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Searching the Footprints of Pioneers on Neurology: A Bibliometric Analysis

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Abstract
Background: We identify the most cited articles that have influenced the clinical practices of neurologists. ***Methods:*** We first analyzed the top 100 cited articles published in 50 neurology journals with high impact factors. We collected all of the original articles on clinical neurology published in all 554 medical journals. The Institute for Scientific Information Web of Science search tools were used to identify the top 100 cited articles in the database of Journal Citation Reports since 1950, which were then manually reviewed to discover their contents. ***Results:*** In the first part of analysis, the top 100 cited articles were all published in 17 journals, with 26 articles published in *Neurology*. The most frequent topic subject of neurodegeneration appeared in 40 articles. The second part of the analysis revealed that the top 100 cited articles were also all published in 17 journals, with 30 articles published in *New England Journal of Medicine*. In contrast to the first part of the analysis, stroke was the most frequent topic subject (in 38 articles). ***Conclusions:*** Our bibliometric analysis has yielded 2 detailed lists of the top 100 cited articles that were listed separately using different methods. This approach can provide information about the trends and academic achievements in the field of clinical neurology.

Introduction

Several bibliometric analyses have identified the most cited articles in various fields of clinical medicine [1–7]. Each of these reports has collected and reviewed the most cited works, which has influenced the practices of clinicians and the basic approaches applied in medical sciences [1–7]. However, unlike in other areas of clinical medicine, there have been no analyses of the citation classics in clinical neurology or the most cited works or contributions in clinical neurology. We presume that this is due to the difficulties associated with the requirement for confidentiality among clinical subjects in neurology.

Various clinical neurology journals focus on basic science, pathology, and experimental neurobiology, as well as on pure clinical neurology. Moreover, the articles in several clinical neurology journals seem to be cited by journals in other subject areas, including basic science, computational science, and neuroscience. These characteristics mean that it is not always possible to estimate or grade influential articles only by performing a citation analysis. Moreover, a considerable proportion of the researches in clinical neurology and neuroscience are characterized by overlapping study purposes or analysis methods, which means that articles on similar subjects can be

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published in clinical neurology and neuroscience journals.

Based on the above considerations, the analysis performed in this study used 2 different approaches. Because the boundaries between clinical neurology and neuroscience are sometimes ambiguous, we firstly analyzed the most cited articles from the top 50 journals on clinical neurology as classified by the Institute for Scientific Information (ISI). In the second part of the analysis, we analyzed the data confined to original contributions that potentially influence the clinical practices of neurologists.

The aim of this study was to identify the most cited works in the field of clinical neurology and review the landmark researches influencing and advancing clinical practices and related basic neuroscience.

Materials and Methods

We searched journals to select the most cited articles by utilizing the ISI Web of Science database (Thomson Reuters, New York, NY, USA). Based on the Science Edition 2014 of Journal Citation Reports, journals covering 3 topics were included: 192 journals on clinical neurology, 252 journals on neuroscience, and 110 journals on general and internal medicine. For each included journal, we retrieved all articles that were cited more than 100 times at the time of the search (February 2016) using the "cited reference search" facility of the expanded version of the Science Citation Index of the ISI Web of Science.

First Part of the Analysis: The Top 100 Cited Articles in Neurology Journals

In the first part of the analysis, we firstly selected the 50 top-ranked journals (based on impact factor) in clinical neurology from the ISI Web of Science (the titles of the journals are listed in online supplementary Table 1; for all online suppl. material, see www.karger.com/doi/10.1159/000455843). Only the journals focusing on clinical neurology were selected, and we excluded specific journals with relatively narrow focuses on pure neuroscience (i.e., *Neuroscientist* and *Brain Stimulation*), pathology, neurosurgery (i.e., *Journal of Neurotrauma*), psychiatry (or psychology), aphasiology (very specific topic), pain (general and broad), rehabilitation, or radiology. However, we included journals on sleep medicine, headache, clinical neurophysiology, and neurogenetics, and journals related to diagnostic tools used in clinical neurology (e.g., electrodiagnostic medicine).

Second Part of the Analysis: The 100 Most Influential Articles for the Clinical Practices of Neurologists

Articles were selected in the second part of the analysis from journals on clinical issues rather than theoretical topics. The selected articles had influenced the clinical practices of neurologists, especially in clinical diagnosis, epidemiological characteristics, key mechanisms of disease, therapeutic trials, and prognosis predictions. In addition, this part of the enrollment was confined to original articles (with clearly stated objectives or hypotheses and containing comprehensive methods and results sections), since many top-ranked articles might only be review articles, reports on consensus statements, or guidelines. Articles on meta-analyses or systematic reviews were also excluded.

The above-described procedure resulted in the top 100 cited articles being selected and reviewed in the first and second parts of the analysis, respectively. Two neurologists (J.S.B. and K.M.P.) manually reviewed the contents of articles independently. If there were any disagreements between these 2 authors about the selections, another 2 neurologists (J.-E.K. and Y.K.) determined the final selections. The following information about the articles was extracted: (i) year of publication, (ii) journal title, (iii) number of citations, (iv) authorship, (v) author affiliations, (vi) author nationalities, and (vii) topic subjects (categorized into stroke and atherosclerosis, neurodegeneration and cognitive impairment, multiple sclerosis [MS], movement disorders, epilepsy, headache, neuromuscular disorders, sleep disorders, or others). When the authors of an article had more than one affiliation, the department, institution, and country of origin were defined by the affiliation of the corresponding author.

This study did not need to be reviewed by an ethics committee since it performed a bibliometric analysis of existing published studies. Data are presented using descriptive statistics, and no tests of statistical significance were performed.

Results

We selected the top 100 cited articles for further analysis and ranked them according to the number of citations in the first and second parts of the analysis (Table 1; online suppl. Tables 2, 3). In the first part of the analysis, the most- and least-cited articles received 18,700 and 1,097 citations, respectively; the corresponding values in the second part of the analysis were 5,182 and 976 citations.

The top cited articles in the first part of the analysis were all published in 17 journals (Table 2). Fifty-seven articles were retrieved from 3 journals: *Neurology* (26 articles), *Annals of Neurology* (21 articles), and *Brain* (10 articles). The top cited articles in the second part of the analysis were also all published in 17 journals (Table 2). Sixty-eight articles were retrieved from 3 journals: *New England Journal of Medicine* (30 articles), *Lancet* (26 articles), and *JAMA – Journal of the America Medical Association* (12 articles). Table 3 lists the top-ranked institutions publishing more than 2 or more citation classics in the first and second parts of the analysis. The 12 institutions provided 2 or more top cited articles in the first part of the analysis. The institutions associated with the largest number of citation classics were Johns Hopkins University School of Medicine, UCLA School of Medicine (3 articles), Beth Israel Hospital (3 articles), and Boston University (3 articles) in the USA. In the second part of

Table 1. Top 10 cited articles

First part of the analysis			Second part of the analysis		
Rank	article	number of citations	rank	article	number of citations
1	McKhann G, Drachman D, Folstein M, et al: Clinical diagnosis of Alzheimer's disease. Neurology 1984;34:939–944.	18,700	1	Marler JR, Brott T, Broderick J, et al: Tissue plasminogen activator for acute ischemic stroke. N Engl J Med 1995;333:1581–1588.	5,182
2	Kurtzke JF: Rating neurologic impairment in multiple sclerosis: an expanded disability status scale (EDSS). Neurology 1983;33:1444–1452.	6,819	2	Taylor DW, Barnett HJM: Beneficial effect of carotid endarterectomy in symptomatic patients with high-grade carotid stenosis. N Engl J Med 1991;325:445–453.	4,021
3	Poser CM, Paty DW, Scheinberg L, et al: New diagnostic criteria for multiple sclerosis: guidelines for research protocols. Ann Neurol 1983;13:227–231.	6,307	3	Gent M, Beaumont D, Blanchard J, et al: A randomised, blinded, trial of clopidogrel versus aspirin in patients at risk of ischaemic events (CAPRIE). Lancet 1996;348:1329–1339.	3,375
4	Hoehn MM, Yahr MD: Parkinsonism: onset, progression and mortality. Neurology 1967;17:427–442.	6,293	4	O'Leary DH, Polak JF, Kronmal RA, et al: Carotid-artery intima and media thickness as a risk factor for myocardial infarction and stroke in older adults. N Engl J Med 1999;340:14–22.	2,862
5	Johns MW. A new method for measuring daytime sleepiness: the Epworth sleepiness scale. Sleep 1991;14:540–545.	5,106	5	MacMahon S, Peto R, Cutler J, et al: Blood pressure, stroke, and coronary heart disease. Part 1, prolonged differences in blood pressure: prospective observational studies corrected for the regression dilution bias. Lancet 1990;335:765–774.	2,847
6	Longa EZ, Weinstein PR, Carlson S, et al: Reversible middle cerebral artery occlusion without craniectomy in rats. Stroke 1989;20:84–91.	4,934	6	Walker MD, Marler JR, Goldstein M, et al: Endarterectomy for asymptomatic carotid artery stenosis. JAMA 1995;273:1421–1428.	2,752
7	Petersen RC, Smith GE, Waring SC, et al: Mild Cognitive Impairment Clinical Characterization and Outcome. Arch Neurol 1999;56:303–308.	4,138	7	Saunders AM, Strittmatter WJ, Schmechel D, et al: Association of apolipoprotein E allele epsilon 4 with late-onset familial and sporadic Alzheimer's disease. Neurology 1993;43:1467–1472.	2,666
8	Hughes AJ, Daniel SE, Kilford L, et al: Accuracy of clinical diagnosis of idiopathic Parkinson's disease: a clinico-pathological study of 100 cases. J Neurol Neurosurg Psychiatry 1992;55:181–184.	4,046	8	Wolf PA, Abbott RD, Kannel WB: Atrial fibrillation as an independent risk factor for stroke: the Framingham study. Stroke 1991;22:983–988.	2,612
9	McDonald WI, Compston A, Edan G, et al: Recommended diagnostic criteria for multiple sclerosis: guidelines from the International Panel on the diagnosis of multiple sclerosis. Ann Neurol 2001;50:121–127.	3,897	9	Go AS, Hylek EM, Phillips KA, et al: Prevalence of diagnosed atrial fibrillation in adults: national implications for rhythm management and stroke prevention: the AnTicoagulation and Risk Factors in Atrial Fibrillation (ATRIA) Study. JAMA 2001;285:2370–2375.	2,507
10	Adams HP Jr, Bendixen BH, Kappelle LJ, et al: Classification of subtype of acute ischemic stroke. Definitions for use in a multicenter clinical trial. Stroke 1993;24:35–41.	3,673	10	Bernard SA, Gray TW, Buist MD, et al: Treatment of comatose survivors of out-of-hospital cardiac arrest with induced hypothermia. N Engl J Med 2002;346:557–563.	2,502

Table 2. Top-ranked journals

First part of the analysis			Second part of the analysis		
Rank	journal	number of citation classics	Rank	journal	number of citation classics
1	*Neurology*	26	1	*New England Journal of Medicine*	30
2	*Annals of Neurology*	21	2	*Lancet*	26
3	*Brain*	10	3	*JAMA – Journal of the American Medical Association*	12
4	*Archives of Neurology*	9	4	*Neurology*	9
4	*Stroke*	9	5	*Annals of Neurology*	7
6	*Journal of the Neurological Sciences*	6	6	*Archives of Neurology*	3
7	*Alzheimers and Dementia*	3	7	*Brain*	2
7	*Clinical Neurophysiology*	3	7	*Journal of the Neurological Sciences*	2
7	*Journal of Neurology, Neurosurgery and Psychiatry*	3	9	*Annals of Internal Medicine*	1
10	*Epilepsia*	2	9	*Archives of Internal Medicine*	1
11	*Lancet Neurology*	2	9	*Brain*	1
12	*Sleep*	2	9	*Epilepsia*	1
14	*Amyotrophic Lateral Sclerosis and Frontotemporal Degeneration*	1	9	*Headache*	1
15	*Developmental Medicine and Child Neurology*	1	9	*Journal of Neuroscience*	1
16	*European Journal of Neuroscience*	1	9	*Journal of Neurosurgery*	1
17	*Sleep Medicine*	1	9	*Sleep Medicine Reviews*	1
			9	*Stroke*	1

Table 3. Top-ranked institutions publishing more than 2 citation classics

First part of the analysis					Second part of the analysis				
Rank	department	institution	location	number of citations	rank	department	institution	location	number of citations
1	Neurology	The Johns Hopkins University School of Medicine	Baltimore, USA	3	1	Clinical Neurosciences	Western General Hospital	Edinburgh, UK	5
2	Neurology	UCLA School of Medicine	Los Angeles, USA	3	2	Neurology	Columbia University	New York, USA	3
3	Neurology	Beth Israel Hospital	Boston, USA	3	3	Neurology	University of Heidelberg	Heidelberg, Germany	3
4	Neurology	Boston University	Boston, USA	3	4	Clinical Neurological Sciences	University of Western Ontario	Ontario, Canada	2

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Table 3. (continued)

First part of the analysis					Second part of the analysis				
Rank	department	institution	location	number of citations	rank	department	institution	location	number of citations
5	Neurology	University of Wisconsin Hospital and Clinics	Madison, USA	2	5	Neurology	Albert Einstein College of Medicine	Bronx, USA	2
6	Neurology	Cornell University Medical College, New York	New York, USA	2	6	Neurology	Boston University School of Medicine	Boston, USA	2
7	Neurology	Hôpital de la Salpêtrière	Paris, France	2	7	Neurology	Cornell University	New York, USA	2
8	Neurology	Manchester Royal Infirmary	Manchester, UK	2	8	Clinical and Biologic Neurosciences	Joseph Fourier University	Grenoble, France	2
9	Neurology	Mayo clinic	Rochester, USA	2	9	Neurology	Massachusetts General Hospital	Boston, USA	2
10	Neurology	Memorial Sloan-Kettering Cancer Center	New York, USA	2					
11	Neurology	National Institute of Neurological Disorders and Stroke	Bethesda, USA	2					
12	Neurosurgery	University of California	San Francisco, USA	2					

USA, United States of America; UK, United Kingdom.

the analysis, 9 institutions provided 2 or more top cited articles. The institution associated with the largest number of citation classics was Western General Hospital in the UK (5 articles), followed by Columbia University in the USA (3 articles), and University of Heidelberg in Germany (3 articles).

M.M. Mesulam, who was the first author of 6 articles, was the most frequently listed author in citation classics in the first part of the analysis, while W. Hacke was listed most frequently in the second part of the analysis (7 articles; online suppl. Table 4).

The top 100 cited articles in the first part of the analysis originated from institutions in 11 countries, with the USA contributing 68 articles, followed by the UK (15 articles), Netherlands (3 articles), Austria (3 articles), and Canada (3 articles; Table 4). In the second part of the analysis, the top 100 cited articles originated from institutions in 16 countries, with the USA contributing 55 articles, followed by the UK (13 articles) and Canada (9 articles; Table 4). These data indicate that more than two-thirds and one-half of the top 100 cited articles originated from the USA in the first and second parts of the analysis, respectively.

The years of publication are listed in Figure 1 for the first and second parts of the analysis. The publication years were concentrated in the 1990s in both parts. In the first part of the analysis, the earliest recorded article was published in 1965 and the most recent article was published in 2011; the corresponding years in the second part of the analysis were 1962 and 2010.

Neurodegeneration and cognitive impairment was the most frequent topic subject (40 articles), followed by MS (12 articles), stroke and atherosclerosis (11 articles), movement disorders (8 articles), sleep disorders (4 articles), epilepsy (3 articles), neuromuscular disorders (1 articles), and others (21 articles; 17 articles on neuroscience, 1 on cerebral palsy, 1 on acquired immunodeficiency syndrome [AIDS], 1 on neurofibromatosis, and

Table 4. Countries of origin associated with articles identified as citation classics

First part of the analysis			Second part of the analysis		
Rank	country	number of citation classics	rank	country	number of citation classics
1	USA	68	1	USA	55
2	UK	15	2	UK	13
3	Netherlands	3	3	Canada	9
4	Austria	3	4	France	4
8	Canada	3	5	Germany	4
5	France	2	6	Australia	3
6	Italy	2	7	Netherlands	3
7	Australia	1	8	Austria	1
9	Spain	1	9	Belgium	1
10	Belgium	1	10	Ireland	1
11	Denmark	1	11	New Zealand	1
			12	Scotland	1
			13	Sweden	1
			14	Japan	1
			15	Denmark	1
			16	Italy	1

USA, United States of America; UK, United Kingdom.

1 on neuromyelitis optica [NMO]). In contrast to the first part of the analysis, the most frequent topic subject in the second part of the analysis was stroke and atherosclerosis (38 articles), followed by neurodegeneration and cognitive impairment (27 articles), MS (9 articles), movement disorders (4 articles), epilepsy (3 articles), headache (2 articles), neuromuscular disorders (2 articles), sleep disorders (2 articles), and others (13 articles; 4 articles on AIDS, 3 on hypothermia, 1 on magnetic stimulation, 1 on myelopathy, 1 on Creutzfeldt-Jakob disease, 1 on reversible posterior leukoencephalopathy syndrome, 1 on NMO, and 1 on progressive multifocal leukoencephalopathy).

Discussion

In this study, we searched journals to select the most cited articles by utilizing the ISI database. The ISI Web of Science is a multidisciplinary database providing the most relevant bibliometric information from published scientific articles since 1950; it fully indexes more than 8,600 major journals across 176 topic subjects. The Web of Science is one of the important databases in ISI for analyzing citation counts and other information related to academic impact [8].

The first part of the analysis involved an essentially technical stratification based only on the rank after quantifying the numbers of citations in specifically selected journals. We chose this method because articles in the clinical neurology field are often difficult to classify into either clinical neurology or basic neuroscience, or into clinical neuroscience or basic neuroscience. The first part of the analysis revealed that the most cited journal was *Neurology*, which is the official journal of the American Academy of Neurology.

Many of the original articles included in the second part of the analysis reported on landmark studies of well-accepted theories that had also been mentioned in neurology textbooks. For example, the top-ranked article on a trial of intravenous recombinant tissue plasminogen activator (t-PA) changed the emergent clinical management of hyperacute stroke [9]. That study demonstrated that the intravenous administration of t-PA within 3 h of the onset of ischemic stroke improved the clinical outcome at 3 months. Additionally, the topic subject in 8 of the 10 top cited articles was stroke, which could be due to stroke being one of the most common neurological diseases.

However, there is a concern regarding the present citation analysis in the field of stroke, which should be addressed. Hypertension and diabetes mellitus (a prototype

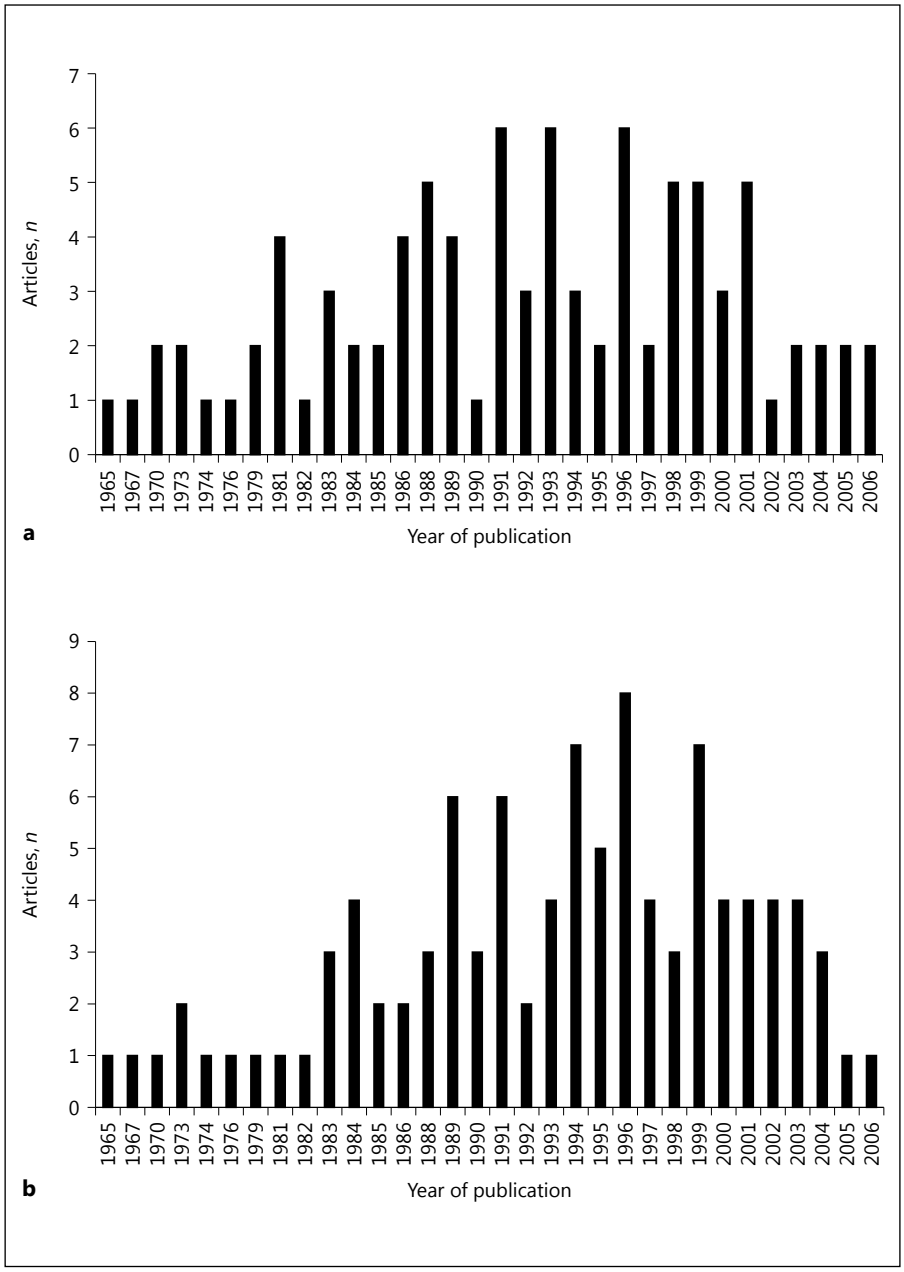

Fig. 1. Years of publication for the top 100 cited articles. **a** First part of analysis; **b** second part of analysis.

of chronic adult disease) are now well-known representative risk factors for ischemic stroke as well as other vascular events [10]. One of the main current goals of anticoagulation in atrial fibrillation is preventing cardioembolic stroke [11]. In this context, ischemic stroke is considered one of many possible types of vascular event, which might result in some overlap among various neurology, cardiology, and endocrinology journals. Because the present analysis was focused on influencing clinical decision-making by neurologists, some relevant articles on stroke published in cardiology and endocrinology journals might have been overlooked.

The second most common topic subject of the top 100 cited articles was neurodegeneration, including dementia. The most frequently cited research in the articles on dementia involved analyses of apolipoprotein E (APOE) alleles in several case reports of sporadic Alzheimer's dementia (AD) [12]. That study revealed that the APOE type-epsilon-4 allele was significantly associated with a series of probable sporadic AD patients, supporting the

involvement of this allele in the pathogenesis of late-onset familial and sporadic AD. The APOE type-epsilon-4 allele is now a well-known risk factor for AD among neurologists [13].

Most of the articles on MS, which was the third most common topic subject among the top 100 cited articles, reported on analyses of the effects of disease-modifying agents, such as interferon beta-1a, interferon beta-1b, and natalizumab [14–18], which are now well-accepted treatment strategies. There was one article on the pathogenic aquaporin-4 antibody for NMO [19]. All neurologists would now identify the aquaporin-4 antibody in the differential clinical diagnosis between MS and NMO [20].

There have been several citation classics on movement disorders. All of them reported researches of Parkinson disease (PD) [21–24], and they focused either on currently well-accepted or epoch-making trials such as deep brain stimulation or embryonic cell transplantation [21–23]. Two of the 4 articles on PD reported on studies involving deep brain stimulation [21, 22]. One of these studies found that electrical stimulation of the subthalamic nucleus was an effective treatment for advanced PD [21], with PD patients exhibiting improved motor function while off medication at 1 year after surgery. The other study demonstrated the long-term benefit of bilateral stimulation of the subthalamic nucleus in patients with advanced PD [22]. Deep brain stimulation is currently the most frequently performed surgical procedure for the patients with medically intractable symptoms of PD.

The top-ranked articles in the field of epilepsy reported on landmark studies regarding epilepsy treatment including pharmacotherapy and surgery [25, 26]. The top-ranked article on epilepsy reported an observational cohort study of newly diagnosed epilepsy suggesting that once a patient had not responded in trials of 2 appropriate antiepileptic drugs (AEDs), the probability of achieving seizure freedom with subsequent AEDs was only modest [26]. That article influenced a consensus regarding the definition of drug-resistant epilepsy proposed by the ad hoc Task Force of the ILAE commission, and provided general neurologists with guidelines for when to refer patients with epilepsy to an epilepsy center [27].

A particular finding of the present study was the identification of 4 AIDS-related articles among the top 100 cited articles [28–31]. Neurological disease occurs frequently in patients infected with the human immunodeficiency virus (HIV). Most of the articles are related to neurological complications or manifestations of AIDS [28, 29], with those of the nervous system consisting of infections, tumors, vascular complications, and cranial and peripheral neuropathies. These articles help neurologists to evaluate and manage HIV-infected patients. In addition, there were 3 articles on treatments for induced hypothermia in patients after resuscitation [32–34]. The top-ranked article on therapeutic hypothermia was authored by Bernard et al. [33] in 2002, which described a study involving patients assigned randomly to treatment with either hypothermia or normothermia. That study was the first to demonstrate that treatment with therapeutic hypothermia appeared to improve outcomes in patients with coma after resuscitation from cardiac arrest. Subsequent clinical trials have confirmed that therapeutic hypothermia improves survival and neurological recovery in comatose survivors of cardiac arrest [32, 34], which has led to therapeutic hypothermia being recommended as a standard care method for survivors of cardiac arrest [35].

Moreover, we identified other landmark researches influencing and advancing the clinical practices and relevant basic neuroscience in various fields. An article proposing that the pathogenic antibody of myasthenia gravis is an antibody for the acetylcholine receptor is one of the citation classics in the field of neuromuscular disorders [36]. In addition, an article about variant Creutzfeldt-Jakob disease originating from the UK was published in 1996, which was a hot social issue during that period and frequently cited in subsequent articles [37]. A riluzole trial in amyotrophic lateral sclerosis was nominated as a citation classic for the treatment trial of this notorious neurological disease [38]. That research, demonstrating that obstructive sleep apnea syndrome significantly increases the risk of stroke or death independently of other risk factors, may have led neurologists to actively engage in the diagnosis and treatment of obstructive sleep apnea syndrome [39].

There were inherent limitations in the current citation classics, such as debate regarding the value of citation rates [40]. In addition, the method of the use of the total citations favors older publications and older journals [40]. The citation of a scientific article usually follows a time lapse and is usually not cited until 1–2 years after publication, reaches a peak after 3–10 years, and then declines [40]. This normal life span of a publication shows that evaluating the rank and significance of recent publications is limited. However, reviewing articles that are cited frequently can provide information about the dominant areas of a discipline and highlight the growth of

particular fields as well as the work that influences clinical practices the most. In addition, the impact factor, which is a marker of citations, is widely used to indicate the importance of a given journal in its specific field of interest, and has emerged as a marker of the quality and rank of journals [40].

In conclusion, our bibliometric analysis has yielded 2 detailed lists of the top 100 cited articles that were listed separately using different methods. This approach can provide information about the trends and academic achievements in the field of clinical neurology.

Disclosure Statement

The authors have no conflicts of interest to disclose.

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