Our Efforts in Understanding Normal Pressure Hydrocephalus: Learning from the 100 Most Cited Articles by Bibliometric Analysis

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Key words
- Bibliometric
- Citations
- Idiopathic
- Normal pressure hydrocephalus
- NPH

Abbreviations and Acronyms
iNPH: idiopathic normal pressure hydrocephalus
NPH: Normal pressure hydrocephaluss

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BACKGROUND: **Normal pressure hydrocephalus (NPH) is a syndrome that was characterized several decades ago; however, its optimal diagnosis and management remain unclear. Our objective was to evaluate citation and bibliometric characteristics of the 100 most cited articles about NPH to better understand the state of research efforts in the field and where improvements may arise.**

METHODS: **Elsevier's Scopus database was searched for the 100 most cited articles that focused on NPH. Articles were characterized and various bibliometric parameters were compared. Categorical data were analyzed using Pearson χ^2, and continuous data were analyzed using either linear regression or a Student *t* test.**

RESULTS: **The 100 most cited articles were published between 1965 and 2014, from 16 unique countries in 38 unique journals. The most common outcome types of these articles were clinical ($n = 77$). Median number of citations and rate of citations were 114 citations and 5.9 citations/year since publication, respectively, with a significant inverse linear relationship between the 2 parameters ($P < 0.01$). The most common year of publication was 2002 ($n = 10$), and the most common country of origin was the United States ($n = 40$). Higher citation rates were associated with more recent articles ($P < 0.01$) and more authors ($P < 0.01$).**

CONCLUSIONS: **In the 100 most cited articles about NPH, there has been a distinct shift toward a more globalized effort in recent decades. The lack of more impactful articles in recent decades highlights that particular classic studies still penetrate practice and the possible need to reconsider our contemporary views on NPH to further advance the field.**

INTRODUCTION

Normal pressure hydrocephalus (NPH) is a syndrome with both radiographic and clinical components. The diagnosis requires ventriculomegaly, in the absence of increased intracranial pressure, accompanied by gait disturbance, cognitive impairment, and incontinence.[1,2] This diagnosis can be classified as either idiopathic NPH (iNPH) or secondary NPH, the primary difference being that iNPH has no obvious precipitant.[3] The traditional approach to management is surgical intervention with cerebrospinal fluid flow diversion (ventriculoperitoneal, ventriculoatrial, and lumboperitoneal shunting). Symptomatic resolution is not universal, but it is expected in more than half of all patients with NPH irrespective of their subtype, with some improvement in gait observed in 80%–85% of patients.[4]

Despite our progress in understanding NPH, the exact pathophysiology and optimal management of NPH remain elusive.[5] This deficit is likely to affect our ability to completely resolve NPH symptoms with current interventions. Correspondingly, the objective of this study was to analyze the bibliometrics of the 100 most cited articles about NPH to highlight the nature and content of the most impactful studies on this matter. In doing so, we can better understand how and where we have progressed in terms of our current understandings and suggest the optimal direction for our future efforts.

METHODS

Search Strategy

The search strategy was designed to capture all relevant published indexed articles referring to NPH. An electronic search was performed using Scopus in September 2019. Elsevier's Scopus contains indexed articles from approximately 22,000 journals and captures one of the widest range of scientific articles among all electronic databases, with articles dating back to the 1800s in some cases.[6] The database was searched and screened for "normal pressure hydrocephalus" or "NPH" in the title, abstract, and keywords. Articles were sorted into descending citation count order, and the first 100 articles pertinent to investigating NPH or reporting its outcomes were selected. Articles that referenced NPH only for context rather than substance were not included. Any discrepancies were resolved by discussion and consensus

Table 1. Ten Most Cited Articles About Normal Pressure Hydrocephalus in the Literature

Rank	Citations		Year	Authors	Title	Journal	Country	PubMed ID
	Count (n)	Rate (n/year)						
1	870	16.1	1965	Adams RD, Fisher CM, Hakim S, Ojemann RG, Sweet WH	Symptomatic occult hydrocephalus with normal cerebrospinal-fluid pressure—a treatable syndrome	*New England Journal of Medicine*	United States	14303656
2	706	13.1	1965	Hakim S, Adams RD	The special clinical problem of symptomatic hydrocephalus with normal cerebrospinal fluid pressure. observations on cerebrospinal fluid hydrodynamics	*Journal of the Neurological Sciences*	Colombia	5889177
3	282	15.7	2001	Hebb AO, Cusimano MD	Idiopathic normal pressure hydrocephalus: a systematic review of diagnosis and outcome	*Neurosurgery*	Canada	11846911
4	250	10.9	1996	Bradley Jr WG, Scalzo D, Queralt J, Nitz WN, Atkinson DJ, Wong P	Normal-pressure hydrocephalus: evaluation with cerebrospinal fluid flow measurements at MR imaging	*Radiology*	United States	8596861
5	237	5.5	1976	Hakim S, Venegas JG, Burton JD	The physics of the cranial cavity. hydrocephalus and normal pressure hydrocephalus: mechanical interpretation and mathematical model	*Surgical Neurology*	Colombia	1257894
6	232	6.3	1982	Børgesen SE, Gjerris F	The predictive value of conductance to outflow of CSF in normal pressure hydrocephalus	*Brain*	Denmark	7066675
7	226	15.1	2004	Greitz D	Radiological assessment of hydrocephalus: new theories and implications for therapy	*Neurosurgical Review*	Sweden	15164255
8	226	8.4	1992	Vanneste J, Augustijn P, Dirven C, Tan WF, Goedhart ZD	Shunting normal-pressure hydrocephalus: do the benefits outweigh the risks?: a multicenter study and literature review	*Neurology*	Netherlands	1734324
9	207	9.4	1997	Boon AJW, Tans JTJ, Delwel EJ, Egeler-Peerdeman SM, Hanlo PW, Wurzer HAL, Avezaat CJJ, De Jong DA, Gooskens RHJM, Hermans J	Dutch Normal-Pressure Hydrocephalus Study: prediction of outcome after shunting by resistance to outflow of cerebrospinal fluid	*Journal of Neurosurgery*	Netherlands	9347976
10	205	10.8	2000	Vanneste JAL	Diagnosis and management of normal-pressure hydrocephalus	*Journal of Neurology*	Netherlands	10701891

between authors. Publications were limited to the English language.

Data Extraction

The following validated bibliometric parameters were extracted: article title, authors, journal, Scopus citations, year, citation count, number of authors, first and senior author names, and country of corresponding author. In the case of studies originating from the United States, state was also recorded.

Statistical Analysis

Characteristics of included studies were evaluated for significant trends in relation to overall citation count and rate. To compare dichotomous groups, categorical data were analyzed using a Pearson χ^2, and continuous data were analyzed using a Student t test. In cases of associating continuous citation rate with continuous citation count rank, a linear regression was performed. Statistical significance was set at 2-sided $P < 0.05$. All statistical analyses were performed using STATA 14.1 (StataCorp LLC, College Station, Texas, USA).

RESULTS

Search Results

An initial search of Scopus yielded 4425 articles. After ranking by citation count and removing irrelevant articles, the 100 most cited articles were selected. The 10 most cited articles are listed in Table 1, and the entire cohort is detailed in Supplementary Table 1.

Overall Characteristics

The 100 most cited articles were published between 1965 and 2014, from 16 unique countries in 38 unique journals. The median number of citations and rate of citations were 114 citations (range, 80–870) and 5.9 citations/year (range, 2.0–27.4), respectively. There were 74 unique first authors and 78 unique senior authors. Fourteen articles were published under the open-access model. In terms of article focus, 77 studies focused on clinical outcomes, 19 focused on radiographic outcomes, and 4 focused on basic science outcomes. In terms of study design, there were 67 retrospective series, 14 reviews, 12 prospective series, 4 basic science studies, and 3 guideline articles. There was 1 single randomized controlled trial among the prospective series by Boon et al.[7] from the Netherlands in 1998 titled "Dutch normal-pressure hydrocephalus study: randomized comparison of low- and medium-pressure shunts."

Citations

A significant inverse linear relationship between citation count rank and citation rate was appreciated (slope, −0.1; $P < 0.01$) (Figure 1). The most cited article by count was the seminal clinical series by Hakim and Adams1 from Harvard Medical School, Boston, Massachusetts, USA. Published in 1965 and titled "Symptomatic occult hydrocephalus with normal cerebrospinal fluid pressure—a treatable syndrome," this *New England Journal of Medicine* article has 870 citations to date. In this work, the investigators posited via a case series a diagnosis that would later become known as NPH. The most cited article by rate (27.4 citations/year) was a series of clinical guidelines by Mori et al.[8] from the University of Tohoku, Sendai, Miyag, Japan, published in 2012 titled "Guidelines for management of idiopathic normal pressure hydrocephalus: second edition" (*Neurologia Medico-Chirurgica (Tokyo)*). These guidelines were created by a multidisciplinary expert working group of the Japanese Society of Normal Pressure Hydrocephalus and disseminated to the international community in this English translation article.

Authors

The median number of authors was 4 (range, 1–15). The article with the greatest number of authors was "Guidelines for management of idiopathic normal pressure hydrocephalus: second edition" by Mori et al.,[8] with 15 contributing authors. Twelve single-author articles were included in the pool of 100 articles, from 6 unique countries with a median citation count of 113 (range, 83–226). In terms of first authorship, the greatest number of contributions to the 100 articles were 5 articles[3,9-12] by Bradley Jr. from the United States. In terms of senior authorship, Wikkelso from Sweden contributed 6 articles,[13-18] which was the greatest number by the same author.

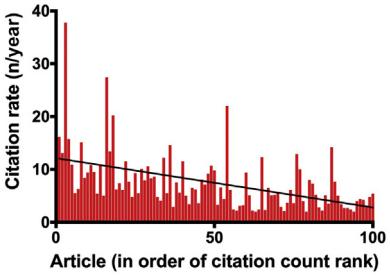

Figure 1. Distribution of citation rate (n/year) of 100 most cited articles about normal pressure hydrocephalus across order of decreasing citation count, with linear regression (line) showing significant inverse relationship between the 2 parameters (slope, −0.1; $P < 0.01$).

Year of Publication

The 100 most cited articles were published between 1965 and 2014, with the median represented year being 1999 (Figure 2). The earliest article was the seminal clinical series by Hakim and Adams[1] from Harvard Medical School, Boston, Massachusetts, USA published in 1965, which also had the most citations to date. The greatest number of highly cited articles published in a single year was 10, which occurred in 2002.

Countries of Correspondence

Of the 16 unique countries that were listed as country of correspondence (Supplementary Table 2 and Figure 3A), the United States made most contributions to the 100 articles, with 40 articles; Massachusetts ($n = 10$), California ($n = 6$), and Minnesota ($n = 5$) were the 3 most contributory states (Supplementary Table 3 and Figure 3B).

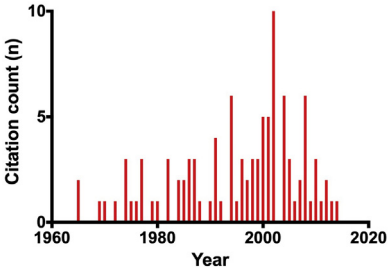

Figure 2. Distribution by year of 100 most cited articles about normal pressure hydrocephalus, which appeared from 1965 to 2014.

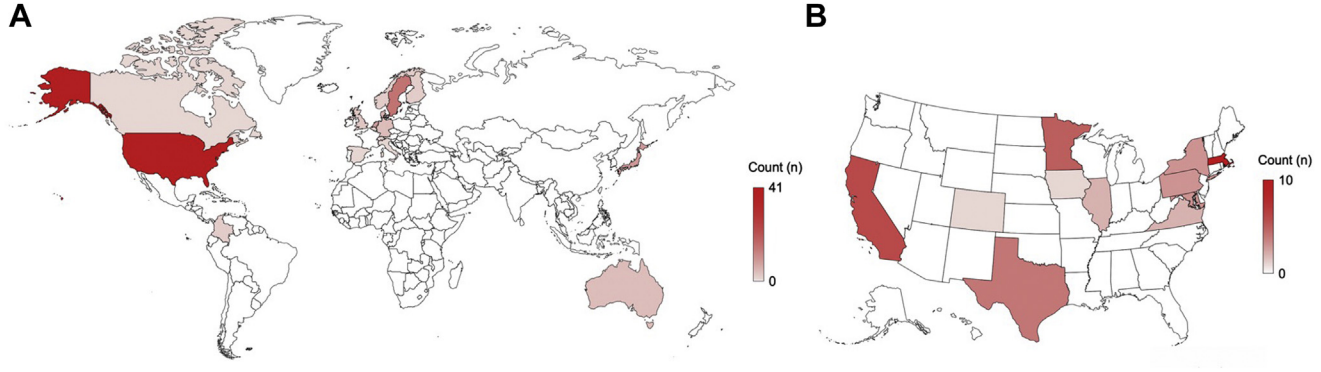

Figure 3. Geographic distribution of 100 most cited articles about normal pressure hydrocephalus (**A**) worldwide and (**B**) in the United States (n = 40) by state.

Of the remaining countries, those that contributed ≥5 articles were Sweden (n = 15), Japan (n = 9), the Netherlands (n = 8), and Denmark (n = 5) (Figure 3B). Articles from outside the United States were statistically more recently published than from inside the United States, with mean publication years of 1999 and 1989, respectively (P < 0.01).

Journals

Of the 38 unique journals in which the 100 most cited articles were published (Supplementary Table 4), the most common journal was *Neurosurgery*, with 16 articles. Of the remaining journals, those that published ≥5 articles were *Journal of Neurosurgery* (n = 12), *Journal of Neurology Neurosurgery and Psychiatry* (n = 8), *Acta Neurochirurgica (Wien)* (n = 6), *American Journal of Neuroradiology* (n = 6), *Neurology* (n = 6), and *Acta Neurologica Scandinavica* (n = 5).

Citation Comparisons

Citation counts and rates were compared (Table 2). Overall citation count was not associated with any tested characteristic. In terms of citation rate, more recent articles (P < 0.01) with more authors (P < 0.01) were significantly associated with higher citation rates. Furthermore, articles from outside the United States (P = 0.01) and published under an open-access model (P = 0.02) had significantly higher citation rates.

DISCUSSION

Our goal in analyzing the 100 most cited articles about NPH was to identify and better understand the nature of the most impactful contributions to the understanding of NPH. The articles were most commonly published in neurosurgical journals, reflecting the neurosurgical nature of managing this syndrome. Analysis of citations yields 2 conclusions: 1) the seminal works by Hakim and Adams continue to penetrate our clinical practice and 2) our interest in optimizing and personalizing NPH treatment dictates much of the current research efforts, which are principally clinical and radiographic. Although the United States has contributed the largest number of articles to this list, our analysis also indicates that the study of NPH is global, with many other countries having made impactful contributions to the literature in more recent decades and with higher citation rates.

When Hakim and Adams[1] first described NPH in their seminal 1965 series, definitions would have classified only 2 of the 6 patients described as having iNPH. One decade later the occurrence of NPH in adults without obvious cause became known as iNPH.[2] Despite the greater awareness of the idiopathic subtype in clinical practice, the preliminary studies[2,19] that established it as an NPH subtype do not feature in the 100 most cited articles. This finding may suggest that the clinical emphasis on NPH in the literature considers NPH more as a collective diagnosis of both idiopathic and secondary subtypes, rather than as separate entities. Although ventriculomegaly is requisite for both NPH subtypes, the causes,

Table 2. Citation Comparisons of the 100 Most Cited Articles on Hydrocephalus

Comparison	*Citation Count (n)**	*P*	Citation Rate (n/year)*	*P*
Continuous data				
Year	−2.7	<0.01	0.2	<0.01
Number of authors	−2.7	0.45	0.4	<0.01
Categorical data				
Clinical versus not	141 versus 134	0.78	7.0 versus 7.4	0.74
Neurosurgery (journal) versus not	122 versus 143	0.47	6.8 versus 7.2	0.76
United States versus not	140 versus 140	0.98	5.7 versus 8.1	0.01
Open access versus not	128 versus 142	0.67	9.7 versus 6.7	0.02

*Continuous and categorical data presented and regression slope and mean values, respectively.

treatments, and management can often be different, and it is highly likely that future impactful studies will tease out these differences.[20]

The clinical and neurosurgical management of NPH continues to be the focus of many of the impactful articles, based on their topic and journal of publication. The management guidelines[8] published by the Japanese Society of Normal Pressure Hydrocephalus are testament to this statement, because it has the highest citation rate of all included articles. Further evidence of clinical management being the dominant focus of the NPH literature is the fact that more than three quarters of the 100 most cited articles described clinical outcomes and their prognostication. In addition to radiographic ventriculomegaly used to describe NPH, there is as well the classically taught symptomatic triad of cognitive impairment, gait disturbance, and urinary incontinence.[1] Given the vast differential diagnoses from which these individual symptoms may manifest, it may explain in part why there are several clinical and radiographic studies making the most impact currently, because all efforts should be made to ensure that the presenting clinical diagnosis is not another driving pathology or disease (e.g., Parkinson disease [gait] or Alzheimer disease [cognitive impairment]).[5]

What perhaps remains the most interesting aspect of this analysis is the direction that the impactful NPH literature has taken since 1965. Most of the early impactful articles[21,22] originated from the United States led by Hakim and Adams, which is not an unexpected trend in the broader neurosurgical field. In contrast, more recent impactful articles have originated from outside the United States, with pockets in Scandinavia, Japan, and Western Europe all key contributors, supported by the fact that Wikkelso from Sweden has been senior author on the most articles ($n = 6$), and the management guidelines article by the Japanese group was the article with the highest citation rate. This globalization of impactful contributions to the NPH literature more recently is an exciting prospect, because future NPH studies and clinical trials may be better positioned for more statistical power and more clinical rigor via international collaborations.

A remarkable finding in our analysis is that the peak year of publication for these 100 articles was more than a decade ago. It seems that gains from impactful contributions have become smaller and stalled somewhat compared with the late 1990s and early 2000s, when scientific investigation of NPH mechanisms were really flourishing.[5] This finding could suggest that we have learned all we can learn about NPH under the current neurosurgical paradigms and that further progress may require a novel series of alterations to how we perceive NPH. Perhaps NPH is a constellation of concomitant diagnoses requiring individual management rather than a unified syndrome requiring a single therapeutic intervention. Future impactful articles will likely shed new light on these possibilities.

It is becoming clearer that the pathophysiology of iNPH is multifactorial in its development as a result of self-reinforcing derangements of cerebrospinal fluid dynamics, simultaneously involving multiple aspects of its production, kinetics, and reabsorption.[23] This shift in our understanding from the more linear model first suggested by Hakim and Adams[1] shows a paradigmatic evolution in our understanding. One could interpret the lack of difference in citation rates between clinical studies and nonclinical studies as a sign that we are continuing to value both perspectives as we try to elucidate the exact mechanisms of this disease.

We hypothesize that other paradigm shifts are likely as we advance our understanding of NPH more. The emergence of molecular biomarkers in the cerebrospinal fluid and gene sequencing to diagnose and prognosticate other neurodegenerative diseases may become more relevant for NPH differential diagnosis.[24-26] New technologies or techniques may inform our decision to intervene or observe, and if intervening, by which technique. Although third ventriculostomy has not proved beneficial for treatment of iNPH, it is useful for treatment of arrested congenital hydrocephalus. For iNPH, use of programmable valves and antisiphon devices has increased recently, with some improvements in clinical outcomes.[27,28] All these avenues require further exploration der to further improve NPH management in the future.

Although there has only been 1 highly cited randomized controlled trial,[7] it is our hope that future studies conducted in a similar manner will affect our understanding of these aspects and others. Although difficulties exist as to institutional approval and time to achieve statistical cohorts prospectively, such studies will provide the highest level of evidence to interpret clinical NPH causes and outcomes. In terms of how efforts have become more multi-institutional and multidisciplinary, the formation of multiple national hydrocephalus interest groups, such as the Japanese Society of Normal Pressure Hydrocephalus and the Hydrocephalus Clinical Research Network in the United States, will undoubtedly lead to greater collaborative efforts in both maintaining contemporary management guidelines as already mentioned[8] as well as improving research opportunities to improve our understanding of this disease clinically and scientifically.

There are limitations to the current study. First, the use of citations to indicate impact is imperfect. Citations may be more representative of academic impact than of clinical or translational use. However, most of the 100 most cited articles were clinical (and/or radiographic), arguing that citation count is likely relatively congruent to clinical usefulness. Second, many other bibliometric measures exist, including journal impact factor, m-quotient, and author h-index, which can modulate the exposure of articles and therefore affect how likely they are to impact wider audiences. The merits of using citation count versus other possible measures of impact remains a subject of debate.[29] In particular, whether or not 2-year citation count since publication is potentially more representative of impact remains to be seen, which such data beyond the scope of our database. Consequently, the granular results of this analysis should be interpreted with caution in terms of absolute article impact, because what constitutes an article worthy of citation largely depends on the author doing the citing. Because of the necessary passage of time to acquire literature citations, it is unclear if the presented trends truly reflect trends in the

recent literature with respect to impact. We anticipate a greater shift in impactful articles toward more novel approaches and considerations as they become more accepted. Future bibliometric analyses with more mature data will confirm or refute our conclusions.

CONCLUSIONS

Many impactful articles have appeared in the literature and have led to our understanding of NPH. These articles have their roots in the United States, with Hakim and Adams more than 50 years ago, since spreading across the world. There are bibliometric and geographic niches within the 100 most cited articles about NPH, and these inform us of how our current understanding has developed. The best clinical diagnostic criteria and management strategies for NPH remain an ongoing effort, and we see that future prospective, carefully designed, and collaborative studies will help us define these elements as we consider improvements to the management and mechanistic paradigms.

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Supplementary Table 1. Complete List of 100-Most Cited Articles About Hydrocephalus

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1	870	16.1	1965	Adams RD, Fisher CM, Hakim S, Ojemann RG, Sweet WH	Symptomatic occult hydrocephalus with normal cerebrospinal fluid pressure—a treatable syndrome	*New England Journal of Medicine*	United States	14303656
2	706	13.1	1965	Hakim S, Adams RD	The special clinical problem of symptomatic hydrocephalus with normal cerebrospinal fluid pressure. Observations on cerebrospinal fluid hydrodynamics	*Journal of the Neurological Sciences*	Colombia	5889177
3	282	15.7	2001	Hebb AO, Cusimano MD	Idiopathic normal pressure hydrocephalus: a systematic review of diagnosis and outcome	*Neurosurgery*	Canada	11846911
4	250	10.9	1996	Bradley WG Jr, Scalzo D, Queralt J, Nitz WN, Atkinson DJ, Wong P	Normal-pressure hydrocephalus: evaluation with cerebrospinal fluid flow measurements at MR imaging	*Radiology*	United States	8596861
5	237	5.5	1976	Hakim S, Venegas JG, Burton JD	The physics of the cranial cavity. Hydrocephalus and normal pressure hydrocephalus: mechanical interpretation and mathematical model	*Surgical Neurology*	Colombia	1257894
6	232	6.3	1982	Børgesen SE, Gjerris F	The predictive value of conductance to outflow of CSF in normal pressure hydrocephalus	*Brain*	Denmark	7066675
7	226	15.1	2004	Greitz D	Radiological assessment of hydrocephalus: new theories and implications for therapy	*Neurosurgical Review*	Sweden	15164255
8	226	8.4	1992	Vanneste J, Augustijn P, Dirven C, Tan WF, Goedhart ZD	Shunting normal—pressure hydrocephalus: do the benefits outweigh the risks?: A multicenter study and literature review	*Neurology*	Netherlands	1734324

CSF, cerebrospinal fluid.

Continues

Supplementary Table 1. Continued

Rank	Citations: Count (n)	Citations: Rate (n/year)	Year	Authors	Title	Journal	Country	PubMed ID
9	207	9.4	1997	Boon AJW, Tans JTJ, Delwel EJ, Egeler-Peerdeman SM, Hanlo PW, Wurzer HAL, Avezaat CJJ, De Jong DA, Gooskens RHJM, Hermans J	Dutch Normal-Pressure Hydrocephalus Study: prediction of outcome after shunting by resistance to outflow of cerebrospinal fluid	*Journal of Neurosurgery*	Netherlands	9347976
10	205	10.8	2000	Vanneste JAL	Diagnosis and management of normal-pressure hydrocephalus	*Journal of Neurology*	Netherlands	10701891
11	199	9.5	1998	Kitagaki H, Mori E, Ishii K, Yamaji S, Hirono N, Imamura T	CSF spaces in idiopathic normal pressure hydrocephalus: morphology and volumetry	*American Journal of Neuroradiology*	Japan	9726467
12	198	5.4	1982	Fisher CM	Hydrocephalus as a cause of disturbances of gait in the elderly	*Neurology*	United States	6890641
13	196	10.9	2001	Stolze H, Kuhtz-Buschbeck JP, Drücke H, Jöhnk K, Illert M, Deuschl G	Comparative analysis of the gait disorder of normal pressure hydrocephalus and Parkinson's disease	*Journal of Neurology Neurosurgery and Psychiatry*	Germany	11181848
14	194	5.0	1980	Black McL P	Idiopathic normal-pressure hydrocephalus. Results of shunting in 62 patients	*Journal of Neurosurgery*	United States	7359191
15	192	27.4	2012	Mori E, Ishikawa M, Kato T, Kazui H, Miyake H, Miyajima M, Nakajima M, Hashimoto M, Kuriyama N, Tokuda T, Ishii K, Kaijima M, Hirata Y, Saito M, Arai H	Guidelines for management of idiopathic normal pressure hydrocephalus: second edition	*Neurologia Medico-Chirurgica (Tokyo)*	Japan	23183074
16	187	13.4	2005	Marmarou A, Young HF, Aygok GA, Sawauchi S, Tsuji O, Yamamoto T, Dunbar J	Diagnosis and management of idiopathic normal-pressure hydrocephalus: a prospective study in 151 patients	*Journal of Neurosurgery*	United States	16028756
17	182	20.2	2010	Hashimoto M, Ishikawa M, Mori E, Kuwana N	Diagnosis of idiopathic normal pressure hydrocephalus is supported by MRI-based scheme: a prospective cohort study	*Cerebrospinal Fluid Research*	Japan	21040519

18	173	6.2	1991	Bradley WG Jr, Whittemore AR, Watanabe AS, Davis SJ, Teresi LM, Homyak M	Association of deep white matter infarction with chronic communicating hydrocephalus: implications regarding the possible origin of normal-pressure hydrocephalus	*American Journal of Neuroradiology*	United States	1899515
19	171	7.4	1996	Krauss JK, Regel JP, Vach W, Droste DW, Borremans JJ, Mergner T	Vascular risk factors and arteriosclerotic disease in idiopathic normal-pressure hydrocephalus of the elderly	*Stroke*	United States	8553398
20	171	6.1	1991	Larsson A, Wikkelsö C, Bilting M, Stephensen H	Clinical parameters in 74 consecutive patients shunt operated for normal pressure hydrocephalus	*Acta Neurologica Scandinavica*	Sweden	1792852
21	161	11.5	2005	McGirt MJ, Woodworth G, Coon AL, Thomas G, Williams MA, Rigamonti D	Diagnosis, treatment, and analysis of long-term outcomes in idiopathic normal-pressure hydrocephalus	*Neurosurgery*	United States	16239882
22	161	7.7	1998	Boon AJW, Tans JTJ, Delwel EJ, Egeler-Peerdeman SM, Hanlo PW, Wurzer HAL, Avezaat CJJ, De Jong DA, Gooskens RHJM, Hermans J	Dutch Normal-Pressure Hydrocephalus Study: randomized comparison of low- and medium-pressure shunts	*Journal of Neurosurgery*	Netherlands	9488303
23	159	4.8	1986	Bradley WG Jr, Kortman KE, Burgoyne B	Flowing cerebrospinal fluid in normal and hydrocephalic states: appearance on MR images	*Radiology*	United States	3704142
24	158	9.3	2002	Newman WD, Hollman AS, Dutton GN, Carachi R	Measurement of optic nerve sheath diameter by ultrasound: a means of detecting acute raised intracranial pressure in hydrocephalus	*British Journal of Ophthalmology*	UK	12234888
25	154	5.5	1991	Bradley WG Jr, Whittemore AR, Kortman KE, Watanabe AS, Homyak M, Teresi LM, Davis SJ	Marked cerebrospinal fluid void: indicator of successful shunt in patients with suspected normal-pressure hydrocephalus	*Radiology*	United States	1987609
26	152	10.1	2004	Momjian S, Owler BK, Czosnyka Z, Czosnyka M, Pena A, Pickard JD	Pattern of white matter regional cerebral blood flow and autoregulation in normal pressure hydrocephalus	*Brain*	UK	15033897

CSF, cerebrospinal fluid.

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Supplementary Table 1. Continued

Rank	Citations: Count (n)	Citations: Rate (n/year)	Year	Authors	Title	Journal	Country	PubMed ID
27	150	7.9	2000	Zemack G, Romner B	Seven years of clinical experience with the programmable Codman Hakim valve: a retrospective study of 583 patients	*Journal of Neurosurgery*	Sweden	10839253
28	149	10.6	2005	Marmarou A, Bergsneider M, Relkin N, Klinge P, Black PMcL	INPH guidelines, part I: development of guidelines for idiopathic normal-pressure hydrocephalus: introduction	*Neurosurgery*	United States	16160426
29	149	8.3	2001	Loth F, Yardimci MA, Alperin N	Hydrodynamic modeling of cerebrospinal fluid motion within the spinal cavity	*Journal of Biomechanical Engineering*	United States	11277305
30	147	8.6	2002	Walchenbach R, Geiger E, Thomeer RTWM, Vanneste JAL	The value of temporary external lumbar CSF drainage in predicting the outcome of shunting on normal pressure hydrocephalus	*Journal of Neurology Neurosurgery and Psychiatry*	Netherlands	11909911
31	139	4.8	1990	Chapman PH, Cosman ER, Arnold MA, Portnoy HD, Sklar F	The relationship between ventricular fluid pressure and body position in normal subjects and subjects with shunts: a telemetric study	*Neurosurgery*	United States	2308665
32	135	4.1	1986	Wikkelsö C, Andersson H, Blomstrand C, Lindqvist G, Svendsen P	Predictive value of the cerebrospinal fluid tap-test	*Acta Neurologica Scandinavica*	Sweden	3751498
33	133	5.5	1995	Aschoff A, Kremer P, Benesch C, Fruh K, Klank A, Kunze S	Overdrainage and shunt technology—a critical comparison of programmable, hydrostatic and variable-resistance valves and flow-reducing devices	*Child's Nervous System*	Germany	7621479
34	131	14.6	2010	Eide PK, Sorteberg W	Diagnostic intracranial pressure monitoring and surgical management in idiopathic normal pressure hydrocephalus: a 6-Year review of 214 patients	*Neurosurgery*	Norway	20023540

35	129	2.9	1974	Stein SC, Langfitt TW	Normal pressure hydrocephalus. Predicting the results of cerebrospinal fluid shunting	*Journal of Neurosurgery*	United States	4479249
36	128	7.5	2002	Luetmer PH, Huston J, Friedman JA, Dixon GR, Petersen RC, Jack CR, McClelland RL, Ebersold MJ, Milhorat TH, Hodge CJ Jr	Measurement of cerebrospinal fluid flow at the cerebral aqueduct by use of phase-contrast magnetic resonance imaging: technique validation and utility in diagnosing idiopathic normal pressure hydrocephalus	*Neurosurgery*	United States	11841721
37	128	5.6	1996	Krauss JK, Droste DW, Vach W, Regel JP, Orszagh M, Borremans JJ, Tietz A, Seeger W	Cerebrospinal fluid shunting in idiopathic normal-pressure hydrocephalus of the elderly: effect of periventricular and deep white matter lesions	*Neurosurgery*	United States	8832666
38	127	11.5	2008	Ishikawa M, Hashimoto M, Kuwana N, Mori E, Miyake H, Wachi A, Takeuchi T, Kazui H, Koyama H	Guidelines for management of idiopathic normal pressure hydrocephalus: Guidelines from the Guidelines Committee of Idiopathic Normal Pressure Hydrocephalus, the Japanese Society of Normal Pressure Hydrocephalus	*Neurologia Medico-Chirurgica (Tokyo)*	Japan	18408356
39	125	5.0	1994	Raftopoulos C, Deleval J, Chaskis C, Leonard A, Cantraine F, Desmyttere F, Clarysse S, Brotchi J	Cognitive recovery in idiopathic normal pressure hydrocephalus: a prospective study	*Neurosurgery*	Belgium	7528358
40	125	3.4	1982	Wikkelso C, Andersson H, Blomstrand C, Lindqvist G	The clinical effect of lumbar puncture in normal pressure hydrocephalus	*Journal of Neurology Neurosurgery and Psychiatry*	Sweden	7062072
41	124	6.5	2000	Bateman GA	Vascular compliance in normal pressure hydrocephalus	*American Journal of Neuroradiology*	Australia	11039334
42	123	6.2	1999	Boon AJW, Tans JTJ, Delwel EJ, Egeler-Peerdeman SM, Patrick WH, Wurzer HAL, Hermans J	Dutch Normal-Pressure Hydrocephalus Study: the role of cerebrovascular disease	*Journal of Neurosurgery*	Netherlands	9950492
43	123	3.6	1985	Petersen RC, Mokri B, Laws ER Jr	Surgical treatment of idiopathic hydrocephalus in elderly patients	*Neurology*	United States	3974888

CSF, cerebrospinal fluid.

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Supplementary Table 1. Continued

Rank	Citations: Count (n)	Citations: Rate (n/year)	Year	Authors	Title	Journal	Country	PubMed ID
44	121	8.1	2004	Czosnyka M, Czosnyka Z, Momjian S, Pickard JD	Cerebrospinal fluid dynamics	*Physiological Measurement*	UK	15535175
45	121	7.1	2002	Savolainen S, Hurskainen H, Paljärvi L, Alafuzoff I, Vapalahti M	Five-year outcome of normal pressure hydrocephalus with or without a shunt: predictive value of the clinical signs, neuropsychological evaluation and infusion test	*Acta Neurochirurgica (Wien)*	Finland	12111484
46	119	9.2	2006	Gallia GL, Rigamonti D, Williams MA	The diagnosis and treatment of idiopathic normal pressure hydrocephalus	*Nature Clinical Practice Neurology*	United States	16932588
47	118	10.7	2008	Brean A, Eide PK	Prevalence of probable idiopathic normal pressure hydrocephalus in a Norwegian population	*Acta Neurologica Scandinavica*	Norway	18205881
48	118	9.8	2007	Kubo Y, Kazui H, Yoshida T, Kito Y, Kimura N, Tokunaga H, Ogino A, Miyake H, Ishikawa M, Takeda M	Validation of grading scale for evaluating symptoms of idiopathic normal-pressure hydrocephalus	*Dementia and Geriatric Cognitive Disorders*	Japan	18025828
49	115	3.3	1984	Børgesen SE	Conductance to outflow of CSF in normal pressure hydrocephalus	*Acta Neurochirurgica (Wien)*	Denmark	6731051
50	113	6.6	2002	Kahlon B, Sundbärg G, Rehncrona S	Comparison between the lumbar infusion and CSF tap tests to predict outcome after shunt surgery in suspected normal pressure hydrocephalus	*Journal of Neurology Neurosurgery and Psychiatry*	Sweden	12438477
51	111	4.4	1994	Vanneste JAL	Three decades of normal pressure hydrocephalus: are we wiser now?	*Journal of Neurology Neurosurgery and Psychiatry*	Netherlands	8089664
52	110	22.0	2014	Jaraj D, Rabiei K, Marlow T, Jensen C, Skoog I, Wikkelsø C	Prevalence of idiopathic normal-pressure hydrocephalus	*Neurology*	Sweden	24682964

53	109	6.1	2001	Mori K	Management of idiopathic normal-pressure hydrocephalus: a multiinstitutional study conducted in Japan	*Journal of Neurosurgery*	Japan	11765841
54	108	2.4	1974	Earnest MP, Fahn S, Karp JH, Rowland LP	Normal pressure hydrocephalus and hypertensive cerebrovascular disease	*Archives of Neurology*	United States	4414845
55	108	2.2	1969	Ojemann RG, Fisher CM, Adams RD, Sweet WH, New PF	Further experience with the syndrome of "normal" pressure hydrocephalus	*Journal of Neurosurgery*	United States	5811831
56	105	3.1	1985	Black PM, Ojemann RG, Tzouras A	CSF shunts for dementia, incontinence, and gait disturbance	*Clinical Neurosurgery*	United States	3905156
57	104	3.2	1986	Thomsen AM, Børgesen SE, Bruhn P, Gjerris F	Prognosis of dementia in normal-pressure hydrocephalus after a shunt operation	*Annals of Neurology*	Denmark	3767314
58	103	9.4	2008	Shprecher D, Schwalb J, Kurlan R	Normal pressure hydrocephalus: diagnosis and treatment	*Current Neurology and Neuroscience Reports*	United States	18713572
59	102	5.1	1999	Savolainen S, Paljärvi L, Vapalahti M, Borgesen SE	Prevalence of Alzheimer's disease in patients investigated for presumed normal pressure hydrocephalus: a clinical and neuropathological study	*Acta Neurochirurgica (Wien)*	Finland	10536721
60	102	2.2	1972	Samuelson S, Long DM, Chou SN	Subdural hematoma as a complication of shunting procedures for normal pressure hydrocephalus	*Journal of Neurosurgery*	United States	5076372
61	100	2.0	1970	Benson DF, Lemay M, Patten DH, Rubens AB	Diagnosis of normal-pressure hydrocephalus	*New England Journal of Medicine*	United States	5450636
62	99	2.4	1977	Fisher CM	The clinical picture in occult hydrocephalus	*Clinical Neurosurgery*	United States	583685
63	98	12.3	2011	Streitberger K-J, Wiener E, Hoffmann J, Freimann FB, Klatt D, Braun J, Lin K, Mclaughlin J, Sprung C, Klingebiel R, Sack I	In vivo viscoelastic properties of the brain in normal pressure hydrocephalus	*NMR in Biomedicine*	Switzerland	20931563

CSF, cerebrospinal fluid.

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Supplementary Table 1. Continued

Rank	Citations: Count (n)	Citations: Rate (n/year)	Year	Authors	Title	Journal	Country	PubMed ID
64	98	2.3	1977	Greenberg JO, Shenkin HA, Adam R	Idiopathic normal pressure hydrocephalus: a report of 73 patients	*Journal of Neurology Neurosurgery and Psychiatry*	United States	874511
65	97	6.5	2004	Gangemi M, Maiuri F, Buonamasa S, Colella G, De Divitiis E	Endoscopic third ventriculostomy in idiopathic normal pressure hydrocephalus	*Neurosurgery*	Italy	15214981
66	97	5.1	2000	Stolze H, Kuhtz-Buschbeck JP, Drücke H, Jöhnk K, Diercks C, Palmié S, Mehdorn HM, Illert M, Deuschl G	Gait analysis in idiopathic normal pressure hydrocephalus—which parameters respond to the CSF tap test?	*Clinical Neurophysiology*	Germany	10964082
67	94	5.2	2001	Tullberg M, Jensen C, Ekholm S, Wikkelsø C	Normal pressure hydrocephalus: vascular white matter changes on MR images must not exclude patients from shunt surgery	*American Journal of Neuroradiology*	Sweden	11673159
68	93	5.5	2002	Zemack G, Romner B, Pickard JD, Sindou MP, Drake JM, Milhorat TH	Adjustable valves in normal-pressure hydrocephalus: a retrospective study of 218 patients	*Neurosurgery*	Sweden	12445344
69	93	2.9	1987	Akai K, Uchigasaki S, Tanaka U, Komatsu A	Normal pressure hydrocephalus: neuropathological study	*Pathology International*	Japan	3577765
70	93	2.1	1974	McCullough DC, Fox JL	Negative intracranial pressure hydrocephalus in adults with shunts and its relationship to the production of subdural hematoma	*Journal of Neurosurgery*	United States	4813717
71	92	3.7	1994	Pang D, Altschuler E	Low-pressure hydrocephalic state and viscoelastic alterations in the brain	*Neurosurgery*	United States	7808607

72	91	6.1	2004	Owler BK, Momjian S, Czosnyka Z, Czosnyka M, Péna A, Harris NG, Smielewski P, Fryer T, Donovan T, Coles J, Carpenter A, Pickard JD	Normal pressure hydrocephalus and cerebral blood flow: a PET study of baseline values	*Journal of Cerebral Blood Flow and Metabolism*	Australia	14688613
73	91	3.6	1994	Larsson A, Bergh A-C, Bilting M, Ärlig Å, Jacobsson L, Stephensen H, Wikkelsö C	Regional cerebral blood flow in normal pressure hydrocephalus: diagnostic and prognostic aspects	*European Journal of Nuclear Medicine*	Sweden	8162934
74	90	12.9	2012	Klinge P, Hellström P, Tans J, Wikkelsø C	One-year outcome in the European multicentre study on iNPH	*Acta Neurologica Scandinavica*	Sweden	22571428
75	90	10.0	2010	Hamilton R, Patel S, Lee EB, Jackson EM, Lopinto J, Arnold SE, Clark CM, Basil A, Shaw LM, Xie SX, Grady MS, Trojanowski JQ	Lack of shunt response in suspected idiopathic normal pressure hydrocephalus with Alzheimer disease pathology	*Annals of Neurology*	United States	20687117
76	89	4.0	1997	Tanaka A, Kimura M, Nakayama Y, Yoshinaga S, Tomonaga M	Cerebral blood flow and autoregulation in normal pressure hydrocephalus	*Neurosurgery*	Japan	9179888
77	89	2.0	1975	Mathew NT, Meyer JS, Hartmann A, Ott EO	Abnormal cerebrospinal fluid-blood flow dynamics: implications in diagnosis, treatment, and prognosis in normal pressure hydrocephalus	*Archives of Neurology*	United States	1180726
78	88	8.0	2008	Bateman GA	The pathophysiology of idiopathic normal pressure hydrocephalus: cerebral ischemia or altered venous hemodynamics?	*American Journal of Neuroradiology*	Australia	17925373
79	88	7.3	2007	Linninger AA, Xenos M, Zhu DC, Somayaji MR, Kondapalli S, Penn RD	Cerebrospinal fluid flow in the normal and hydrocephalic human brain	*IEEE Transactions on Biomedical Engineering*	United States	17278586
80	88	5.2	2002	Stephensen H, Tisell M, Wikkelsö C, Hodge CJ Jr, Gjerris F, Børgesen SE, Bech-Azeddine R, Sutton LN, McComb JG, Pickard JD	There is no transmantle pressure gradient in communicating or noncommunicating hydrocephalus	*Neurosurgery*	Sweden	11904027
81	88	2.8	1988	Haan J, Thomeer RTWM	Predictive value of temporary external lumbar drainage in normal pressure hydrocephalus	*Neurosurgery*	Netherlands	3352890

CSF, cerebrospinal fluid.

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Supplementary Table 1. Continued

Rank	Citations: Count (n)	Citations: Rate (n/year)	Year	Authors	Title	Journal	Country	PubMed ID
82	88	2.2	1979	Engel M, Carmel PW, Chutorian AM	Increased intraventricular pressure without ventriculomegaly in children with shunts: 'normal volume' hydrocephalus	*Neurosurgery*	United States	534062
83	87	5.1	2002	Bateman GA	Pulse-wave encephalopathy: a comparative study of the hydrodynamics of leukoaraiosis and normal-pressure hydrocephalus	*Neuroradiology*	Australia	12221445
84	87	3.5	1994	Black PM, Hakim R, Bailey NO	The use of the Codman-Medos programmable Hakim valve in the management of patients with hydrocephalus: illustrative cases	*Neurosurgery*	United States	8084404
85	85	14.2	2013	Malm J, Graff-Radford NR, Ishikawa M, Kristensen B, Leinonen V, Mori E, Owler BK, Tullberg M, Williams MA, Relkin NR	Influence of comorbidities in idiopathic normal pressure hydrocephalus—research and clinical care. A report of the ISHCSF task force on comorbidities in INPH	*Fluids and Barriers of the CNS*	Sweden	23758953
86	85	7.7	2008	Pujari S, Kharkar S, Metellus P, Shuck J, Williams MA, Rigamonti D	Normal pressure hydrocephalus: long-term outcome after shunt surgery	*Journal of Neurology Neurosurgery and Psychiatry*	United States	18356257
87	85	5.0	2002	Tullberg M, Hultin L, Ekholm S, Månsson J-E, Fredman P, Wikkelsø C	White matter changes in normal pressure hydrocephalus and Binswanger disease: specificity, predictive value and correlations to axonal degeneration and demyelination	*Acta Neurologica Scandinavica*	Sweden	12027829
88	85	3.4	1994	Gideon P, Ståhlberg F, Thomsen C, Gjerris F, Sørensen PS, Henriksen O	Cerebrospinal fluid flow and production in patients with normal pressure hydrocephalus studied by MRI	*Neuroradiology*	Denmark	8041442

89	85	2.7	1987	Jack CR Jr, Mokri B, Laws ER Jr, Houser OW, Baker HL Jr, Petersen RC	MR findings in normal-pressure hydrocephalus: significance and comparison with other forms of dementia	*Journal of Computer Assisted Tomography*	United States	3680706
90	85	2.7	1987	Graff-Radford NR, Godersky JC	Idiopathic normal pressure hydrocephalus and systemic hypertension	*Neurology*	United States	3574694
91	85	2.4	1984	Conner ES, Foley L, Black McL P	Experimental normal-pressure hydrocephalus is accompanied by increased transmantle pressure	*Journal of Neurosurgery*	United States	6737056
92	85	2.0	1977	Koto A, Rosenberg G, Zingesser LH, Horoupian D, Katzman R	Syndrome of normal pressure hydrocephalus: possible relation to hypertensive and arteriosclerotic vasculopathy	*Journal of Neurology Neurosurgery and Psychiatry*	United States	845610
93	84	4.0	1998	Tullberg M, Rosengren L, Blomsterwall E, Karlsson J-E, Wikkelsö C	CSF neurofilament and glial fibrillary acidic protein in normal pressure hydrocephalus	*Neurology*	Sweden	9566405
94	83	4.4	2000	Bradley WG	Normal pressure hydrocephalus: new concepts on etiology and diagnosis	*American Journal of Neuroradiology*	United States	11039335
95	83	4.2	1999	Bech RA, Waldemar G, Gjerris F, Klinken L, Juhler M	Shunting effects in patients with idiopathic normal pressure hydrocephalus; correlation with cerebral and leptomeningeal biopsy findings	*Acta Neurochirurgica (Wien)*	Denmark	10929729
96	83	3.0	1991	Sahuquillo J, Rubio E, Codina A, Molins A, Guitart JM, Poca MA, Chasampi A	Reappraisal of the intracranial pressure and cerebrospinal fluid dynamics in patients with the so-called "normal pressure hydrocephalus" syndrome	*Acta Neurochirurgica (Wien)*	Spain	1763684
97	82	4.8	2002	Dixon GR, Friedman JA, Luetmer PH, Quast LM, McClelland RL, Petersen RC, Maher CO, Ebersold MJ	Use of cerebrospinal fluid flow rates measured by phase-contrast MR to predict outcome of ventriculoperitoneal shunting for idiopathic normal-pressure hydrocephalus	*Mayo Clinic Proceedings*	United States	12059119

CSF, cerebrospinal fluid.

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Supplementary Table 1. Continued

Rank	Citations: Count (n)	Citations: Rate (n/year)	Year	Authors	Title	Journal	Country	PubMed ID
98	81	5.4	2004	Krauss JK, Halve B, Sahuquillo J, Thomeer RTWM	Normal pressure hydrocephalus: survey of contemporary diagnostic algorithms and therapeutic decision-making in clinical practice	*Acta Neurochirurgica (Wien)*	Germany	15057532
99	80	8.0	2009	Iseki C, Kawanami T, Nagasawa H, Wada M, Koyama S, Kikuchi K, Arawaka S, Kurita K, Daimon M, Mori E, Kato T	Asymptomatic ventriculomegaly with features of idiopathic normal pressure hydrocephalus on MRI (AVIM) in the elderly: a prospective study in a Japanese population	*Journal of the Neurological Sciences*	Japan	18990411
100	80	6.7	2007	Kapaki EN, Paraskevas GP, Tzerakis NG, Sfagos C, Seretis A, Kararizou E, Vassilopoulos D	Cerebrospinal fluid tau, phospho-tau181 and β-amyloid 1—42 in idiopathic normal pressure hydrocephalus: a discrimination from Alzheimer's disease	*European Journal of Neurology*	Greece	18990411

CSF, cerebrospinal fluid.

Supplementary Table 2. Countries of Correspondence of 100 Most Cited Articles About Normal Pressure Hydrocephalus

Country	n
United States	40
Sweden	15
Japan	9
Netherlands	8
Denmark	5
Australia	4
Germany	4
United Kingdom	3
Colombia	2
Finland	2
Norway	2
Belgium	1
Canada	1
Greece	1
Italy	1
Spain	1
Switzerland	1

Supplementary Table 3. U.S. States of Correspondence for the 41 Articles Originating from the United States in the 100 Most Cited Articles About Normal Pressure Hydrocephalus

State	n
Massachusetts	10
California	6
Minnesota	5
Texas	4
Maryland	3
New York	3
Philadelphia	3
Illinois	2
Virginia	2
Colorado	1
Washington, DC	1
Iowa	1

Supplementary Table 4. Journals of 100 Most Cited Articles About Normal Pressure Hydrocephalus

Journal	n
Neurosurgery	16
Journal of Neurosurgery	12
Journal of Neurology Neurosurgery and Psychiatry	8
Acta Neurochirurgica (Wien)	6
American Journal of Neuroradiology	6
Neurology	6
Acta Neurologica Scandinavica	5
Radiology	3
Annals of Neurology	2
Archives of Neurology	2
Brain	2
Clinical Neurosurgery	2
Journal of the Neurological Sciences	2
Neurologia Medico-Chirurgica (Tokyo)	2
Neuroradiology	2
New England Journal of Medicine	2
British Journal of Ophthalmology	1
Cerebrospinal Fluid Research	1
Child's Nervous System	1
Clinical Neurophysiology	1
Current Neurology and Neuroscience Reports	1
Dementia and Geriatric Cognitive Disorders	1
European Journal of Neurology	1
European Journal of Nuclear Medicine	1
Fluids and Barriers of the CNS	1
IEEE Transactions on Biomedical Engineering	1
Journal of Biomechanical Engineering	1
Journal of Cerebral Blood Flow and Metabolism	1
Journal of Computer Assisted Tomography	1
Journal of Neurology	1
Mayo Clinic Proceedings	1
NMR in Biomedicine	1
Nature Clinical Practice Neurology	1
Neurosurgical Review	1

Continues

Supplementary Table 4. Continued

Journal	n
Pathology International	1
Physiological Measurement	1
Stroke	1
Surgical Neurology	1