Research Article

Citation analysis of the most influential articles on traumatic spinal cord injury

Ronak H. Jani [1], Arpan V. Prabhu [2], James J. Zhou[3], Nima Alan[1], Nitin Agarwal[1]

[1]Department of Neurological Surgery, University of Pittsburgh Medical Center, Pittsburgh, Pennsylvania, USA,
[2]Department of Radiation Oncology, University of Pittsburgh Cancer Institute, Pittsburgh, Pennsylvania, USA,
[3]Department of Neurosurgery, Barrow Neurological Institute, Phoenix, Arizona, USA

Objective: We conducted a citation analysis in order to catalog and pay tribute to the 100 most influential clinical research articles in traumatic spinal cord injury.
Design: The Thomson Reuters Web of Science was searched in a two-step process without time period limitations. Review articles were excluded. In the first stage of data extraction, a Boolean query was used to identify the top 100 most cited clinical papers on traumatic spinal cord injury. One hundred and seven keywords were manually chosen and extracted from titles and abstracts. A second Boolean query used these keywords to broaden search results. The top 100 articles from this second stage search comprised the final list.
Outcome Measures: For each article, measures evaluated were number of citations, average number of citations per year, time elapsed before first citation, and time elapsed until the year in which each article received its respective highest number of citations in a one-year period.
Results: 119,991 articles were found in the second stage search. The top 100 most cited articles meeting inclusion criteria were identified within the first 2,104 results. Archives of Physical Medicine and Rehabilitation was the most represented journal, with 20 of the top 100 articles. The top 100 list averaged 255 citations per article. The most highly cited article was the NASCIS 2 trial by Bracken *et al.*, cited 1500 times, which investigated the efficacy of methylprednisolone or naloxone for spinal cord injury.
Conclusion: Clinical research in traumatic spinal cord injury has grown over time, expanding to encompass rehabilitation and experimental therapies in addition to acute management trials. The list may serve as an archive and reference for further studies in this field.

Keywords: Spinal cord injury, Acute, Traumatic, Citation analysis, Bibliometric study

Introduction

As research in spinal cord injury (SCI) races forward, neurologists, neurosurgeons, and rehabilitation specialists must sort through an increasing number of studies in order to understand how the field has developed over time. The past several decades have brought advances in understanding SCI. Key papers have played a critical role in defining the management of SCI and have formed a basis for many exciting technologies now in development, such as brain-computer interfaces that may allow people with tetraplegia to independently execute manual tasks. In order to organize the multitude of studies, and to recognize those who contributed key knowledge to the SCI community, the most influential papers should be codified for future reference.

Bibliometric studies, also known as citation analyses, are one such method of identifying the most relevant and impactful articles within a field. In a bibliometric analysis, research articles are ranked by their relative impacts on their respective fields. Bibliometric studies are a valued method to identify and collect seminal studies in many medical and scientific fields.[1–3] These analyses have been employed to compile key works across medical specialties such as rehabilitation as well as to analyze literature pertaining to specific disorders.[4–10] Multiple papers detailing the top cited articles for spine diseases such as scoliosis, metastasis,

Correspondence to: Nitin Agarwal, Department of Neurological Surgery, University of Pittsburgh Medical Center, 200 Lothrop Street, Suite B-400, Pittsburgh, PA 15213, USA. Email: agarwaln@upmc.edu
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and deformity exist.[11–18] A 2017 citation analysis of SCI exists in the literature; however, the study included predominantly review articles and did not exclude basic science papers.[19] No bibliometric study to date has specifically examined original clinical research on SCI, *i.e.* studies generating novel information from human clinical, outcome, epidemiological, survey, or psychometric or qualitative data.

In this study, we conduct citation analysis using the Thomson Reuters Web of Science to identify the top 100 most cited clinical research articles pertaining to SCI published in any journal from 1945 to 2016.

Methods

Inclusion criteria

Studies must have met specific criteria to be included on the final 100-article list. First, studies must have focused on clinical aspects of traumatic SCI. These could include SCI treatment, management of SCI complications, outcome studies, quality of life analyses including psychometric analyses and survey responses, epidemiology of SCI, or insights into radiographic interpretation of spinal cord trauma, among other possibilities. Further, clinical studies involving other spinal cord disorders, such as multiple sclerosis, were included if people with traumatic SCI made up the majority of the study population. Manual review of abstracts and article text was performed to verify majority representation of traumatic SCI in instances of mixed study populations. Basic science studies, such as experiments using mice, rats, human cell lines, or human cells obtained from deceased people with SCI, were excluded. The decision to exclude basic science research was made to formulate a list of clinical studies that may be perused by clinicians and those interested in translational or clinical work. There is a rich history of molecular and cellular SCI studies forming the foundation for subsequent clinical research; these warrant full consideration in a separate bibliometric analysis.

Data collection

All databases and journals accessible within the Thomson Reuters Web of Science were considered in

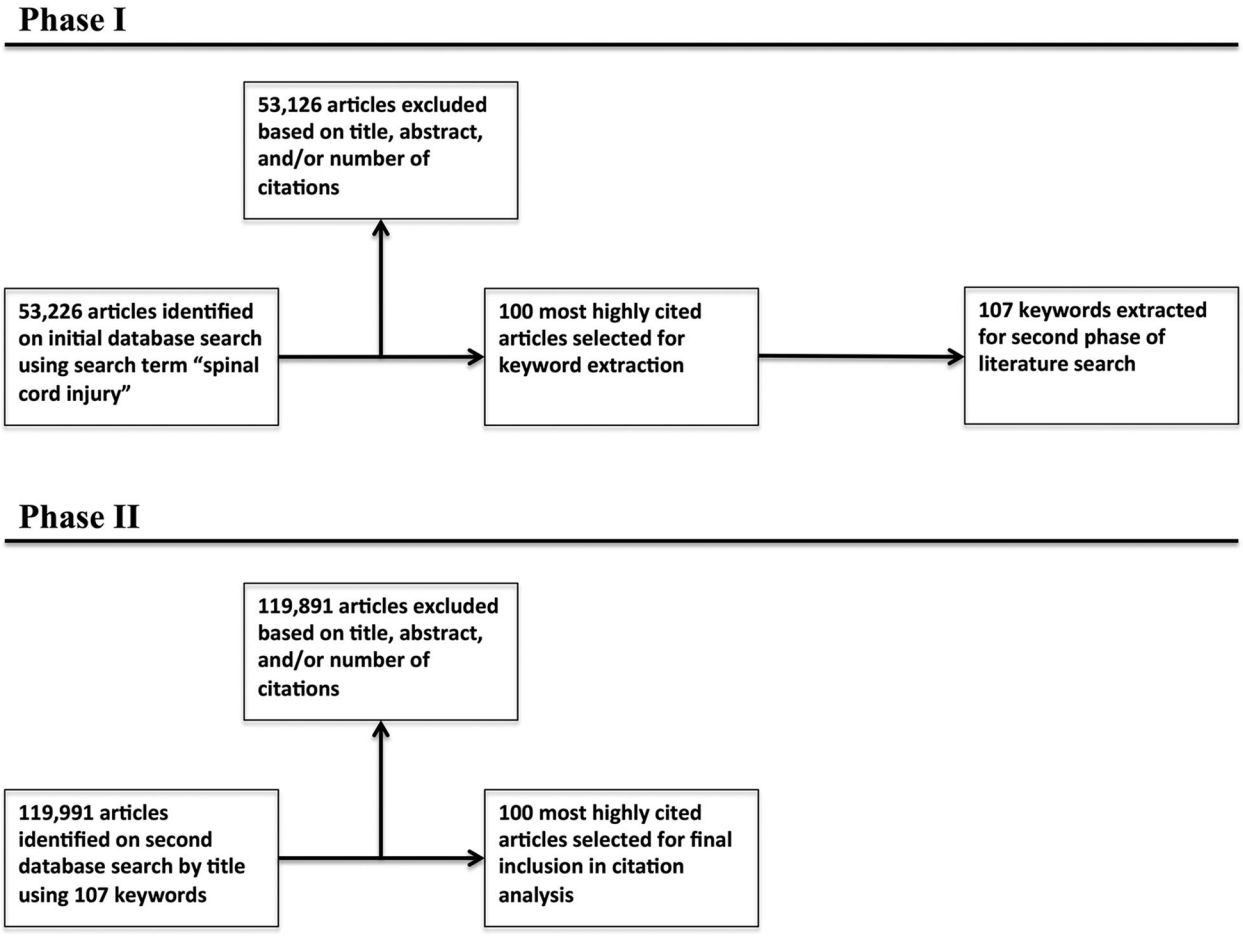

Figure 1 Flowchart showing literature search strategy.

identifying eligible articles. Literature search was conducted in a two-step process (Fig. 1).

In phase one, a topic search was conducted by the primary author using the following Boolean query: *spinal cord injury*. The search yielded 53,226 results, which were then sorted by total number of citations in descending order. The first 100 clinical research papers involving traumatic SCI were identified via manual review of titles and abstracts. 1,255 studies required review to identify these 100 clinical articles, as the majority of results consisted of reviews and basic science articles, which were excluded from the present study. The 100 articles were reviewed for relevance and adherence to inclusion and exclusion criteria by the senior author. All 100 articles collected were then further examined to create a list of keywords to be used in the second stage of data collection.

One hundred and seven keywords were extracted from the 100 papers collected during the first step of data collection (Supplementary Table 1). Keywords were extracted from each article's associated Web of Science Keywords as well as created based on careful review of titles and abstracts. All keywords were grouped by relevant category of paper (problem name, acute management, short-term complications and treatment, long-term outcomes and treatment, rehabilitation, comorbidities, regeneration, and brain-computer interface). These 107 keywords were used to construct the Boolean search query during a second search of the Web of Science. This phase of the search yielded 119,991 studies, which were again sorted in descending order by cumulative citations. Within the first 2,104 results, the top 100 most highly cited articles meeting inclusion criteria were extracted and reviewed for relevance and adherence to inclusion and exclusion criteria by the senior author. After review, the top 100 articles were chosen for inclusion in the present study.

Several characteristics were collated for each entry in the final 100 study list: title, authors, year of publication, year of first citation, year of peak number of citations, cumulative citation count, and number of citations in 2016, the most recent year for which full citation metric data were available. We then used this data to calculate average citations per year, time to first citation, and time until year of peak citations. The average number of citations per year was calculated using only complete annual data; the year 2017, for which only data through May 2017 were available, was therefore excluded for this calculation. Metrics were selected to provide context to each entry in the top 100. Year of first citation and year of peak citation were metrics intended to reflect speed of incorporation into the referenced literature, *i.e.* whether an article enjoyed immediate or delayed influence. Citation count in 2016 was recorded in order to examine ongoing influence on the literature, particularly for older studies with citations amassed in the distant past. Finally, average citation count per year assessed citation frequency relative to article age in order to offset the time advantage enjoyed by studies published long ago. Citation count per year for older articles is tempered by the many years during which citations were accumulated.

Graphs were drawn to illustrate the relationships between length of time until first citation or maximum citation and average citation count per year. Logarithmic regression curves were generated to fit the data (Microsoft Excel, 2011). For each regression curve, the logarithmic transformation applied to the citation count parameter (x-axis).

Results

Gross outcome of citation analysis

The top 10 most cited articles at time of analysis are listed in Table 1 (full top 100 list is available in Supplementary Table 2). Citation metrics collected on each article are also shown. These descriptive statistics include total citations at time of analysis, total citations through the end of 2016, number of citations in 2016, year of most frequent citation, average yearly citations since date of publication, and number of years that passed from publication until year of most citations.

Archives of Physical Medicine and Rehabilitation was the most represented journal with 20 articles, and *Spinal Cord* was second with 10 articles. The third-most highly represented journal was *Journal of Neurosurgery* with 9 articles. Together, these three journals accounted for 39 of the 100 articles.

"Bracken, M.B." appeared as first author on 7 articles, the highest representation of any first author in the top 100. Four first authors tied for second-highest representation on the list, appearing on 3 articles apiece: Whiteneck, GG; Siddall, PJ; Schurch, B; and Brindley, GS.

The most highly cited article identified was the NASCIS 2 trial for methylprednisolone or naloxone use in traumatic SCI by Bracken *et al.* with 1500 citations.[20] Across all 100 articles, the list averaged 255 cumulative citations per publication, with a standard deviation of 199.

Spinal cord injury subtopic citation analysis

Figure 2 sorts the top 100 articles by subtopic category. Each article was categorized into one or more of 6

Table 1 The top 10 articles in spinal cord injury research.

Rank	Publication	Years until first citation	Most cited year	Years until most cited year	Average citations per year since publication (± SD)	Number of citations in 2016	Total number of citations through 12/31/2016	Total number of citations at analysis 5/31/2017
1	Bracken *et al.*[20]	0	1997	7	57.69 ± 14.11	47	1500	1512
2	Hochberg *et al.*[22]	0	2009	3	141.90 ± 44.68	127	1419	1450
3	Bracken *et al.*[23]	0	2012	15	39.05 ± 11.65	30	742	759
4	Anderson[25]	1	2015	11	44.17 ± 24.08	71	530	553
5	Colombo *et al.*[24]	1	2015	15	32.25 ± 17.73	42	516	531
6	Whiteneck *et al.*[34]	0	2011	19	20.92 ± 8.32	22	502	507
7	Bracken *et al.*[35]	0	1999	7	18.38 ± 6.06	13	441	442
8	Kirshblum *et al.*[36]	1	2016	5	75.4 ± 67.79	151	377	439
9	Schurch *et al.*[37]	1	2006	6	25.94 ± 12.58	24	415	419
10	DeVivo *et al.* [38]	0	2010	11	23.00 ± 11.01	26	391	399

different subtopics within the field of SCI: acute management, complications, rehabilitation, SCI outcomes, epidemiology, and experimental therapies. Complications and outcomes were most highly represented on the top 100 list, with 30 and 24 publications on each subtopic, respectively. Rehabilitation was third most highly represented, with 21 publications on the subtopic. Ten articles were assigned to two different categories each.

Increase in spinal cord injury research

Figure 3 depicts the number of articles on the list published each year. The number of articles published within each subtopic for any given decade is shown in

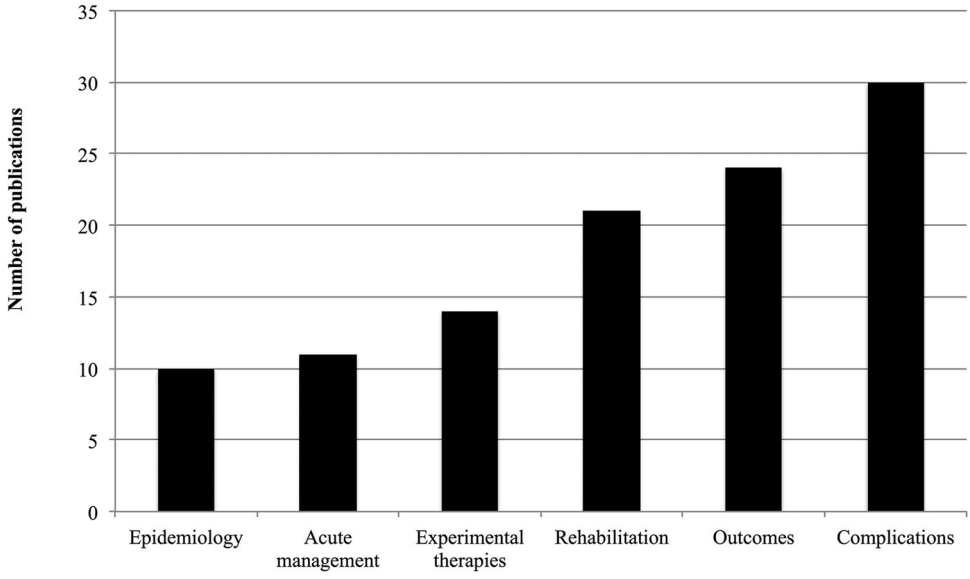

Figure 2 Bar chart showing top 100 articles sorted by subtopic category. Ten articles were assigned to two subtopics each: Kulkarni *et al*. (1987): outcomes/epidemiology; Hadley *et al*. (1988): outcomes/epidemiology; Whiteneck *et al*.:[34] rehabilitation/outcomes; Devivo *et al*. (1993): outcomes/epidemiology; Levi *et al*. (1995): complications/epidemiology; Frankel *et al*. (1998): outcomes/epidemiology; McKinley *et al*. (1999): complications/outcomes; Washburn *et al.* (2002): rehabilitation/outcomes; Hicks *et al*. (2003): rehabilitation/outcomes; and Cardenas *et al*. (2004): complications/outcomes.

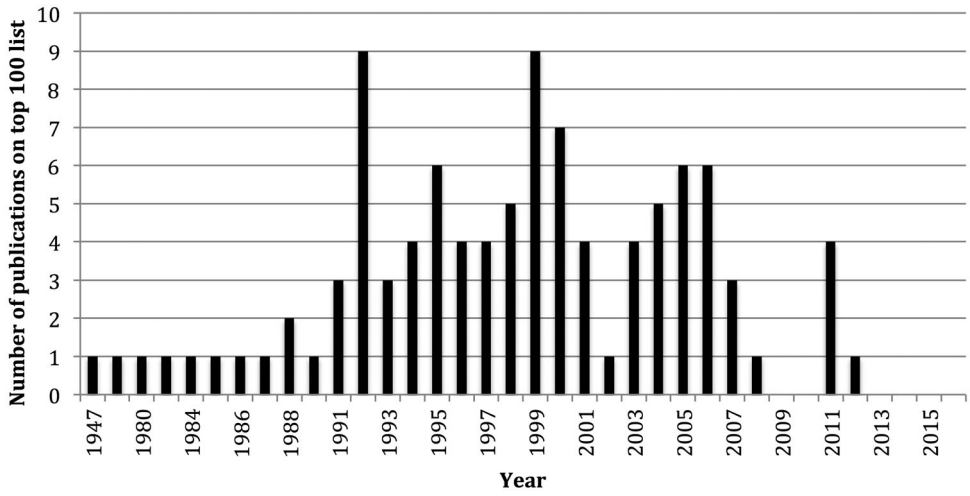

Figure 3 Bar chart showing number of top 100 articles by year.

Supplementary Figure 1. The number of articles on the list rose from just one in 1947 to a maximum of nine in both 1992 and 1999. The most highly represented subtopics, complications and outcomes, peaked with 15 and 13 articles respectively in the 1990s, which were also the decade during which the most articles on the list were published. No experimental therapies subtopic papers on the top 100 list had publication dates before the 1990s. The first experimental therapies subtopic article was Topka *et al*.'s transcranial magnetic stimulation study examining post-SCI changes in cortical motor evoked potentials.[21]

Article recognition and incorporation

In an effort to identify relationships between citation frequency and rapidity of incorporation into the literature, logarithmic regressions were applied to citation metrics. A negative correlation was revealed between average citations per year since publication and time until first citation (regression equation: $y = -0.36\ln(x) + 1.56$) ($R^2 = 0.11$) (Supplementary Figure 2). Logarithmic regression also revealed negative correlation between average citations per year since publication and years until maximum citation (regression equation: $y = -5.06\ln(x) + 23.19$) ($R^2 = 0.15$) (Supplementary Figure 3). Similarly, a negative correlation was observed between average number of citations per year from publication until maximum citation year and years until maximum citation year (regression equation: $y = -7.13\ln(x) + 33.86$) ($R^2 = 0.49$) (Supplementary Figure 4). The data indicate that articles with more influential findings tend to be more quickly identified and cited in the literature, and become rapidly incorporated into the body of frequently cited works. Furthermore, articles that are cited at a higher rate until reaching year of maximum citations seem to achieve peak citations earlier than those cited at lower rates.

Year-by-year citation frequency for the top five most highly cited articles is depicted in (Fig. 4). Hochberg *et al*., which reported neuro-prosthetic use by a person with tetraplegia, peaked at 185 citations in 2009, declining slightly since but remaining highly referenced in 2016 with 127 citations.[22] Bracken *et al*.[20] (NASCIS 2) and Bracken *et al*.[23] (NASCIS 3), comparing methylprednisolone administered over 24 h, methylprednisolone administered over 48 h, and treatment with tirilazad mesylate have maintained relatively steady numbers of citations since the initial five years post-publication.[20, 23] Colombo *et al*., describing a robotic driven gait orthosis to assist treadmill training rehabilitation, experienced steadily increasing citation frequency until 2008 and has since been cited at a steady rate.[24] Finally, citations per year of Anderson *et al*., a survey-based study reporting individuals' highest priority functional goals after SCI, have continued to climb since publication in 2004 and have not appeared to reach a plateau as of 2016.[25]

Discussion

The most highly cited article identified was "A Randomized, Controlled Trial of Methylprednisolone or Naloxone in the Treatment of Acute Spinal-Cord Injury – Results of the 2nd National Acute Spinal-Cord Injury Study," published in 1990 by Bracken *et al*. in the *New England Journal of Medicine*.[20] This paper presented the results of the NASCIS 2 trial, which concluded that treatment with methylprednisolone steroid within eight hours of SCI produced significantly better neurologic outcomes at six months post-

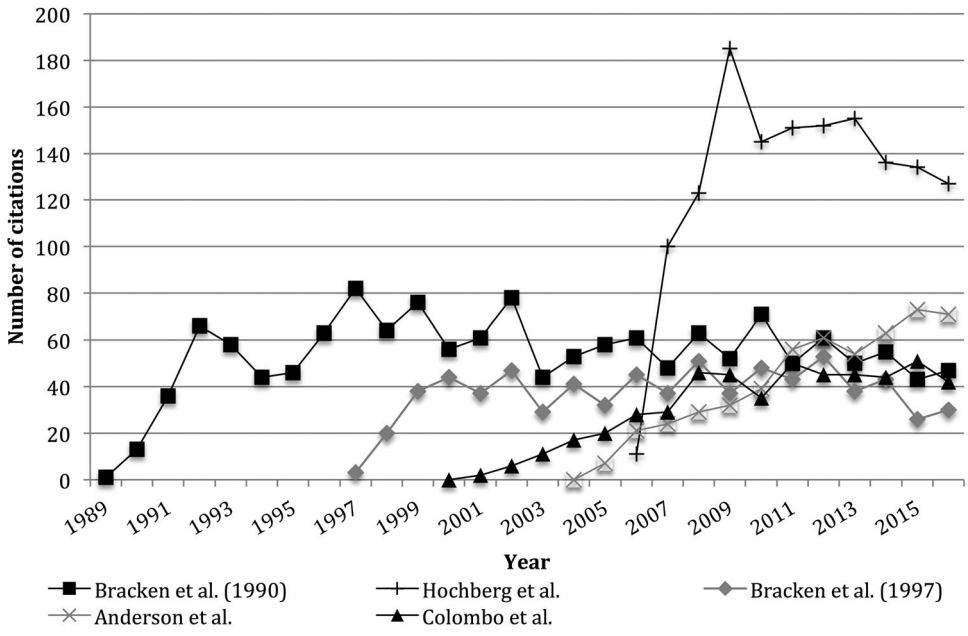

Figure 4 Line graph showing number of citations by year for top 5 articles on the top 100 list.

injury. The NASCIS 2 trial purported to support an effective acute intervention for SCI, a condition with very few acute management options. NASCIS 2 has been critiqued by a re-analysis in 2000 by Hurlbert in *Journal of Neurosurgery*, also appearing on the top 100 list.[26] The large number of citations accumulated by NASCIS 2, including critiques, suggests that a given study's influence may extend beyond the application of its findings in clinical practice and research. Rather, the ability to inspire debate in the literature may itself constitute a form of influence exerted by such contested articles.

Application of logarithmic regression to bibliometric data revealed a negative correlation between average citations per year and time to first citation in the literature. This relationship likely reflects a connection between early recognition of studies with major implications and the lasting influence thereof. Studies quickly garnering citations after publication therefore may continue to be referenced in the literature. In contrast, longer time to first reference may predict delayed discovery of a study's significance, resulting in reduced citation per year rate.

The oldest paper was "Effects of Bladder Distension on Autonomic Mechanisms After Spinal Cord Injuries," published in 1947 by Guttmann and Whitteridge in *Brain*.[27] The paper examines various autonomic reactions to bladder distension in 30 people who had SCI. With exception of one person, all injuries were complete transverse transections of the spinal cord, predominantly due to gunshot wounds. The phenomenon of hypertension, sweating, and bradycardia following bladder distension in individuals with SCI above T6 described in the article is now recognized as the clinical entity autonomic dysreflexia.[28] Representing a potentially lethal condition in those with SCI, autonomic dysreflexia has been of enduring importance for clinicians and patients in the 70 years since its initial description. Illustrating the continued significance of the original 1947 article, a 2009 study found 22% of individuals with chronic SCI suffered from symptoms of unrecognized autonomic dysreflexia.[29] A significant proportion of individuals with autonomic dysreflexia remain asymptomatic.

Subtopic analysis of the top 100 articles in SCI (Fig. 2) revealed that articles on SCI complications were the most common. Papers describing SCI outcomes (neurologic, quality of life, and functional) were the second most common. Rehabilitation was the third most common subtopic. Acute management articles, in contrast, were second-least common out of the list of six possible subtopics. Together, these findings reflect the status of SCI as a condition with few options for acute interventions. Instead, the literature's most influential articles focus on the identification and management of SCI's many long-term consequences, such as motor disability and urinary and bowel symptoms. Decade-by-decade analysis of subtopics within the top 100 revealed the rise of experimental SCI therapy research and development in the 1990s. These articles include stem cell transplantation and brain-computer interface advances.

Study limitations

Our citation analysis has limitations. The present study did not include basic science articles or those applying to SCI due to non-traumatic causes, many of which have had significant effect on the field of traumatic SCI. Animal model and human cell line studies frequently lay the basic knowledge base for subsequent clinical investigations, and exclusion of such articles has inevitably left many critical paper in the field of SCI research unmentioned in the present work. Furthermore, multiple highly cited experimental and theoretical brain-computer interface studies were not included in the present study as the focus of this work was on clinical articles on traumatic spinal cord injury.[30] The literature contains a citation analysis of SCI research conducted without exclusion of basic science or review articles, which found 40% of the top 50 most highly-cited SCI papers identified were systematic reviews or meta-analyses.[19] Our study, in contrast, excluded review and meta-analyses. These results suggest that many of the most influential articles in SCI are early basic science studies and reviews of established or theoretical concepts. Future studies may consider focusing solely on original basic science research within the field of SCI in order to give these studies their due credit.

Citation analyses are inherently unable to detect recently published articles that are quickly gaining citations but have not yet accumulated enough to appear in the top 100. It is possible such papers will eventually surpass articles seen on the current top 100 list as their findings become more widely appreciated and incorporated into the literature. Citation count may be artificially inflated through the practice of self-citation, a bias in favor of studies produced by prolific authors. Finally, citation analysis is not necessarily a measure of influence of studies on clinical practice. It must be kept in mind that clinical studies may spur on new basic and translational work, amassing many citations, without having immediate practical correlates. Similarly, studies with questionable or debatable findings may accumulate many citations by inspiring negative critiques and reviews. Such "negative citations" point to the possibility that a given study's influence need not reflect practical findings. Rather, highly cited studies may exert influence through creation and direction of debate or discussion. Despite these limitations, we believe it is worthwhile to perform this research in order to more readily identify impactful research that has been recognized by the scientific community through increased citations; this study also highlights the clinicians and scientists who have made substantial contributions to the field.

Utilizing a two-step literature search method has been previously demonstrated to increase results for citation analysis compared to a single-step search,[11,31] our methods allow a more complete search capable of identifying a greater number of relevant articles. However, we do acknowledge limitations of citation analysis, in addition to those noted above, which have been put forth in previous publications.[32,33]

Conclusion

In this study, the top 100 most highly cited original clinical research articles in traumatic spinal cord injury, published between 1945 and 2016, were identified. The resulting collection of 100 articles points to progress in the field over the past 70 years and highlights those researchers whose work has been particularly influential.

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ORCID

Ronak H. Jani http://orcid.org/0000-0002-5687-6488

Arpan V. Prabhu http://orcid.org/0000-0002-9928-2911

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