Peruvian Journal of
Health Care and Global Health

Artículo Original

Patterns of research and scientific growth on complex regional pain syndrome: bibliometric analysis of global scope

Patrones de investigación y crecimiento científico sobre el síndrome doloroso regional complejo: Análisis bibliométrico de alcance global

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Article information

Cite as: Moscoso-Organista, JL, Zárate-Saavedra MA, Prieto-Gutiérrez V, Carreño-Barrera VD, Gómez-Jiménez NA, Palacios-Izquierdo V, González-Villarreal A, Santodomingo-Vasquez JR, Coronell-Marimon JP, Ortega-Sierra M. Patterns of research and scientific growth on complex regional pain syndrome: bibliometric analysis of global scope. Health Care & Global Health.2024;8(1):17-23.

DOI: 10.22258/hgh.2024.81.170

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History:
Received: 02/06/2024
Accepted: 13/06/2024
Online: 15/06/2024

Funding:
None.

Abstract

Introduction: Complex Regional Pain Syndrome (CRPS) is a pathological entity that carries a high burden of disease and reduces disability-free life expectancy and quality of life. Previously, the research patterns and general characteristics of the scientific production on CRPS have not been evaluated or analyzed. **Methods:** Cross-sectional bibliometric study that used Scopus as the data source. **Results:** A total of 3081 documents were selected, published between 1969 and 2024. Of these, 69% (n=2126) were original articles, followed by 13.2% (n=406) for reviews. It was observed that international collaboration accounted for 11.49% and annual scientific growth accounted for 7.63%. The most frequently used terms in CRPS research are causalgia, rehabilitation, allodynia, treatment, and inflammation. Reflex sympathetic dystrophy, causalgia, and spinal cord stimulation are the most popular topics to date. As an emerging central theme, there is increasing research on cortical reorganization. The construction of the thematic map revealed that niches of topics include depression and quality of life, as well as autoimmunity. **Conclusions:** This study revealed a significant increase in global research and scientific publications on CRPS, with the United States being the most prolific country and achieving the greatest impact. However, it is Dutch institutions that have made the most substantial contributions to this research field. Among the most common research patterns, it is found that causalgia, rehabilitation, allodynia, treatment, and inflammation are the most frequently used keywords, while reflex sympathetic dystrophy, causalgia, and spinal cord stimulation are the most addressed topics to date.

Keywords: Complex Regional Pain Syndromes; Autonomic Nervous System Diseases; Peripheral Nervous System Diseases; Research; Bibliometrics (Source: MeSH, NLM).

Resumen

Introducción: El Síndrome Doloroso Regional Complejo (SDRC) es una entidad patológica que conlleva una elevada carga de enfermedad y reduce la esperanza y la calidad de vida sin discapacidad. Anteriormente, no se habían evaluado ni analizado los patrones de investigación ni las características generales de la producción científica sobre el SDRC. **Métodos:** Estudio bibliométrico de corte transversal, que utilizó como fuente de datos la base Scopus. **Resultados:** Se seleccionaron 3081 documentos publicados entre 1969 y 2024. El 69% (n=2126) de los artículos correspondían a artículos originales, seguidos del 13,2% (n=406) por revisiones. Se observó que la colaboración internacional representaba el 11,49% y el crecimiento científico anual el 7,63%. Los términos más utilizados en la investigación del SDRC son causalgia, rehabilitación, alodinia, tratamiento e inflamación. La distrofia simpática refleja, la causalgia y la estimulación de la médula espinal son los temas más populares hasta la fecha. Como tema central emergente, cada vez se investiga más la reorganización cortical. La construcción del mapa temático reveló que entre los nichos de temas figuran la depresión y la calidad de vida, así como la autoinmunidad. **Conclusiones:** Este estudio reveló un aumento significativo de la investigación mundial y de las publicaciones científicas sobre el SDRC, siendo Estados Unidos el país más prolífico y el que ha logrado un mayor impacto. Sin embargo, son las instituciones holandesas las que han realizado las contribuciones más sustanciales a este campo de investigación. Entre los patrones de investigación más comunes, se observa que causalgia, rehabilitación, alodinia, tratamiento e inflamación son las palabras clave más utilizadas, mientras que distrofia simpática refleja, causalgia y estimulación de la médula espinal son los temas más abordados hasta la fecha.

Palabras clave: Síndromes de Dolor Regional Complejo; Enfermedades del Sistema Nervioso Autónomo; Enfermedades del Sistema Nervioso Periférico; Investigación; Bibliometría (Fuente: DeCS, BIREME).

Introduction

Complex Regional Pain Syndrome (CRPS) is an acute or chronic condition, typically of unknown etiology and without the potential for definitive resolution, characterized by hyperalgesia and allodynia [1][2][3]. This syndrome is usually managed medically through pharmacological treatment (which can even involve polypharmacy) or more invasive interventions, such as neural blockade, for temporary pain control [4]. In this context, CRPS is a pathological entity that carries a high burden of disease and reduces disability-free life expectancy and quality of life by affecting various health outcomes and impacting some health determinants, such as work, due to functional limitations caused by pain [1][2][5].

Currently, the absence of definitive therapies positions this pathological condition as a topic of global interest in the biomedical sciences. Some authors have proposed strengthening basic and translational research in neuroinflammation and neuromodulators [6]. However, to propose this perspective, it is necessary to know what has been studied. In this way, knowledge gaps and opportunities can be identified, and multidisciplinary research groups and lines of inquiry can be designed to generate valuable new knowledge about this syndrome [7]. Previously, the research patterns and general characteristics of the scientific production on CRPS have not been evaluated or analyzed.

With the aim of providing solid data for the first time on the scientific landscape of this topic, this study analyzed the research patterns and scientific growth of global research on CRPS.

Methods

A cross-sectional bibliometric study was conducted using the Scopus database as the data source. This database is used for this type of analysis because it provides extensive information on metadata variables and citation behavior. Additionally, it is described as the largest database that indexes peer-reviewed literature globally, which is why previous studies have used it [8][9].

The inclusion criteria defined for this analysis were scientific publications whose primary or secondary topic was CRPS. This was confirmed through the publication's objective, title, and keywords. Retractions, erratum, and data papers were excluded. There were no language restrictions.

To obtain the information, a semi-structured search was designed based on MeSH terms and synonyms to identify studies on CRPS regardless of the research approach. Following a pilot test for label testing, the following search strategy was defined: TITLE("Complex regional pain syndrome") OR TITLE(CRPS) OR TITLE("Regional Complex Pain Syndromes") OR TITLE("Acute Regional Pain Syndrome") OR TITLE("Chronic Regional Pain Syndrome"). This search was conducted on May 22, 2024, and did not specify a time inclusion window.

Once the results were obtained, data related to citation domains, bibliographic information, and general metadata (titles, keywords, abstracts, authors, etc.) were exported in .CSV format for manual review in Microsoft Office Excel 2016. During the first review, duplicates and articles not directly related to the topic of interest were removed. In the second review, the information was standardized and verified to ensure it corresponded to the registered domain.

With the final database established, a visual and bibliometric analysis of the general characteristics, patterns, and co-occurrence of topics, as well as an evaluation of scientific growth over time, was conducted. For this analysis, the Bibliometrix package of R (version 4.3.1) was used, which provides quantitative and qualitative bibliometric indicators [10]. Synonyms, errors, plurals, and variants were carefully grouped using a thesaurus to homogenize the analysis. Frequency and percentage calculations were carried out using Microsoft Office Excel 2016.

This study did not require approval from an ethics committee, considering that it did not involve research on humans, biological models, or the use of medical records.

Results

A total of 3081 documents were selected, published between 1969 and 2024. Of these, 69% (n=2126) were original articles, followed by 13.2% (n=406) for reviews. It was observed that international collaboration accounted for 11.49% and annual scientific growth accounted for 7.63% (Table 1). Regarding the evolution of publications on this topic, there was a very slow growth since the first publication, with a notable rise starting in the 1990s, which has been fluctuating up to 2024 (Figura 1). Similarly, the behavior of received citations has been fluctuating, with a marked decrease in recent years (Figura 1). Lotka's law revealed that 78.1% of the authors had published only one article, followed by 12.3% with two articles.

In the analysis of the evolution of CRPS research over time, it was identified that Erasmus MC (Netherlands) has been the most prolific institution (n=91), followed by Leids Universitair Medisch Centrum (Netherlands) with 74 publications. On the other hand, the United States has been the country with the highest volume of publications (n=907) and impact to date (h-index = 80), followed by Germany (n=416; h-index = 75) (Table 2).

When visualizing research patterns, it was shown that the most frequently used terms in CRPS research are causalgia, rehabilitation, allodynia, treatment, and inflammation (Figure 2-A). Reflex sympathetic dystrophy, causalgia, and spinal cord stimulation are the most popular topics to date (Figure 2-B). Compared to the

Table 1. Baseline characteristics of global research on complex regional pain syndrome (N=3081).

	n	%
Article type		
Article	2126	69
Book	2	0.1
Book chapter	147	4.78
Conference paper	33	1.08
Editorial	55	1.79
Letter	200	6.5
Note	80	2.6
Review	406	13.2
Short Survery	32	1.04
Authors		
Authorships	7903	-
Authors of documents with single authorship (N=7903)	313	3.96
Collaboration		
Single-authored articles	427	-
Co-authorships per article (average)	4.21	-
International co-authorship	-	11.49
Key words	3619	-
Average age of article (years)	11.2	-
Average number of citations per paper	24.22	-
Annual growth	7.63	-

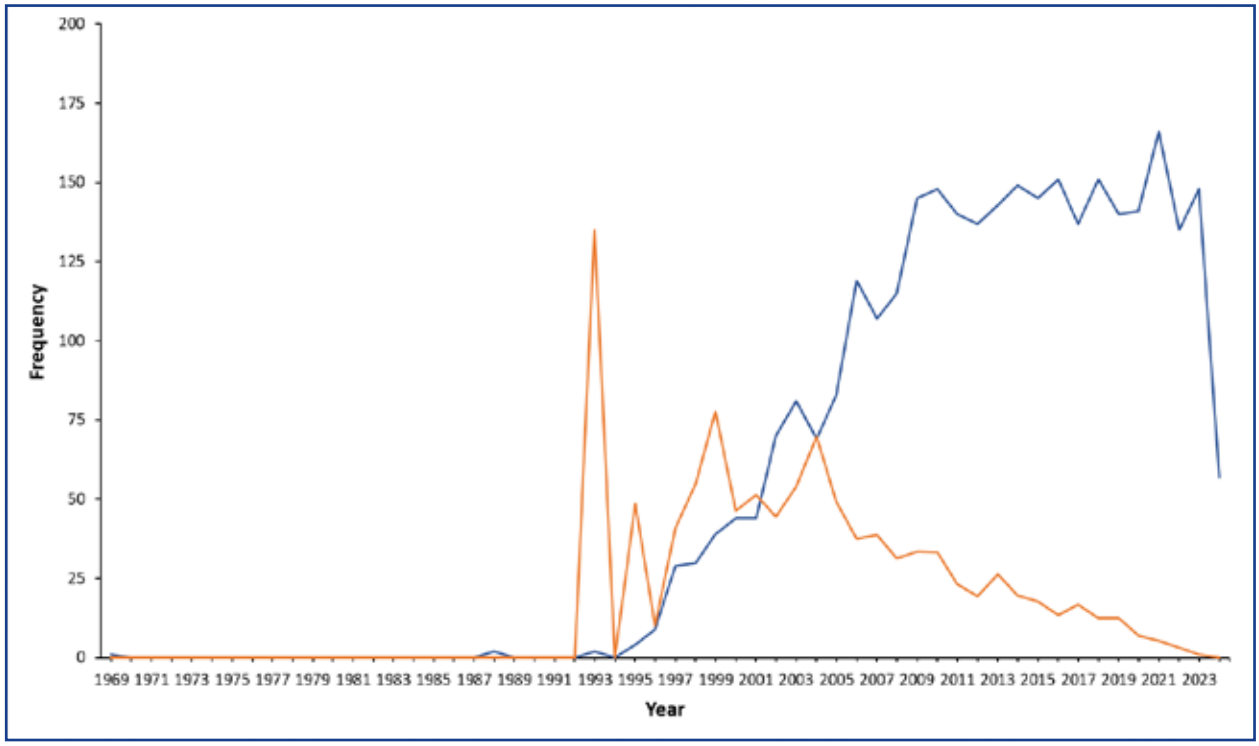

Figure 1. Evolution of publications on complex regional pain syndrome. Blue: Annual scientific production from 1969 to 2024. Orange: Average number of citations received per article per year.

Table 2. Evolution of the most prolific institutions and countries on complex regional pain syndrome research over time.

Affiliation	Documents over time				Total documents	h-index	Country
	1969 – 1982	1983 – 1995	1996 – 2009	2010 - 2024			
Erasmus MC	0	0	42	49	91	35	Netherlands
Leids Universitair Medisch Centrum	0	0	28	46	74	35	Netherlands
Johannes Gutenberg-Universität Mainz	0	0	25	35	60	30	Germany
Universitätsmedizin Mainz	0	0	1	56	57	23	Germany
Drexel University College of Medicine	0	0	21	36	57	26	United States
Country	Documents over time				Total documents*	h-index	
	1969 – 1982	1983 – 1995	1996 – 2009	2010 - 2024			
United States	0	1	345	561	907	80	
Germany	0	0	155	261	416	75	
United Kingdom	0	3	63	231	297	47	
Netherlands	0	0	132	144	276	63	
South Korea	0	0	7	148	155	22	

*The production was counted individually. Therefore, a document could have been counted several times depending on international collaboration.

2000s, when the most prominent topics related to CRPS were reflex sympathetic dystrophy, CRPS type I, and neurogenic inflammation (Figure 2-C), since 2010, there has been a particular emphasis on neuromodulation, rehabilitation, spinal cord stimulation, and allodynia (Figure 2-D). Closely related, the co-occurrence of topics revealed that reflex sympathetic dystrophy is correlated with treatment opportunities and quality of life (Figure 2-E). The construction of the thematic map revealed that niches of topics include depression and quality of life, as well as autoimmunity. As an emerging central theme, there is increasing research on cortical reorganization;

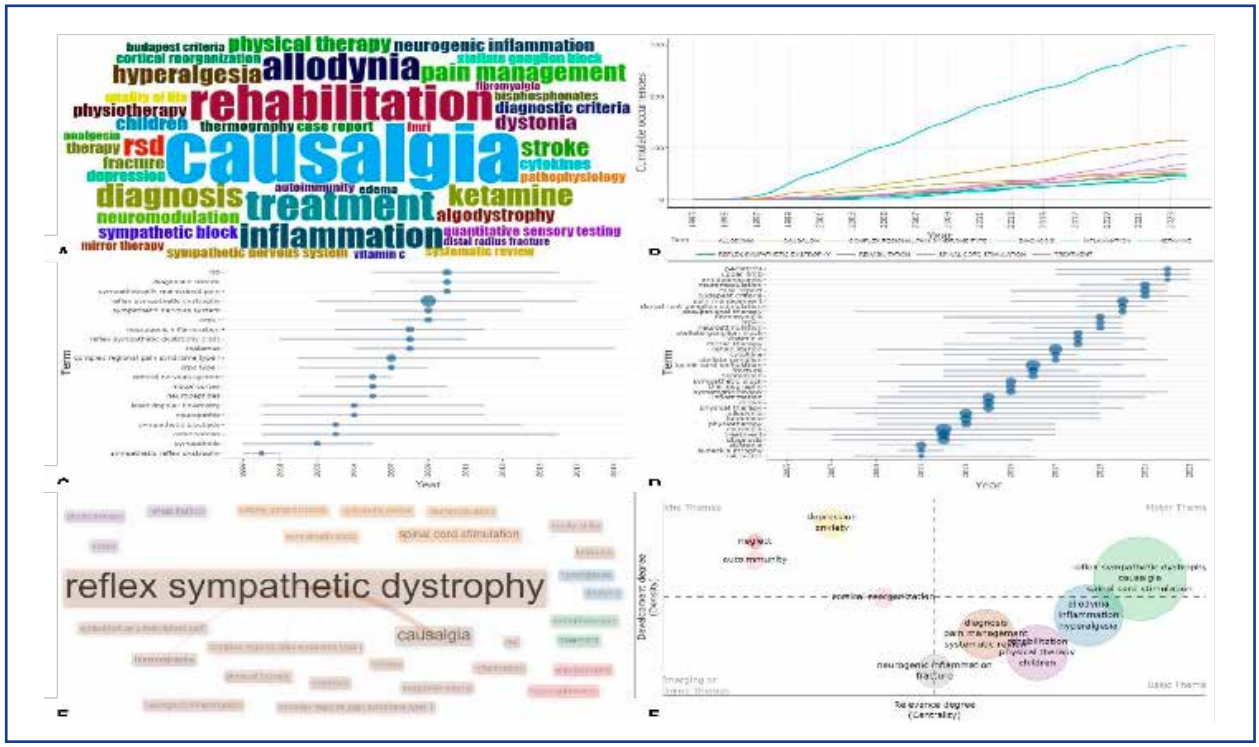

Figure 2. Patterns, trends, and topic co-occurrence in research on complex regional pain syndrome. A. Cloud of most frequently used keywords. B. Cumulative occurrence of most frequent topics over time. C. Evolution of topics from 2000 to 2010. D. Evolution of topics from 2011 to 2024. E. Co-ocurrence of topics F. Thematic map with degree of development of the topics studied.

while the basic themes include diagnosis, treatment, and clinical manifestations (Figure 2-F).

Finally, another perspective allowed for the appreciation that compared to the years prior to 2013, the last 10 years have seen a significant focus on central sensitization, inflammation, and the approach to the pediatric population (Figure 3-A). The multiple correspondence analysis revealed that the previously discussed topics have a central and concentrated relationship, isolating the themes of stroke and dystonia, which are associated with CRPS (Figure 3-B).

Regarding scientific collaboration, it was found that globally, there is a network between the United States and Asian countries, and another European network, primarily led by the United Kingdom, Germany, and the Netherlands (Figure 3-C). Similarly, in assessing the frequency of international cooperation, the low participation of Latin American and African countries is evident, with Brazil and Chile standing out in Latin America. In contrast, there is a strong concentration of cooperation in Europe, with allies in the United States and Australia (Figure 3-D).

Among the articles with the highest impact obtained to date, three original studies stand out: 1) "Validation of proposed diagnostic criteria (the "Budapest Criteria") for Complex Regional Pain Syndrome " (847 citations - Pain – 2010 – DOI: 10.1016/j.pain.2010.04.030); 2) " Proposed New Diagnostic Criteria for Complex Regional Pain Syndrome" (702 citations – Pain Medicine – 2007 – DOI: 10.1111/j.1526-4637.2006.00169.x); and 3) "The incidence of complex regional pain syndrome: A population-based study" (639 citations – Pain – 2007 – DOI: 10.1016/j.pain.2006.09.008).

Discussion

This study provides, for the first time, data on the global research landscape concerning CRPS. According to guidelines and suggestions from international researchers in scientometrics, research policy, and evidence-based research, it is essential to have bibliometric data as a foundation to justify gaps, pluralism, and opportunities in biomedical research in order to build robust work routes and research lines [11][12]. This study fulfills that argument by providing data, patterns, and trends in this research field.

Given the absence of previous studies, it is challenging to specifically compare methodologies and results. However, some bibliometric analyses focused on chronic pain and pain neuromodulation have included CRPS [13][14]. These studies have identified similar characteristics, such as notable growth in recent decades (p <0.001) and the leadership of the United States in research volume and impact. Nonetheless, other fields have focused on the evaluation and intervention of pain, specifically on spinal cord stimulation, intrathecal drug administration, and dorsal root ganglion and peripheral nerve stimulation [13][14]. Another study with a similar objective also identified that the United States, the United Kingdom, and Germany stood out in pain research [15]. Therefore, there is a clear trend that in these countries, there are strong research groups focused on pain and its various phenotypes, making them potential international collaborators.

No clear niches were identified in basic and translational research on CRPS or pain, with clinical research and studies focused on general health outcomes predominating. This reveals a potential tool and opportunity for research to

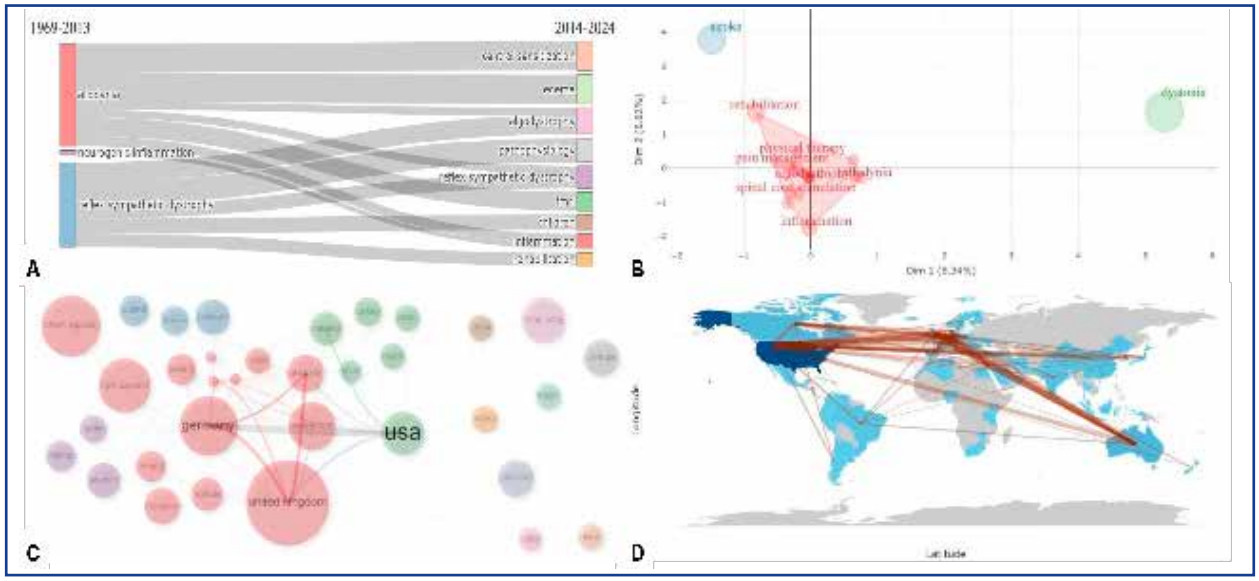

Figure 3. Transition and correspondence of topics, and international collaboration in research on complex regional pain syndrome. A. Transition of topics from 1969 – 2013 to 2014 – 2024. B. Multiple correspondence analysis based on keywords. C. Strength of collaboration between countries. D. Frequency of collaboration between countries

promote molecular and computational research [16], aimed at identifying therapeutic targets or definitive therapies to address this debilitating condition.

Notably, and similar to another global bibliometric study [17], it was observed that Latin America and Africa have minimal participation in research. Therefore, it is necessary to develop a roadmap and programs driven by actors in the science, technology, and innovation systems, offering incentives to researchers interested in generating new knowledge that advances the understanding and treatment of CRPS.

As a limitation, there is the use of a single database, which limits and excludes evidence that may have been published in other sources. However, due to the methodology and statistical analysis performed, Scopus is one of the few databases that allows these analyses based on the metadata deposited.

Conclusions

This study revealed a significant increase in global research and scientific publications on CRPS, with the United States being the most prolific country and achieving the greatest impact. However, it is Dutch institutions that have made the most substantial contributions to this research field. Among the most common research patterns, it is found that causalgia, rehabilitation, allodynia, treatment, and inflammation are the most frequently used keywords, while reflex sympathetic dystrophy, causalgia, and spinal cord stimulation are the most addressed topics to date. Emerging niches include the assessment of clinical outcomes such as the depression and quality of life, as well as autoimmunity associated with CRPS. International collaboration is concentrated, with very little participation from Latin American and African countries in this research field. These results will help identify gaps and opportunities for research on CRPS worldwide.

Author contributions

JLMO, MAZS, VPG, VDCB, NAGJ, VPI, AGV, and JRSV: Study conception and design, obtaining results, data analysis and interpretation, manuscript writing, and approval of the final version. JPCM and MOS: Study conception and design, obtaining results, data analysis and interpretation, manuscript writing, critical revision of the manuscript, approval of the final version, and technical or administrative advice.

Data availability: N/A

Acknowledgments: None

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