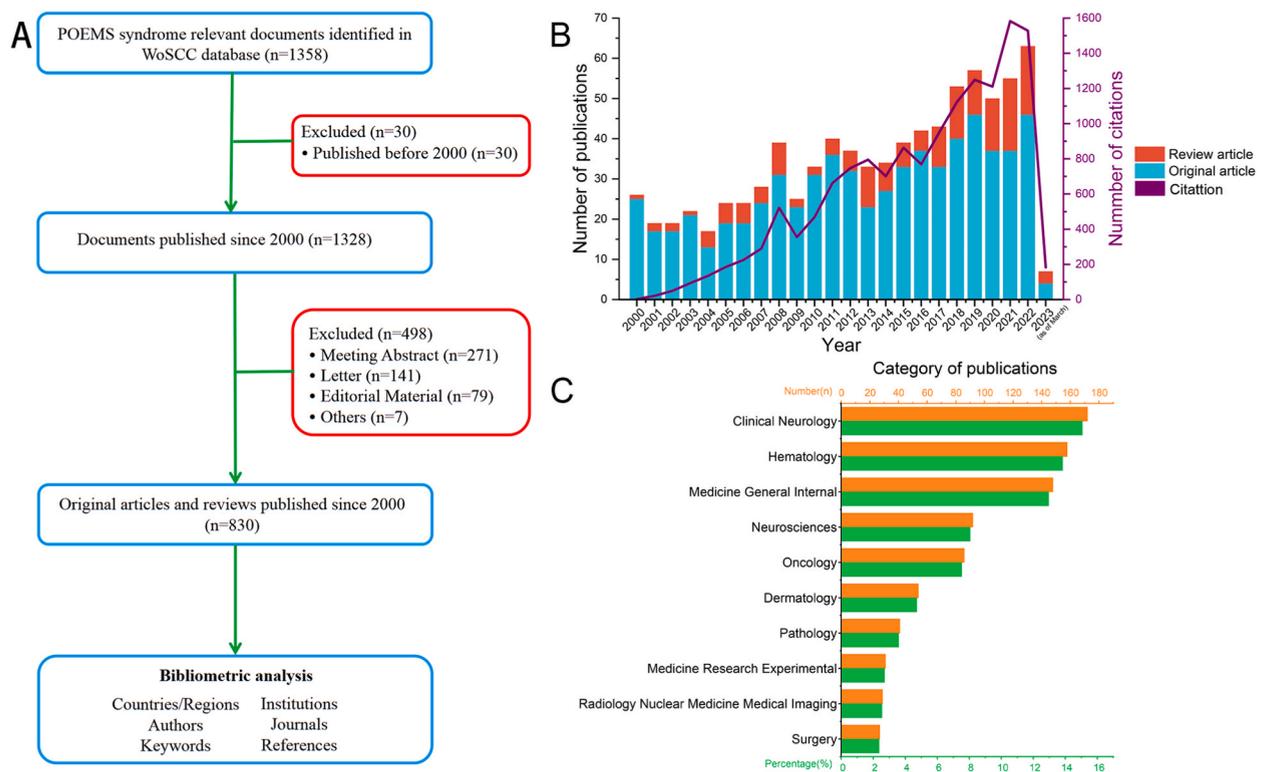


Fig. 1. Search strategy and summary of publications. (A) The inclusion and exclusion of publications, (B) annual number of publications and citations, and (C) categories of publications on POEMS syndrome.

3. Results

3.1. Overview

As of March 8, 2023, WoSCC indicates that there have been a total of 830 publications about POEMS syndrome across the globe since the start of the 21st century, comprising 671 original papers and 159 review articles. In Fig. 1A, the graphic illustrates the process of including and excluding publications. The majority of identified literature was published in English (n = 758, 91.3%), followed by French (n = 33, 4.0%), Spanish (n = 16, 2.0%), German (n = 10, 1.2%), and 5 other languages. Fig. 1B shows the annual number of publications related to POEMS syndrome, which has overall exhibited an increasing trend, particularly for review articles, the proportion of which has increased from 3.8% in 2000 to 27.0% in 2022. Supplementary Table S1 presents the yearly distribution of original articles and review articles, showing the proportion of each category. POEMS syndrome involves multiple organ systems throughout the body, and its clinical manifestations are diverse. Articles related to POEMS syndrome have been published in various

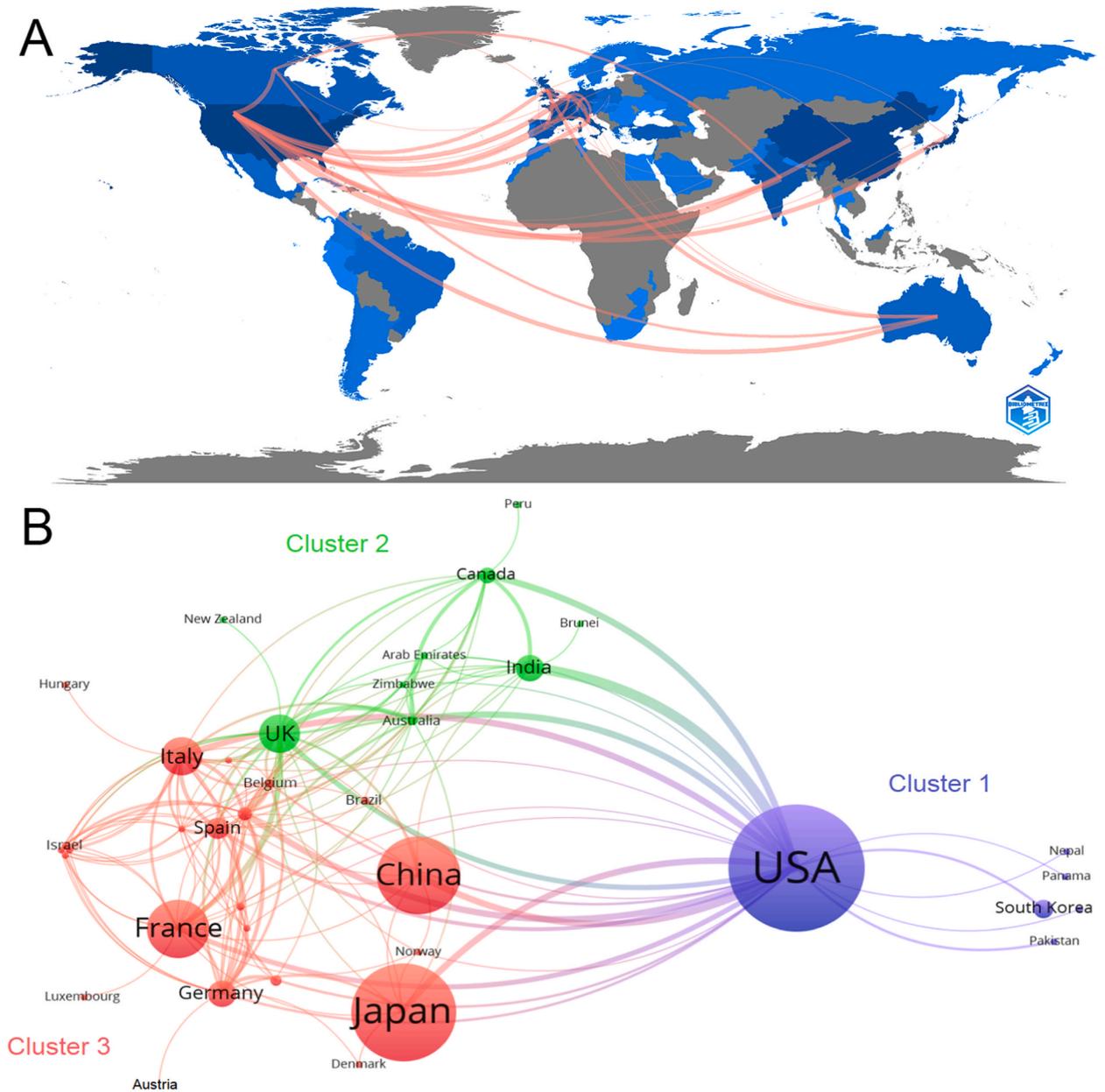


Fig. 2. Leading Countries or Regions in terms of publications on POEMS syndrome. (A) Distribution of collaborations and publications among countries/regions and (B) clustering of partnership among countries/regions on POEMS syndrome research.

categories of medicine. Fig. 1C lists the top ten categories of publications on POEMS syndrome. As POEMS syndrome is a plasma cell disorder characterized by neurological disease and skin changes, research on POEMS syndrome has focused on the fields of neurology, hematology, oncology, and dermatology, categories of which primarily are clinical neurology (n = 172, 15.1%), hematology (n = 158, 13.8%), internal medicine (n = 148, 13.0%), neuroscience (n = 92, 8.1%), and oncology (n = 86, 7.5%). To date, this collection of articles has garnered a total of 14,680 citations, with the number of citations steadily rising each year. On average, each article in the collection has received 17.7 citations, as depicted in Fig. 1B.

3.2. Leading countries/regions

Between January 1, 2000, and March 8, 2023, Articles on POEMS syndrome were published by 68 countries/regions spanning across 6 continents, with a significant concentration in North America, East Asia, and Western Europe, as illustrated in Fig. 2A. The 10 leading countries/regions in terms of publication are detailed in Table 1. The USA is the country with the highest output in POEMS syndrome research, accounting for over one-fifth (n = 178, 21.4%) of POEMS syndrome relevant publications, followed by Japan (n = 142, 17.1%), China (n = 117, 14.1%), France (n = 73, 8.8%), and Italy (n = 43, 5.2%). The USA is also the nation with the highest total number of article citations (n = 5697) and the highest average number of citations per article (n = 32). Based on cooperation between countries, three collaborative clusters were identified (Fig. 2B). The USA is not only the most important node in the global network of country cooperation, collaborating with most of the countries that have published on POEMS syndrome, with up to 13 multi-country publications, but also the most collaborative country in Cluster 1. Cluster 2 mainly involves close cooperation among Commonwealth of Nations countries, primarily led by the UK. Cluster 3 is mainly composed of East Asian countries excluding South Korea and Western European countries excluding the UK. Collaboration centrality assesses the location of a country/institution, or author within the network of research collaboration, and higher levels of collaboration centrality reflect more research connections with partners [23]. In this study, the USA is the dominant collaborative center, followed by France, Italy, and the UK.

3.3. Productive institutions and authors

A total of 3677 authors affiliated with 1125 institutions have published articles on POEMS syndrome. Table 2 highlights the top 10 most productive institutions, which are distributed across the USA, China, Japan, France, and the UK. The Mayo Clinic (n = 74, 8.9%) emerged as the leading institution, followed by Udice French Research Universities (n = 48, 5.8%), Chinese Academy of Medical Sciences & Peking Union Medical College (n = 43, 5.2%), Chiba University (n = 42, 5.1%), and Peking Union Medical College Hospital (n = 41, 4.9%). Fig. 3A illustrates the identification of three clusters of collaborations among institutions. Cluster 1 shows close collaborations among West European and North American institutions, with collaborations initially spearhead by Udice French Research Universities and Sorbonne University in the first decade of the 21st century, and more recently by the Mayo Clinic and University College London. Collaborations in Cluster 2 was limited to Peking Union Medical College and its affiliated institutions in China. Chiba University was centrally located in the network of collaborations of Cluster 3, which was predominantly composed of Japanese institutions. The Mayo Clinic exhibited the highest level of collaboration centrality, with Udice French Research Universities and Chiba University following behind.

The top 10 authors with the highest productivity were dominated by three institutions, with four from the Mayo Clinic in the USA, three from Peking Union Medical College in China, and three from Chiba University in Japan (Table 3). The top three most productive authors were Dispenzieri Angela from the Mayo Clinic (n = 47, 5.7%), Kuwabara Satoshi from Chiba University (n = 36, 4.3%), and Misawa Sonoko from Chiba University (n = 35, 4.2%). Dispenzieri Angela from the Mayo Clinic also had the highest H-index (n = 30), total citations (n = 3240), average citations (n = 68.9), and centrality (n = 0.02) among authors. Authors were grouped into three clusters based on their collaborations on POEMS syndrome research. Fig. 3B displays the cooperative relationships among authors who have published more than five articles, revealing that close collaboration among authors is almost limited within the same institution, while collaborations across countries and institutions are relatively infrequent. This indicates a lack of sufficient collaboration between research groups conducting POEMS syndrome research. The centrality scores for all authors fell below the threshold of 0.10, demonstrating insufficient collaboration among researchers in POEMS syndrome field as well. Fig. 3C visualizes the relationships among active countries, institutions, and authors. Fig. 3D depicts the yearly output of the top 10 most prolific authors.

Table 1

The top 10 most productive countries in terms of POEMS syndrome research. SCP: single country publications; MCP: multi-country publications.

Rank	Country	Publications n (%)	SCP	MCP	Cluster	Total citations	Average citations	Collaborative centrality
1	USA	178 (21.4)	165	13	1	5697	32.0	0.18
2	Japan	142 (17.1)	139	3	3	2209	15.6	0.01
3	China	117 (14.1)	113	4	3	1141	9.8	0.07
4	France	73 (8.8)	72	1	3	1417	19.4	0.06
5	Italy	43 (5.2)	40	3	3	1068	24.8	0.06
6	UK	39 (4.7)	34	5	2	428	11.0	0.06
7	India	26 (3.1)	20	6	2	131	5.0	0.01
8	Germany	25 (3.0)	21	4	3	268	10.7	0.07
9	South Korea	19 (2.3)	18	1	1	143	7.5	0.02
10	Spain	18 (2.2)	17	1	3	220	12.2	0.02

Table 2
The top 10 most productive institutions on POEMS syndrome research.

Rank	Institution	Country	Publications n (%)	Total citations	Average citations	Collaborative centrality
1	Mayo Clinic	USA	74 (8.9)	3796	51.3	0.11
2	Udice French Research Universities	France	48 (5.8)	1313	27.4	0.07
3	Chinese Academy of Medical Sciences & Peking Union Medical College	China	43 (5.2)	667	15.5	0
4	Chiba University	Japan	42 (5.1)	986	23.5	0.05
5	Peking Union Medical College Hospital	China	41 (4.9)	664	16.2	0
6	Peking Union Medical College	China	38 (4.6)	574	15.1	0
7	Assistance Publique Hopitaux Paris (APHP)	France	33 (4.0)	1000	30.3	0.1
8	University of London	UK	24 (2.9)	457	19.04	0.04
9	University College London	UK	21 (2.5)	266	12.7	0
10	Sorbonne University	France	17 (2.0)	298	17.5	0.02

3.4. Core journals and references

408 journals in total have published research on POEMS syndrome since 2000. Table 4 provides a summary of the ten journals that have the highest number of publications on POEMS syndrome. *Internal Medicine* has the greatest output ($n = 29$, 3.5%), followed by the *American Journal of Hematology* ($n = 23$, 2.8%), *Muscle & Nerve* ($n = 22$, 2.7%), *Revue Neurologique* ($n = 15$, 1.8%), and *Blood* ($n = 14$, 1.7%). Publications from *Blood* have the highest total citations ($n = 1800$) and average citations per article ($n = 128.6$) on PEMS syndrome. Due to the rarity of POEMS syndrome, even core journals only publish a very small number of articles on it each year—up to 5 articles at their height and occasionally 0 (Fig. 4A), suggesting that the pace of research in this area is somewhat slow. The dual-map overlay in Fig. 4B reveals numerous inter-domain connections among journals. Journals on the left side represent citing journals, while those on the right side are cited journals, with lines indicating citation relationships between them. Two primary citation paths were identified: Publications from Health/Nursing/Medicine and Molecular/Biology/Genetics journals were primarily cited by publications in Medicine/Medical/Clinical journals.

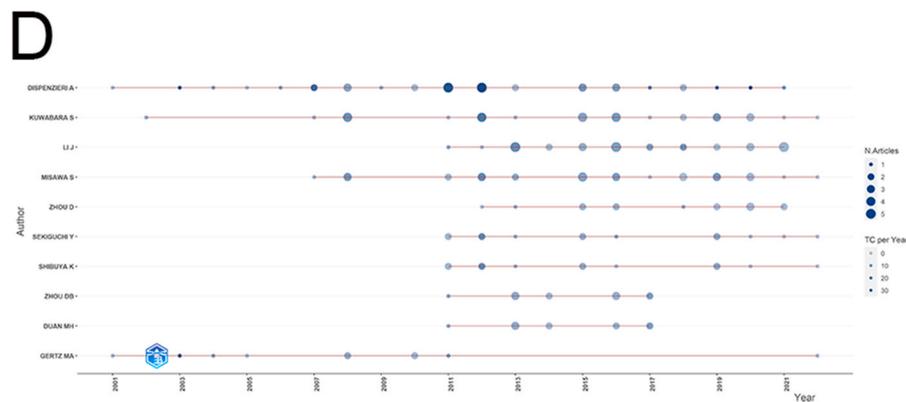
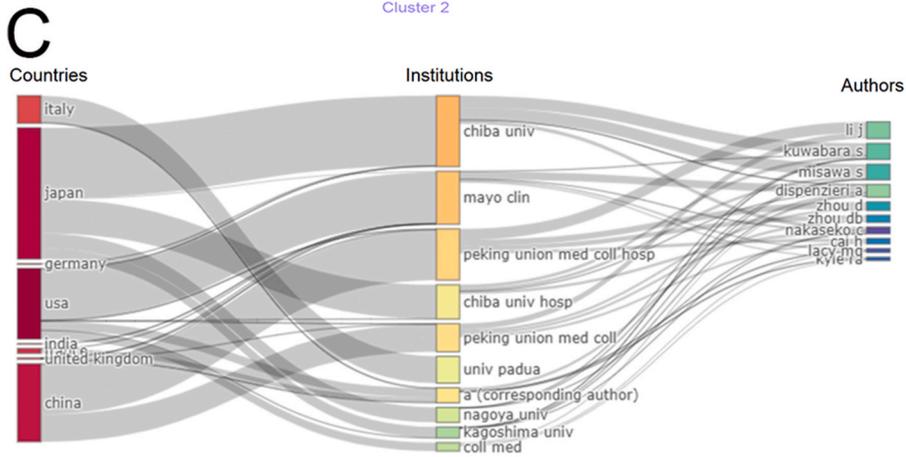
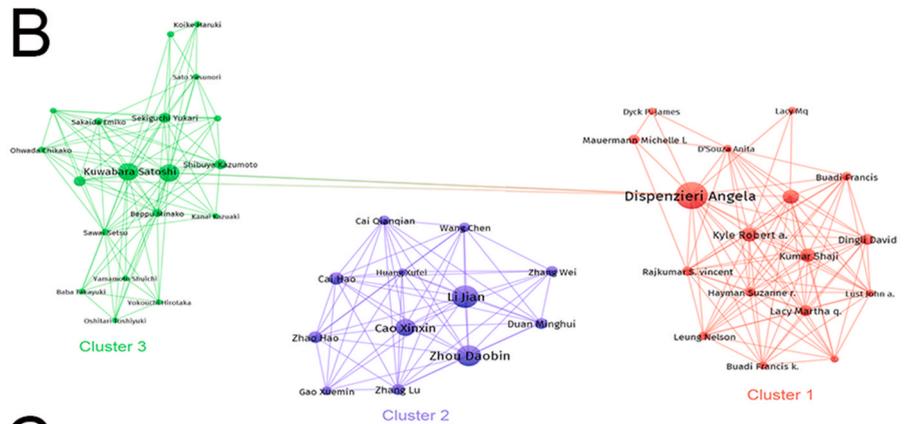
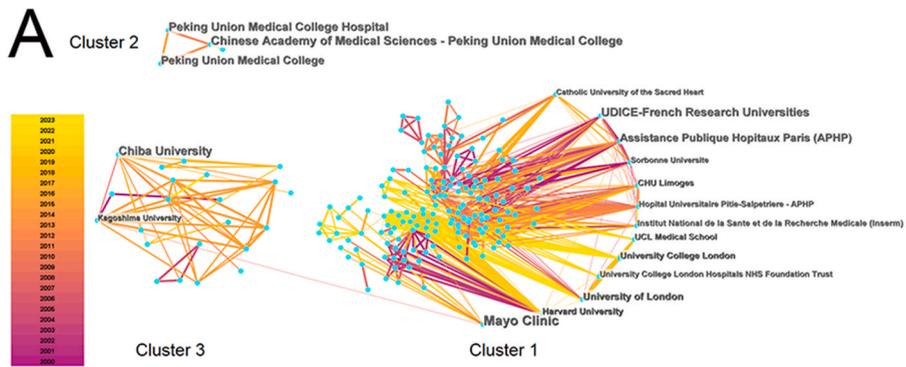
Table 5 showcases the top 10 most cited references, with half of them attributed to contributions by Angela Dispenzieri from the Mayo Clinic. In 2003, Dispenzieri et al. [24] established the minimal criteria for diagnosing POEMS syndrome and outlined the disease's natural progression, and reported long-term outcome data, the citation of which has reached 527 times so far, making it the most cited reference in the area of POEMS syndrome since the 21st century. In 2005, Scarlato et al. [25] proposed that the polyneuropathy observed in POEMS syndrome may be attributed to the direct or indirect impacts of angiogenic factors. Additionally, alterations in serum levels of VEGF and erythropoietin (EPO) have diagnostic, prognostic, and pathogenic significance. In 2012, Dispenzieri [26] provided a summary of the connection between POEMS syndrome and Castleman disease. In essence, the top 10 core references primarily emphasize aspects related to the diagnosis, pathogenesis, and treatment of POEMS syndrome.

An analysis was conducted on the cited references to detect bursts and track the evolution of research hotspots on POEMS syndrome. Fig. 4C shows the top 25 most frequently cited references from January 1, 2000, to March 8, 2023. "Year" denotes the year when a specific keyword initially emerged in the field of POEMS syndrome. "Begin" and "End" represent the commencement and conclusion years that serve as boundaries for the presence of these keywords. Meanwhile, "Strength" quantifies the level of emergence or significance associated with each keyword. The red line indicates an abrupt increase in the number of citations for the reference during this period, while the blue line indicates relative unpopularity. Three articles with a strength exceeding 30 were all contributed by Dispenzieri Angela. Among hot references cited in recent years, "POEMS syndrome: 2019 update on diagnosis, risk-stratification, and management" by Dispenzieri et al. [27] had the greatest outbreak.

3.5. Analysis of keywords

The titles and abstracts of 830 publications on POEMS syndrome throughout search were used to generate a graph containing 85 keywords (totaling 1400), which appeared at least 10 times and were divided into 6 clusters (Fig. 5A). Table 6 lists the top 10 keywords by frequency. Clusters led by "POEMS syndrome" and "endothelial growth factor" appeared most frequently, followed by "polyneuropathy" and "stem-cell transplantation", and then "multiple-myeloma" and "diagnosis" [28–32]. Fig. 5B shows an overlay visualization of the keywords, with earlier keywords in blue and more recent keywords in yellow. Early hot topics included keywords such as "interleukin-6", "kaposi-sarcoma", and "igm monoclonal gammopathy". In contrast, keywords such as "bevacizumab", "lenalidomide", "dexamethasone", and "management" have been at the forefront in recent years. The construction of the keyword density chart is based on their frequency (Fig. 5C).

Keyword burst detection is regarded as an indicator of evolving research frontiers or emerging topics within a particular field as they develop over time. Fig. 5D displays the top 25 keywords with the most pronounced citation bursts, signifying areas of active and rapidly advancing research in the context of POEMS syndrome. "Diagnosis" was the focus of research from 2018 to 2020, with a strength of 9.96 being the strongest occurrence. "Safety", "blood", "castleman disease", and "case report" are recent research frontiers. Fig. 5E shows a topic trend map generated when analyzing the keywords. It can be seen from the figure that the main hotspots after 2020 are "blood", "free light-chain", "multi-center", "safety" and "risk-factors". The two-dimensional matrix representing the keyword



(caption on next page)

Fig. 3. Productive institutions and prolific authors. (A) Clustering of cooperation among institutions, (B) clustering of collaboration among authors, (C) association between active countries, institutions, and authors, and (D) the yearly publications of the top 10 most prolific authors.

topic map is instrumental in identifying present focal points and forecasting research directions in recent times, as depicted in Fig. 5F. Quadrant 4, situated in the lower right section, highlights fundamental themes that possess significance but have yet to be fully explored within this field. It is worth noting that a cluster (keyword "diagnosis") located in Quadrant 4 corresponds to the analysis result chart that shows keyword bursts, indicating potential research topics.

4. Discussion

Here, we firstly performed a bibliometric analysis and visualization of the publications on POEMS syndrome since the beginning of the 21st century. From 2000 to 2023, the count of publications and citations exhibited a rising pattern. We assessed and provided an overview of the countries/regions with high productivity, active institutions and authors, essential journals, and key references in the field of POEMS syndrome, as well as keywords, and some milestone articles were identified since 2000 (Fig. 6). As far as we are aware, this marks the inaugural bibliometric analysis of POEMS syndrome.

The United States, followed by Japan and China, are the absolute leaders in the field of POEMS syndrome, jointly contributing over 50% of POEMS syndrome research and dominating the top ten authors with greatest article productions. However, the scattered collaboration network reveals a relative lack of cooperation across countries and institutions. Mayo Clinic stands out as the most prolific institution, and its researcher Dispenzieri Angela is the most prolific author with the highest academic impact on POEMS syndrome. In addition, half of the ten most cited references were written by Dispenzieri Angela. Every one to two years, Dispenzieri Angela summarizes and updates research and clinical information on POEMS syndrome from the perspectives of diagnosis, risk stratification, and management [12,27,33–37]. Hematology and neurology are the two main categories, according to an analysis of high-yield journal features, indicating the communication platforms and focus sources of POEMS syndrome research. The journal's dual-map overlay suggests POEMS syndrome has developed from a single discipline to an interdisciplinary field, drawing more and more attention from researchers.

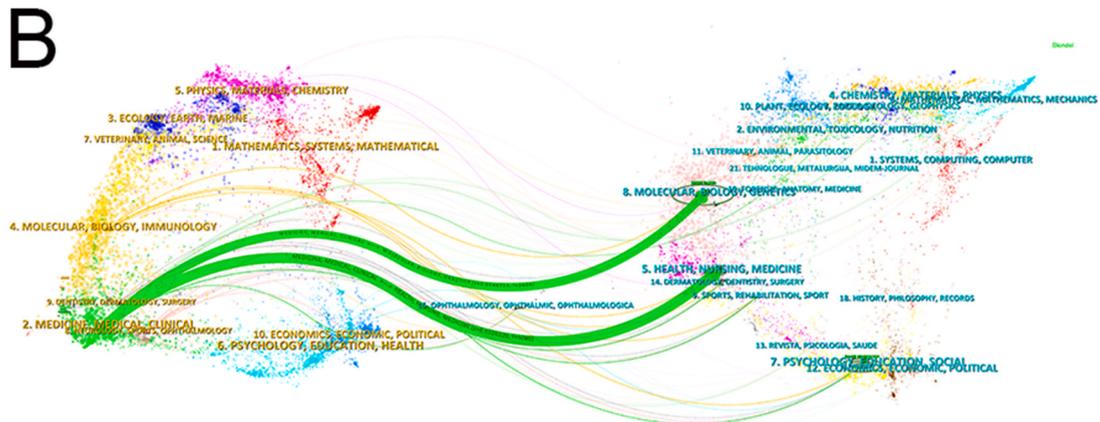
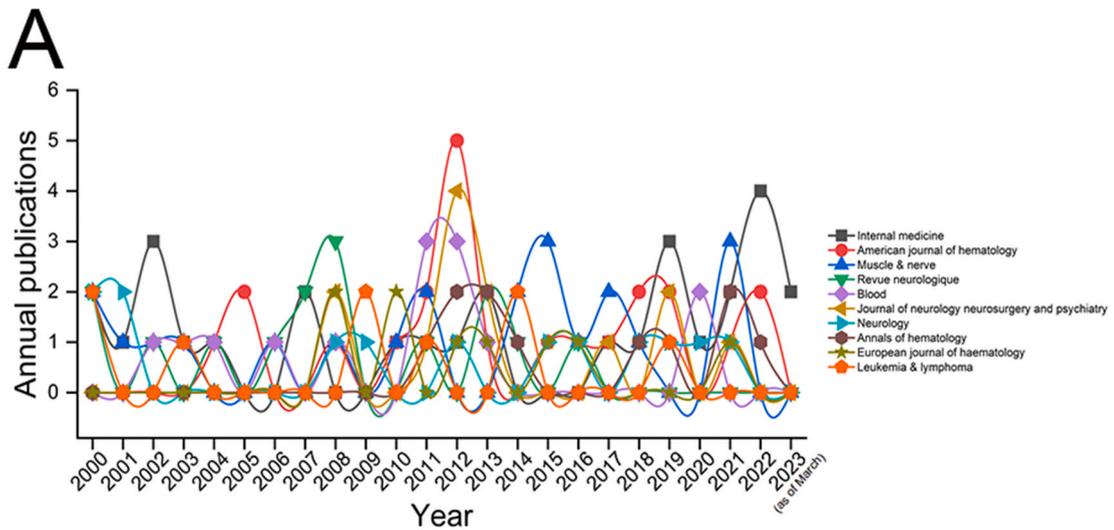
Analysis of keyword burst and co-occurrence distribution reveals that "diagnosis" and "therapy" are significant research hotspots in the field of POEMS syndrome. Diagnosis has long been a challenging issue for POEMS syndrome due to its rarity and the potential for misdiagnosis. Polyneuropathy is the most prominent clinical characteristic and the reason for patients' initial attention and medical consultation, making it easy to misdiagnose as chronic inflammatory demyelinating polyneuropathy (CIDP). More than half of POEMS syndrome patients are at first misdiagnosed as CIDP, which not only leads to delayed therapy and gradual deterioration of clinical presentations, particularly neuropathy, but also causes serious waste of medical resources and increased healthcare expenditure. Recently, Marsh ES et al. [38] performed a significant model-based cost-effectiveness analysis and found that the average cost of each

Table 3
The top 10 most productive authors on POEMS syndrome research.

Rank	Authors	Institution	Country	Publications n (%)	Total citations	Average citations	H-index	Centrality
1	Dispenzieri Angela	Mayo Clinic	USA	47 (5.7)	3240	68.9	30	0.02
2	Kuwabara Satoshi	Chiba University	Japan	36 (4.3)	947	26.3	19	0.01
3	Misawa Sonoko	Chiba University	Japan	35 (4.2)	774	22.1	18	0.01
4	Li Jian	Peking Union Medical College	China	26 (3.1)	582	22.4	14	0
5	Zhou Daobin	Peking Union Medical College	China	23 (2.8)	492	21.4	12	0
6	Cao Xinxin	Peking Union Medical College	China	23 (2.8)	296	12.9	10	0
7	Lacy Martha Q.	Mayo Clinic	USA	19 (2.3)	1294	68.1	14	0
8	Kyle Robert A.	Mayo Clinic	USA	18 (2.2)	1675	93.1	15	0
9	Nakaseko Chiaki	Chiba University	Japan	17 (2.0)	479	28.2	12	0
10	Gertz Morie	Mayo Clinic	USA	15 (1.8)	1253	83.5	13	0

Table 4
The top 10 core journals in terms of POEMS syndrome research. JCR: Journal Citation Report; IF: impactor factor.

Rank	Journal	Publications n (%)	Total citations	Average citations	2021 JCR quartile	2021 IF
1	<i>Internal medicine</i>	29 (3.5)	275	9.5	Q4	1.282
2	<i>American journal of hematology</i>	23 (2.8)	980	42.6	Q1	13.265
3	<i>Muscle & nerve</i>	22 (2.7)	541	24.6	Q2	3.852
4	<i>Revue neurologique</i>	15 (1.8)	50	3.3	Q2	4.313
5	<i>Blood</i>	14 (1.7)	1800	128.6	Q1	25.476
6	<i>Journal of neurology neurosurgery and psychiatry</i>	13 (1.6)	735	56.5	Q1	13.654
7	<i>Neurology</i>	13 (1.6)	410	31.5	Q1	11.8
8	<i>Annals of hematology</i>	11 (1.3)	183	16.6	Q2	4.03
9	<i>European journal of hematology</i>	9 (1.1)	224	24.9	Q3	3.674
10	<i>Leukemia & lymphoma</i>	9 (1.1)	166	18.4	Q3	2.996



C

Top 25 References with the Strongest Citation Bursts

References	Year	Strength	Begin	End	2000 - 2023
Watanabe O, 1998, MUSCLE NERVE, V21, P1390, DOI 10.1002(SICI)1097-4598(199811)21:111390-AID-MUS5<3.3.CO;2-S, DOI	1998	13.08	2000	2003	█
Dispenzieri A, 2003, BLOOD, V101, P2496, DOI 10.1182/blood-2002-07-2299, DOI	2003	39.77	2003	2008	█
Dispenzieri A, 2004, BLOOD, V104, P3400, DOI 10.1182/blood-2004-05-2046, DOI	2004	20.58	2005	2009	█
Scarlato M, 2005, BRAIN, V128, P1911, DOI 10.1093/brain/awh519, DOI	2005	15	2006	2010	█
Kuwabara S, 2006, NEUROLOGY, V66, P105, DOI 10.1212.01.wnl.0000188757.38495.23, DOI	2006	13.09	2006	2011	█
Badros A, 2005, BLOOD, V106, P1135, DOI 10.1182/blood-2005-03-0910, DOI	2005	11.35	2006	2010	█
Dispenzieri A, 2007, BLOOD REV, V21, P285, DOI 10.1016/j.bbrc.2007.07.004, DOI	2007	37.41	2008	2012	█
Dispenzieri A, 2007, BLOOD, V110, P1075, DOI 10.1182/blood-2007-03-082354, DOI	2007	11.44	2008	2012	█
Kuwabara S, 2008, J NEUROL NEUROSUR PS, V79, P1255, DOI 10.1136/jnnp.2008.150177, DOI	2008	12.39	2010	2013	█
Kuwabara S, 2008, NEUROLOGY, V71, P1691, DOI 10.1212.01.wnl.0000323811.42080.a4, DOI	2008	11.39	2010	2013	█
DSouza A, 2011, BLOOD, V118, P4663, DOI 10.1182/blood-2011-06-362392, DOI	2011	15.7	2012	2016	█
Dispenzieri A, 2011, AM J HEMATOL, V86, P592, DOI 10.1002/ajh.22050, DOI	2011	14.99	2012	2015	█
Li J, 2011, BLOOD, V117, P6445, DOI 10.1182/blood-2010-12-328112, DOI	2011	12.94	2012	2016	█
Nasu S, 2012, J NEUROL NEUROSUR PS, V83, P476, DOI 10.1136/jnnp-2011-301706, DOI	2012	11.54	2012	2017	█
Mauermann ML, 2012, J NEUROL NEUROSUR PS, V83, P480, DOI 10.1136/jnnp-2011-301472, DOI	2012	11.16	2012	2017	█
DSouza A, 2012, BLOOD, V120, P56, DOI 10.1182/blood-2012-04-423178, DOI	2012	14.83	2013	2017	█
Royer B, 2013, AM J HEMATOL, V88, P207, DOI 10.1002/ajh.23374, DOI	2013	11.72	2013	2018	█
Li J, 2013, BRIT J HAEMATOL, V161, P303, DOI 10.1111/bjh.12236, DOI	2013	12.14	2014	2018	█
Dispenzieri Angela, 2014, AM J HEMATOL, V89, P214, DOI 10.1002/ajh.23644, DOI	2014	17.51	2015	2019	█
Dispenzieri A, 2015, AM J HEMATOL, V90, P952, DOI 10.1002/ajh.24171, DOI	2015	15.8	2016	2020	█
Misawa S, 2016, LANCET NEUROL, V15, P1129, DOI 10.1016/S1474-4422(16)30157-0, DOI	2016	11.04	2017	2021	█
Dispenzieri A, 2017, AM J HEMATOL, V92, P814, DOI 10.1002/ajh.24802, DOI	2017	19.75	2018	2020	█
Nozza A, 2017, BRIT J HAEMATOL, V179, P748, DOI 10.1111/bjh.14966, DOI	2017	11.66	2019	2023	█
Dispenzieri A, 2019, AM J HEMATOL, V94, P812, DOI 10.1002/ajh.25495, DOI	2019	33.56	2020	2023	█
Zhao H, 2019, LEUKEMIA, V33, P1023, DOI 10.1038/s41375-019-0391-2, DOI	2019	11.02	2020	2023	█

(caption on next page)

Fig. 4. Core journals and references. (A) Annual outputs of the top 10 core academic journals on POEMS syndrome, (B) the dual-map thematic overlay of journals that publish POEMS syndrome studies, and (C) the top 25 most cited references with the largest citation bursts.

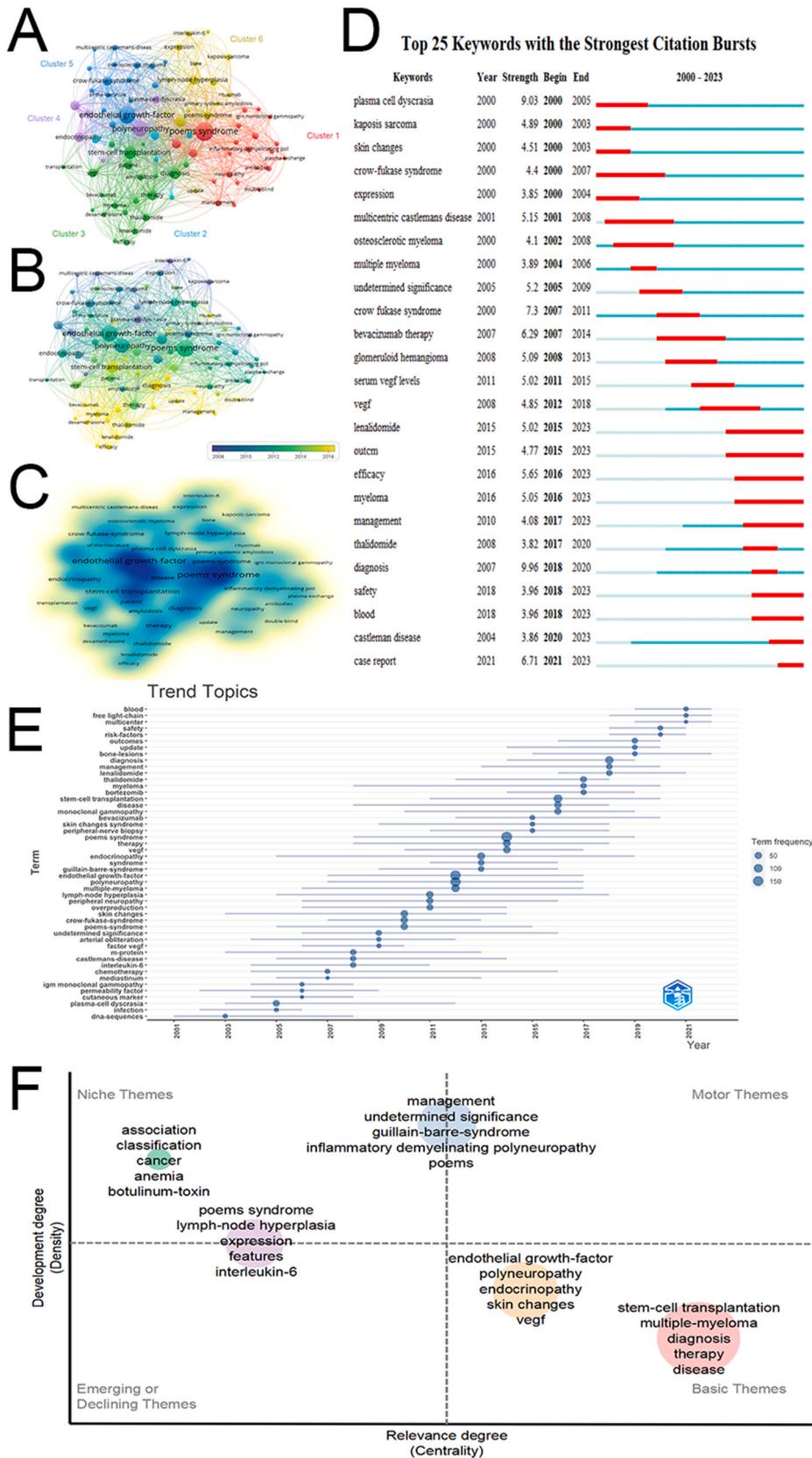
misdiagnosed POEMS patient ranges from £14,701 to £20,214. The implementation of obligatory testing for VEGF to differentiate POEMS syndrome from CIDP could save the National Health Service £107,398 annually and reduce misdiagnosis by 16 cases per year in the UK. In addition to serum VEGF, other new diagnostic markers for POEMS syndrome have been discovered in recent years. Wang C et al. [39] found that compared to healthy volunteers and patients with diseases resembling POEMS syndrome, including CIDP, Castleman disease, MM, and primary light chain amyloidosis (LCA), the serum level of total N-terminal propeptide of type 1 collagen (P1NP) in POEMS syndrome patients is significantly elevated, and P1NP can be used to diagnose POEMS syndrome, with a sensitivity of 80% and specificity of 91.5% when the cut-off value is set at 70 ng/mL.

The therapy for POEMS syndrome continues to evolve. With the development of high-dose chemotherapy with ASCT and the renaissance of myeloma therapies, these therapies have considerably enhanced the prognosis of POEMS syndrome patients in the 21st century, with a 10-year survival rate increasing from 55% before 2003 to 79% after 2003 [40]. There are currently multiple treatment options for POEMS syndrome, including high-dose melphalan and autologous hematopoietic cell transplantation for eligible patients, and lenalidomide and dexamethasone for those who are not eligible for transplantation. The main treatment goal is to achieve complete hematologic and VEGF responses and alleviate symptoms. Thalidomide and bortezomib, which have anti-VEGF and anti-TNF (tumor necrosis factor) effects, are also promising treatment options, as reflected in the hot keywords. In addition, novel treatments for POEMS syndrome are continuously advancing as well, particularly targeted therapies based on anti-CD38 monoclonal antibodies (such as daratumumab) and immunotherapies utilizing chimeric antigen receptor T-cell (CAR-T). Several single-center clinical trials have explored the use of daratumumab as single agent [41,42], or in combination with lenalidomide and dexamethasone [43], or in conjunction with lenalidomide, bortezomib, and dexamethasone [44], for the treatment of POEMS syndrome patients with inadequate responses to conventional therapies, all demonstrating rapid, profound, and sustained responses. These findings suggest promising prospects for daratumumab in the treatment of POEMS syndrome; however, due to the limited number of cases, the exact therapeutic efficacy of daratumumab necessitates further assessment. Recently, a report concerning the application of anti-B cell maturation antigen (BCMA) CAR-T cell therapy in the treatment of POEMS syndrome demonstrated excellent response [45], indicating anti-BCMA CAR-T cell could be a viable therapeutic option for refractory POEMS syndrome. However, due to the rarity of patients and death of randomized clinical trials, therapy recommendations for POEMS syndrome are based on scant trial data, case studies, and anecdotes, as well as drawn from other plasma cell disorders, most notably MM and LCA. Therefore, it is vital to strengthen cooperation between countries and institutions to enhance research on the treatment of POEMS syndrome. Future studies should concentrate on "multi-centers" and "outcomes", consolidate separate centers, standardize follow-up data collecting, and create prospective studies to produce more precise therapies and improve patient outcomes, as suggested by trend topics.

This study has multiple constraints. Firstly, the data was solely gathered from WoSCC, which is a widely used database employed for bibliometric analysis, known for its timely and thorough updates of citation networks. Nevertheless, The software utilized for bibliometric analysis faces challenges when it comes to smoothly integrating data from various origins, and therefore, we refrained from exploring additional databases like Embase and MEDLINE, which may have resulted in overlooking some relevant literature. Secondly, there has been a substantial increase in scientific output in the field of medicine over the last two decades, which may be

Table 5
The top 10 most cited references in terms of POEMS syndrome research.

	First author	Title	Journal	Year of publication	Total citations	Citations per year
1	Dispenzieri Angela	POEMS syndrome: definitions and long-term outcome	<i>Blood</i>	2003	527	25.10
2	Dorfmueller P	Inflammation in pulmonary arterial hypertension	<i>European respiratory journal</i>	2003	443	21.10
3	Giampaolo Merlino	Dangerous small B-cell clones	<i>Blood</i>	2006	297	16.50
4	Dispenzieri Angela	POEMS syndrome	<i>Blood reviews</i>	2007	267	15.71
5	Katzmann Jerry	Screening panels for detection of monoclonal gammopathies	<i>Clinical chemistry</i>	2009	224	14.93
6	Scarlato Marina	Polyneuropathy in POEMS syndrome: role of angiogenic factors in the pathogenesis	<i>Brain</i>	2005	164	8.63
7	Dispenzieri Angela	Peripheral blood stem cell transplantation in 16 patients with POEMS syndrome, and a review of the literature	<i>Blood</i>	2004	146	7.30
8	Dispenzieri Angela	The clinical spectrum of Castleman's disease	<i>American journal of hematology</i>	2012	142	11.83
9	Rajkumar S Vincent	Monoclonal gammopathy of undetermined significance, Waldenström macroglobulinemia, AL amyloidosis, and related plasma cell disorders: diagnosis and treatment	<i>mayo clinic proceedings</i>	2006	132	7.33
10	Dispenzieri Angela	Overview of Castleman disease	<i>Blood</i>	2020	121	30.25



(caption on next page)

Fig. 5. Keywords and research trends. (A) 6 clusters of the top 85 keywords with the most occurrences on POEMS syndrome publications, (B) a time-series keyword map based on the frequency of co-occurrence, (C) a density keyword map for visualizing co-occurrence, (D) the top 25 keywords with the most robust emergent strength, (E) trend topics mapped by keyword occurrences, (F) thematic graphic for keyword occurrences.

used as an explanation for the rise in the number of publications on POEMS syndrome from 2000 to 2023. Additionally, high-impact articles newly published may not have been included in our analysis because of their low citations, as citation-based bibliometric algorithms may not have detected their academic value. Lastly, due to the preferences of the algorithms utilized in the bibliometric analysis, certain emergent themes connected to POEMS syndrome might not have been discovered. Despite these drawbacks, we think that our findings offer a comprehensive overview of POEMS syndrome research, which provides a clearer perspective for current research and guidance for further study on POEMS syndrome.

Table 6
The top 10 most common keywords in terms of POEMS syndrome research.

Rank	Keyword	Cluster	Occurrence
1	poems syndrome	1	175
2	endothelial growth-factor	4	158
3	polyneuropathy	4	147
4	stem-cell transplantation	3	85
5	multiple-myeloma	5	71
6	diagnosis	3	70
7	therapy	3	61
8	endocrinopathy	6	54
9	skin changes	4	51
10	vegf	3	48

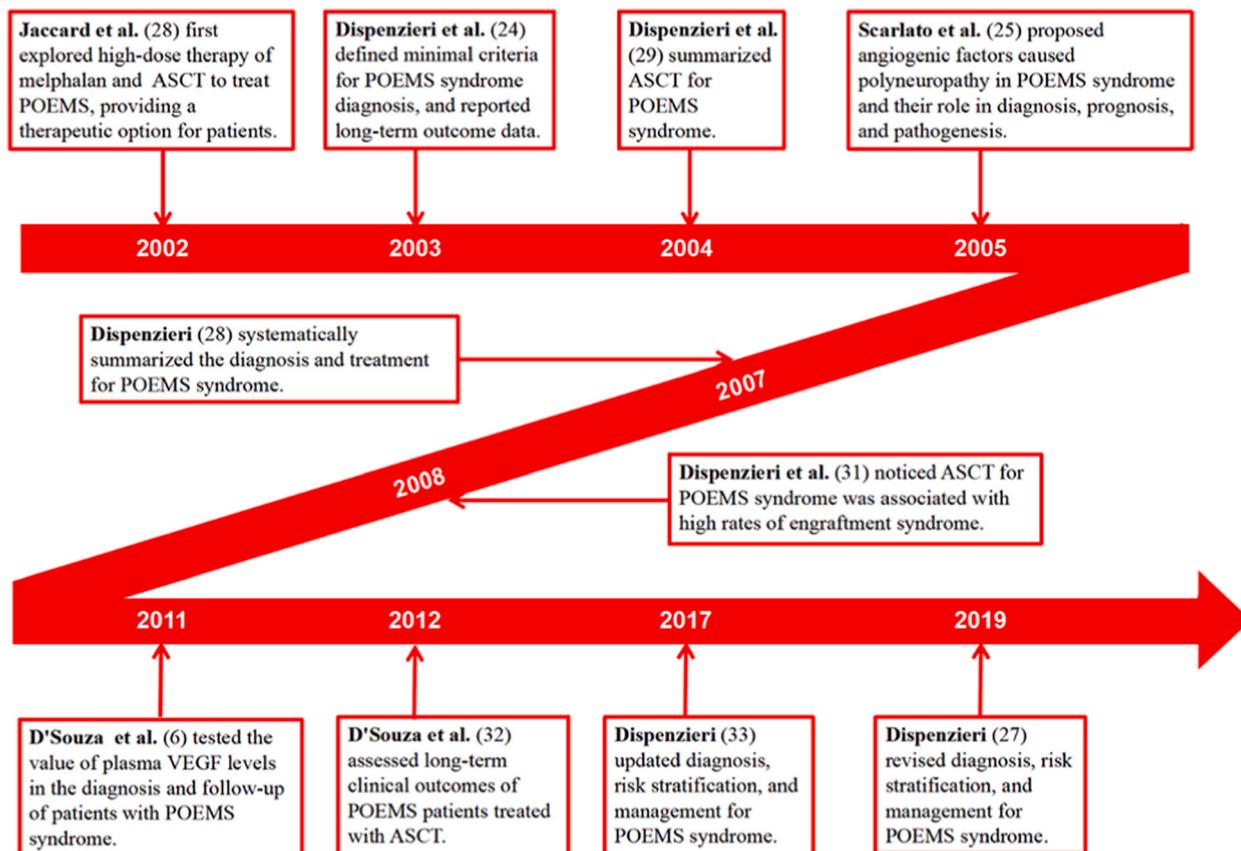


Fig. 6. Timeline of the top 10 landmark publications of POEMS syndrome since 2000.

5. Conclusion

Our research findings indicate that the study of POEMS syndrome has taken off with steady growth of publications and citations in the 21st century. However, there is insufficient collaboration between nations, institutions, and authors, which needs to be strengthened to promote progress in this field. Diagnosis and treatment have been the focus of research in recent years and deserve close attention. In conclusion, our research results will enhance researchers' understanding of the current hot topics and cutting-edge research in POEMS syndrome.

Funding

This project is supported by the National Natural Science Foundations of China (81870166).

Data availability statement

Data will be made available on request.

Ethical approval

Not applicable.

Guarantor

Dr. Yi Chen will act as the guarantor of the article.

CRediT authorship contribution statement

Fangrong Zhang: Formal analysis, Investigation, Methodology, Writing – original draft, Writing – review & editing. **Zhimin Wu:** Formal analysis, Investigation, Methodology, Writing – original draft, Writing – review & editing. **Shanyi Sun:** Conceptualization, Formal analysis, Investigation, Methodology, Writing – original draft, Writing – review & editing. **Yunfeng Fu:** Data curation, Formal analysis, Software, Writing – original draft, Writing – review & editing. **Yi Chen:** Conceptualization, Data curation, Project administration, Resources, Supervision, Writing – original draft, Writing – review & editing. **Jing Liu:** Conceptualization, Data curation, Funding acquisition, Project administration, Resources, Supervision, Writing – original draft, Writing – review & editing.

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Acknowledgments

We extend our gratitude to our tutor, Dr. Jing Liu, for his funding support (National Natural Science Foundations of China (81870166)). Additionally, we would like to express our thanks to Yi Chen, Yunfeng Fu, Zhimin Wu and Shanyi Sun, who provided assistance.

Appendix A. Supplementary data

Supplementary data to this article can be found online at <https://doi.org/10.1016/j.heliyon.2023.e20612>.

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