



Top-100 Highest-Cited Original Articles in Ischemic Stroke: A Bibliometric Analysis

Konark Malhotra¹, Omar Saeed², Nitin Goyal³, Aristeidis H. Katsanos^{4,5}, Georgios Tsivgoulis³⁻⁵

■ **OBJECTIVE:** The total number of citations of a research article can be used to determine its impact on the scientific community. We aimed to identify the top-100 articles published on ischemic stroke and evaluate their characteristics.

■ **METHODS:** Based on the database of Journal Citation Reports, 934 journals were selected that published original ischemic stroke articles. We used Web of Science citation search tool to identify top-100 citation classics, i.e., articles with more than 400 citations, in the field of ischemic stroke. All original articles were evaluated for publication year, journal category, journal and its impact factor, number of total and annual citations, research topic, publishing country, and institutional affiliation.

■ **RESULTS:** The top-100 citation classics in ischemic stroke were published from 1970 to 2015, with the decade of 1990–1999 contributing 47 articles of historical significance. Median of total citations and annual citations in our analysis were 625.0 (interquartile range [IQR] 851.3–494.5) and 35.7 (IQR 79.9–25.9), respectively. The majority of the articles originated from the United States ($n = 57$), focused over the medical management ($n = 26$), and were published in the *New England Journal of Medicine* or *Stroke* ($n = 25$ each) journals. The median impact factor for the journals that published top-100 ischemic stroke citation classics was 9.11 (IQR 21.49–6.11).

■ **CONCLUSIONS:** Our list of top-100 citation classics specific to ischemic stroke provide a detailed insight into academic achievements, historical perspective and serves as a guide for the scientific progress in stroke.

INTRODUCTION

Since the approval by the Food and Drug Administration of intravenous tissue plasminogen activator (IV tPA) in 1995, the field of ischemic stroke has steadily expanded. Public awareness, rapid triage of patients with stroke, use of state-of-the-art stentriever devices in strokes due to large vessel occlusion, and advancements in neuroimaging are few of the major advancements in stroke community. Recent landmark endovascular stroke trials demonstrated improved poststroke morbidity with combined use of mechanical thrombectomy and standard care in patients with proximal large vessel occlusion involving anterior circulation.¹ With a focused approach to improve stroke care, especially secondary prevention, stroke-related mortality has gradually reduced and now ranks fifth in the United States compared with other disease processes.²

The growth of a particular discipline majorly revolves around the research advancements over time. Assessment of the research trend and impact of published literature in a specific field could be performed via citation analyses and remains critical. Citation by a scientific article (citing article) refers to an acknowledgement of a cited article in literature. The number of citations depicts the impact of that individual article over scientific community that corresponds to the impact factor (IF) of the publishing journal.³ Bibliometric analysis of most-cited articles or “citation classics,” i.e., cited more than 400 times,⁴ provides the most robust data to analyze the progress and growth of a scientific field. In this study, we aimed to analyze the 100-most cited original articles published on ischemic stroke and gauge the growth and development in the field of ischemic stroke.

METHODS

Our study analyzed the top 100-cited articles in ischemic stroke. Since there was no use of human subjects, our study was exempt

Key words

- Bibliometric
- Citation classic
- Ischemic stroke
- Stroke trials

Abbreviations and Acronyms

- IF:** Impact factor
IQR: Interquartile range
ISI: Institute for Scientific Information
IV tPA: Intravenous tissue plasminogen activator
NEJM: *New England Journal of Medicine*

From the ¹West Virginia University-Charleston Division, Charleston, West Virginia, USA; ²Zeenat Qureshi Stroke Institute, Department of Neurology, University of Minnesota, Minneapolis, Minnesota, USA; ³University of Tennessee Health Science Center, Memphis, Tennessee, USA; ⁴Department of Neurology, University of Ioannina School of Medicine, Ioannina, Greece; and ⁵Second Department of Neurology, National & Kapodistrian University of Athens, “Attikon,” University Hospital, Athens, Greece

To whom correspondence should be addressed: Konark Malhotra, M.D.
 [E-mail: konark.malhotra@yahoo.com]

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from the institutional review board approval. Two authors (K.M., O.S.) independently conducted the journal search and identifications of articles. Any disagreements that arose were mutually resolved.

Selection of Journals

To identify the 100 most-cited articles in ischemic stroke, we used Institute for Scientific Information (ISI) Web of Knowledge Journal Citation Reports Science Edition 2015 (Thomson Reuters, New York, New York, USA). Journals listed under the following broad categories were included in our evaluation: “Clinical Neurology” (193 journals), “Neurosciences” (256 journals), “Cardiac & Cardiovascular Systems” (124 journals), “Medicine, General & Internal” (155 journals), “Neuroimaging” (14 journals), “Radiology, Nuclear Medicine & Medical Imaging” (124 journals), “Critical Care Medicine” (33 journals), “Emergency Medicine” (24 journals), “Peripheral Vascular Disease” (63 journals), and “Rehabilitation” (65 journals). We identified articles that were published between 1900 and 2017, and our last search was performed on September 30, 2017. After excluding 117 duplicates from a total of 1051 journals, 934 journals were selected in our evaluation.

Definitions and Selection Criteria

We selected the highest cited original articles and referred these as “citation classics.” We included articles pertaining to ischemic events limited to vascular territories of intracranial arteries, extracranial portion of the internal carotid and vertebral arteries, external carotid artery and its branches, common carotid artery,

spinal artery, or intracerebral venous system. No restrictions were applied for patient’s age or language in our study. Articles were excluded if they explored basic science research, surgical techniques, and animal studies. Our search was strictly limited to original research articles, whereas other subtypes, including abstracts, letters, editorials, corrections, meta-analysis, guidelines, viewpoints, and book reviews were excluded.

Identification of 100-Most Cited Articles

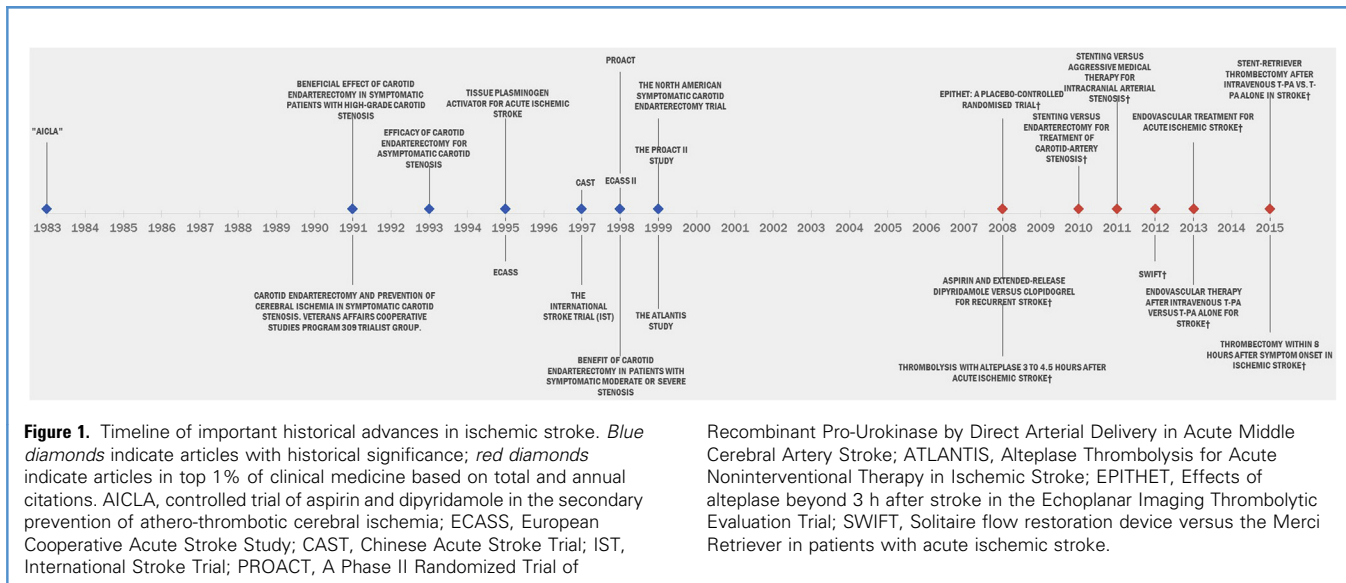
All 934 journals were evaluated via the “cited reference search” in the Science Citation Index Expanded of the ISI Web of Knowledge-Web of Science (Thomson Reuters). The Web of Science remains as one of the important online databases in ISI for analysis of citation counts. We recorded all the articles with at least 400 or more citations in a single database and ranked them based on the citations numbers. Our initial search yielded 116,591 articles using the following terms: cerebral ischemia or transient ischemic attack or acute ischemic stroke. After refining per the journal categories, articles were reduced to 88,553. Because original articles majorly contribute to citation classics, we limited our search to original articles only that further reduced our total articles to 66,705.

Analysis

The following data were collected: article title, total number of citations, total citations during initial 5 years of publication, annual citations, year of publication, publishing journal, Web of Science categories, publishing institution and country, and journal

Table 1. The 10 Most-Cited Articles in Ischemic Stroke Ranked in Order of Citation Numbers

Rank	Year	Article Title	Number of Citations	Number of Annual Citations (Rank)	Number of Citations in Initial 5 Years of Publication
1	1995	Tissue-plasminogen activator for acute ischemic stroke	5284	240.2 (9)	793
2	1991	Beneficial effect of carotid endarterectomy in symptomatic patients with high-grade carotid stenosis	4165	160.2 (15)	92
3	1993	Classification of subtype of acute ischemic stroke—definitions for use in a multicenter clinical-trial	4478	186.6 (11)	119
4	1995	Endarterectomy for asymptomatic carotid-artery stenosis	2821	128.2 (18)	563
5	2008	Thrombolysis with alteplase 3 to 4.5 hours after acute ischemic stroke	2656	295.1 (6)	1118
6	2001	Validation of clinical classification schemes for predicting stroke: results from the National Registry of Atrial Fibrillation	2581	161.3 (14)	127
7	1995	Intravenous thrombolysis with recombinant tissue-plasminogen activator for acute hemispheric stroke—the European Cooperative Acute Stroke Study (ECASS)	2115	96.1 (23)	630
8	1999	Intra-arterial prourokinase for acute ischemic stroke. The PROACT II study: a randomized controlled trial	1988	110.4 (20)	491
9	1998	Benefit of carotid endarterectomy in patients with symptomatic moderate or severe stenosis	1945	102.4 (21)	485
10	1991	MRC European Carotid Surgery Trial: interim results for symptomatic patients with severe (70–99%) or with mild (0–29%) carotid stenosis	1723	66.3 (28)	69



IF. If an article had multiple institutions and country affiliations, we took the first author information as primary affiliation. All publishing journal metrics were also identified and analyzed by

reviewing journal IF, and Cite Score, i.e., average number of citations per article. Data in our study are presented as descriptive statistics, and detailed statistical analysis was not performed.

Table 2. Ranking of Journals in Which the 100 Most-Cited Ischemic Stroke Articles Were Published

Rank	Journals	Number of Citation Classics	Average Citations per Paper	IF (2016)
1a	<i>New England Journal of Medicine</i>	25	12.82	72.699
1b	<i>Stroke</i>	25	4.94	6.032
3	<i>Lancet</i>	12	6.93	47.831
4	<i>Journal of the American Medical Association</i>	10	6.67	44.405
5	<i>Annals of Neurology</i>	8	7.10	9.890
6a	<i>Circulation</i>	4	8.41	19.309
6b	<i>Neurology</i>	4	3.81	8.320
8	<i>Archives of Neurology*</i>	2	5.10	10.029
9a	<i>Lancet Neurology</i>	1	9.60	26.284
9b	<i>Journal of the American College of Cardiology†</i>	1	7.96	19.896
9c	<i>Current Opinion in Neurobiology</i>	1	7.39	6.133
9d	<i>Radiology</i>	1	5.67	7.296
9e	<i>Journal of Cerebral Blood Flow and Metabolism</i>	1	4.78	5.081
9f	<i>Chest</i>	1	3.58	6.147
9g	<i>Journal of Neurology, Neurosurgery, and Psychiatry</i>	1	4.62	7.349
9h	<i>Archives of Internal Medicine*</i>	1	3.93	16.538
9i	<i>Journal of Neurosurgery</i>	1	2.53	4.059
9j	<i>Journal of Neurological Sciences</i>	1	1.98	2.295

IF, impact factor.

*In 2013, *Archives of Neurology* and *Archives of Internal Medicine* changed to *JAMA Neurology* and *JAMA Internal Medicine*, respectively.

†Journal metrics were not published on Scopus journal metrics, so they were retrieved from the journal website.

RESULTS

We selected the 100-most cited original articles on ischemic stroke (**Supplementary Table 1**), and have presented the top-10 articles ranked ordinally based on the total number of citations in **Table 1**. The number of citations for the top 100 most cited articles ranged from 5284 to 420 (median: 625.0; interquartile range [IQR] 851.3–494.5). The number of annual citations ranged from 597.5 to 10.8 (median 35.7; IQR 79.9–25.9). The most-cited article based on historical importance was published in 1995 by National Institute of Neurological Disorders and Stroke rt-PA Study Group that described favorable efficacy of IV tPA in ischemic stroke patients when used within 3 hours of symptom onset.⁵ The article published by Berkhemer et al.,⁶ 1 of the 5 landmark endovascular trials that demonstrated efficacy and safety of intra-arterial treatment, was the highest cited article in the categories of annual citations (597.5) and ranked second for number of citations ($n = 1194$) during initial 5 years since publication. A timeline of most impactful and relevant articles in the history of ischemic stroke is presented in **Figure 1**.

The top-100 ischemic stroke articles were published in 18 of the 934 medical journals included in our analysis. The median IF and Cite Score for these journals was 9.11 (IQR 21.49–6.11) and 5.39 (IQR 7.53–3.90), respectively (**Table 2**). Two journals, the *New England Journal of Medicine* (NEJM) and *Stroke*, contributed equally ($n = 25$ each) to the top-100 list of citation classics. All the articles were published between 1970 and 2015, with the most productive decade being 1990–1999 ($n = 47$), followed by 2000–2009 ($n = 34$).

The top-100 articles in ischemic stroke originated from 12 countries worldwide, with United States ($n = 57$) publishing the majority of the citation classics, followed by Germany ($n = 11$) and United Kingdom ($n = 9$) (**Table 3**). Depending on the first author's affiliation, the institute that contributed the most articles was University of Heidelberg in Germany ($n = 8$), followed by Harvard University ($n = 5$) in United States (**Table 4**). The most frequently discussed topic in the list of highly cited ischemic stroke articles involved the management of ischemic stroke (both medical and surgical treatment; $n = 38$) with medical management and IV tPA contributing 26 articles, followed by epidemiological analyses ($n = 18$) (**Figure 2**).

DISCUSSION

Bibliometric analysis of the most-cited articles highlights the most influential articles, trending topics, and prolific institutions that contribute in the evolution of a scientific subspecialty. Our study depicts the top-100 citation classics that have played a significant role in bolstering the progress in the field of ischemic stroke.

Highlights Over 5 Decades: Historical and Current Impact?

Our cross-sectional analysis of top-100 citation classics demonstrated that nearly half of the articles ($n = 47$) were published during 1990–1999, suggesting the 1990s have been the most productive decade in the history of ischemic stroke. These findings are similar to previous citation analyses conducted in neurosurgery,⁸ radiology,⁹ and neuroimaging¹⁰ specialties. The premillennial decade likely corresponds to the time period that

Table 3. Countries of Origin of the 100 Most-Cited Ischemic Stroke Articles

Country	Number of Citations	Number of University Hospitals ⁷
United States	57	404
Germany	11	42
United Kingdom	9	167
Canada	8	119
France	4	44
Australia	3	45
Netherlands	2	10
Italy	2	78
Japan	1	18
Denmark	1	29
Spain	1	34
Sweden	1	7

noticed the approval of varied medical therapies in ischemic stroke including IV tPA^{5,11} and surgical treatment options such as carotid endarterectomy and stenting.^{12,13} These citation classics carry historical significance in the field of ischemic stroke. However, the assessments of citation classics have inherent limitations as citations tend to accumulate over time, and therefore underestimate recently published articles irrespective of their true impact.¹⁴

To overcome this limitation, we used annual citations for top-100 original ischemic stroke articles in our analysis (**Supplementary Table 1**). In addition, citations gradually reach a summit in 3–10 years after publication and tend to decrease afterwards.¹⁵ Accordingly, we assessed the total citations accumulated during initial 5 years since publication for the articles published until 2012, and ranked them accordingly. The annual citations and total citations in initial 5 years of publications seem to be the best method to assess the “true” impact of citation classics, and thus carry greater clinical relevance for clinicians.

Although the majority of citation classics were condensed in the 1990–1999 decade, the continued research efforts in ischemic stroke resulted in recent success of endovascular trials. Recent endovascular landmark trials (with highest annual citations) were aptly referred as *hot papers* by Web of Sciences with ranking amongst top 0.1% of papers in the academic field of clinical medicine, and likely have potential to be listed with the articles of historical significance in future bibliometric analyses.^{6,16–19}

Which Journals Are Involved in Impactful Research?

Although top-100 citation classics in ischemic stroke articles were published in 18 journals, half of the articles appeared in

Table 4. Institutions That Contributed Three or More of the Top 100-Cited Ischemic Stroke Articles

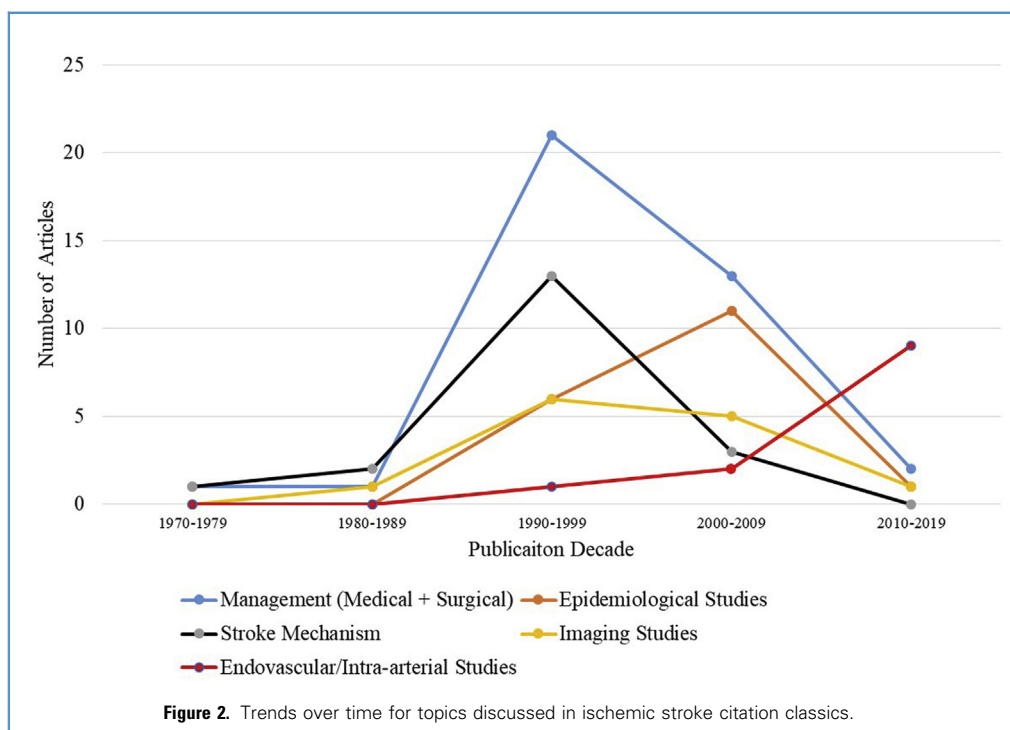
Institution, Country	Number of Articles
Heidelberg University, Germany	8
Harvard University, USA	5
University of Cincinnati, USA	4
Washington University, USA	4
University of Oxford, UK	4
University of California Los Angeles, USA	4
University of Iowa, USA	3
University of Edinburgh, UK	3
University of California San Francisco, USA	3
University of Calgary, Canada	3

NEJM or *Stroke* journals. Equivalent to NEJM, *Stroke* being a relatively low-impact journal, contributed one-fourth ($n = 25$) of total citation classics as compared to other high-IF journals including *JAMA*, *Lancet*, and *Lancet Neurology*. This further confirms the concept of Bradford's law,²⁰ as researchers tend to use citations from the well-renowned core journals of their respective field, and deviations, if any, from this concept portends lower impact or citation frequency for their article. As expected, the number of citations was significantly greater for a total of 48 citation classics published in NEJM, *Lancet*, and *JAMA*. Except *Lancet Neurology*,

43 articles published in neurologic journals with IF less than 10 made to the list of top-100 citation classics in ischemic stroke. Overall, 55 citation classics appeared in non-neurologic journals with an IF greater than 10, including cardiovascular, radiology, and general internal medicine specialties. This demonstrates the impact of ischemic stroke articles in different medical specialties. Although a neurologic pathology, risk factors for ischemic stroke including hypertension, hyperlipidemia, diabetes mellitus, or hypercoagulability encompass systemic disease entities.

Which Topics Are Highly Acknowledged in Stroke Community?

Overall, we observed that one fourth of ischemic stroke citation classics focused on thrombolysis and medical management. These articles discussed the primary and secondary prevention strategies of ischemic stroke, and likely carry greater clinical relevance among clinicians that treat patients with ischemic stroke. However, this trend seems to have faded, as only single study entered the list of citation classics in the current decade. The current decade has already witnessed 9 citation classics in the top-100 list, demonstrating the impact of the recent success of endovascular trials in ischemic stroke. Interestingly, our analysis depicts that the studies on stroke epidemiology have declined. This is likely due to the concept of obliteration by incorporation, i.e., lack of citations for major articles secondary to widely perceived and accepted knowledge on that particular topic. Additionally, epidemiologic data are commonly published as guideline statements; however, our analysis focused on citation classics involving original articles published in ischemic stroke.



How Do Citation Classics Compare with Other Disciplines?

The number of citations for top-100 citation classics in ischemic stroke (414–5329; mean 853.02) is significantly greater as compared with other neurologic subspecialties, including neuro-intervention (170–1912; mean 363.45),²¹ neurosurgery (287–1515; mean 452.6),⁸ and epilepsy (401–3749; mean 648).²² This highlights the bulk of research conducted in ischemic stroke community that has resulted in major growth of this field during last few decades. In addition, multitude of risk factors leading to ischemic stroke involve other disciplines especially cardiology, medicine, radiology, and even oncology. This noticeable overlap among different subspecialties likely explains greater number of citation numbers for ischemic stroke.

Do Countries and Institutions Impact Citation Classics?

The United States was observed to be at the forefront, with 57 contributions in top-100 ischemic stroke citation classics. These findings corroborate the previous literature that has described citations classics in other specialties. This further underscores the strong emphasis for clinical research laid in the United States over a large scientific community (composed of more than 400 university hospitals).^{7,23} In comparison, Germany (with only 42 university hospitals countrywide) ranked second in the list of citation classics, with maximum contributions from University of Heidelberg. Although institutions from the United States had a major contribution in our citation analysis of ischemic stroke, these statistics seem to be less concentrated as compared with previous analyses.^{24,25} These findings likely correlate to the lack of

reporting of trial results to the public and stroke community, as our recent analysis have demonstrated that only one fifth of stroke trials in United States tend to report their results within the mandated time frame, whereas similar fractions remain unreported.²⁶

Our study has few limitations. First, citation analyses usually favor studies of historical significance as citations accumulate over the years and ignore recently published articles. To overcome this limitation, we assessed the annual citation counts and total citations within initial 5 years of publication, which provides the true impact and clinical significance of a scientific article. Second, we limited our selection to original ischemic stroke articles, which could have resulted in missing a few articles involving textbook, systematic reviews, and meta-analyses. Third, inappropriate citations of articles pose concern for various citation biases, such as in-house citations, self-citations, omission biases, tendency to cite articles published in high-IF core journals, and obliteration by incorporation. Lastly, bibliometric analyses tend to portray the articles with widespread acknowledgement in the scientific community, and could omit the ones that represent the highest quality or deserve scientific merit in the literature.

Our study highlights the top-100 most influential and highly impactful research work performed in ischemic stroke past 5 decades. These findings provide insight over the growth trend and development in ischemic stroke, highlights the perspective on current topics of research and practical applications, and bolster future implications on clinical practice.

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SUPPLEMENTARY DATA

Supplementary Table 1. 100 Most-Cited Articles in Ischemic Stroke†

Rank	Year of Publication	Article Title	Number of Citations	Number of Annual Citations (Rank)	Number of Citations in Initial 5 Years of Publication
1	1995	Tissue-plasminogen activator for acute ischemic stroke	5284	240.2 (9)	793
2	1993	Classification of subtype of acute ischemic stroke—definitions for use in a multicenter clinical-trial	4478	186.6 (11)	119
3	1991	Beneficial effect of carotid endarterectomy in symptomatic patients with high-grade carotid stenosis	4165	160.2 (15)	92
4	1995	Endarterectomy for asymptomatic carotid-artery stenosis	2821	128.2 (18)	563
5	2008	Thrombolysis with alteplase 3 to 4.5 hours after acute ischemic stroke*	2656	295.1 (6)	1,118
6	2001	Validation of clinical classification schemes for predicting stroke—results from the National Registry of Atrial Fibrillation	2581	161.3 (14)	127
7	1995	Intravenous thrombolysis with recombinant tissue-plasminogen activator for acute hemispheric stroke—the European Cooperative Acute Stroke Study (ECASS)	2115	96.1 (23)	630
8	1999	Intra-arterial prourokinase for acute ischemic stroke. The PROACT II study: a randomized controlled trial	1988	110.4 (20)	491
9	1998	Benefit of carotid endarterectomy in patients with symptomatic moderate or severe stenosis	1945	102.4 (21)	485
11	2010	Refining clinical risk stratification for predicting stroke and thromboembolism in atrial fibrillation using a novel risk factor-based approach the Euro Heart Survey on Atrial Fibrillation*	1925	275.0 (7)	1,261
12	1998	Randomised double-blind placebo-controlled trial of thrombolytic therapy with intravenous alteplase in acute ischaemic stroke (ECASS II)	1727	90.9 (24)	428
10	1991	MRC European Carotid Surgery Trial: interim results for symptomatic patients with severe (70–99%) or with mild (0–29%) carotid stenosis	1723	66.3 (28)	69
13	2006	High-dose atorvastatin after stroke or transient ischemic attack*	1319	119.9 (19)	707
15	2010	Stenting versus endarterectomy for treatment of carotid-artery stenosis*	1224	174.9 (12)	961
18	2015	A randomized trial of intra-arterial treatment for acute ischemic stroke*†	1195	597.5 (1)	(1194)
14	1996	European Stroke Prevention Study. 2. Dipyridamole and acetylsalicylic acid in the secondary prevention of stroke	1147	54.6 (34)	253
21	2013	Saxagliptin and cardiovascular outcomes in patients with type 2 diabetes mellitus*	1069	267.3 (8)	(1064)
16	1997	The International Stroke Trial (IST): a randomized trial of aspirin, subcutaneous heparin, both, or neither among 19 435 patients with acute ischaemic stroke	1033	51.7 (35)	416
24	2015	Endovascular therapy for ischemic stroke with perfusion-imaging selection*†	1026	513.0 (2)	(1026)
17	1993	Secondary prevention in non-rheumatic atrial-fibrillation after transient ischemic attack or minor stroke	981	40.9 (45)	99
19	1993	Efficacy of carotid endarterectomy for asymptomatic carotid stenosis	934	38.9 (49)	340
20	1994	Viability thresholds and the penumbra of focal ischemia	932	40.5 (47)	246
37	2015	Randomized assessment of rapid endovascular treatment of ischemic stroke*†	922	461.0 (3)	(922)
22	1991	Stroke prevention in atrial-fibrillation study—final results	867	33.3 (56)	42

Continues

Supplementary Table 1. Continued

Rank	Year of Publication	Article Title	Number of Citations	Number of Annual Citations (Rank)	Number of Citations in Initial 5 Years of Publication
25	2013	Endovascular therapy after intravenous t-PA versus t-PA alone for stroke*	856	214.0 (10)	(862)
23	2003	Analysis of pooled data from the randomised controlled trials of endarterectomy for symptomatic carotid stenosis	837	59.8 (31)	300
26	2005	Safety and efficacy of mechanical embolectomy in acute ischemic stroke—results of the MERCI trial	811	67.6 (26)	337
28	2005	Comparison of warfarin and aspirin for symptomatic intracranial arterial stenosis	785	65.4 (29)	346
27	1995	Acute human stroke studied by whole-brain echo-planar diffusion-weighted magnetic resonance imaging	765	34.8 (54)	313
29	1998	PROACT: a phase II randomized trial of recombinant pro-urokinase by direct arterial delivery in acute middle cerebral artery stroke	763	40.2 (48)	242
32	2004	Endarterectomy for symptomatic carotid stenosis in relation to clinical subgroups and timing of surgery	762	58.6 (32)	348
35	2000	Validity and reliability of a quantitative computed tomography score in predicting outcome of hyper acute stroke before thrombolytic therapy	761	44.8 (42)	92
31	2008	Mechanical thrombectomy for acute ischemic stroke—final results of the multi merci trial*	756	84.0 (25)	513
30	2001	Recurrent cerebrovascular events associated with patent foramen ovale, atrial septal aneurysm, or both.	754	47.1 (39)	249
33	2000	Short-term prognosis after emergency department diagnosis of TIA	734	43.2 (44)	134
34	1999	Recombinant tissue-type plasminogen activator (alteplase) for ischemic stroke 3 to 5 hours after symptom onset—the ATLANTIS study: a randomized controlled trial	733	40.7 (46)	205
36	2006	Magnetic resonance imaging profiles predict clinical response to early reperfusion: the diffusion and perfusion imaging evaluation for understanding stroke evolution (DEFUSE) study*	702	63.8 (30)	334
38	1977	Controlled trial of aspirin in cerebral ischemia	663	16.6 (94)	266
39	1996	"Malignant" middle cerebral artery territory infarction: clinical course and prognostic signs	685	32.6 (59)	98
40	2005	The desmoteplase in acute ischemic stroke trial (DIAS)—a phase II MRI-based 9-hour window acute stroke thrombolysis trial with intravenous desmoteplase	671	55.9 (33)	418
41	1992	Fast magnetic-resonance diffusion-weighted imaging of acute human stroke	653	26.1 (73)	132
42	2003	Morning surge in blood pressure as a predictor of silent and clinical cerebrovascular disease in elderly hypertensives—a prospective study	681	48.6 (37)	240
43	1992	Recombinant tissue plasminogen-activator in acute thrombotic and embolic stroke	660	26.4 (71)	145
44	1997	CAST: randomised placebo-controlled trial of early aspirin use in 20,000 patients with acute ischaemic stroke	659	33.0 (57)	237
45	1991	Carotid endarterectomy and prevention of cerebral-ischemia in symptomatic carotid stenosis	640	24.6 (78)	128

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Supplementary Table 1. Continued

Rank	Year of Publication	Article Title	Number of Citations	Number of Annual Citations (Rank)	Number of Citations in Initial 5 Years of Publication
46	2012	Solitaire flow restoration device versus the Merci Retriever in patients with acute ischaemic stroke (SWIFT): a randomised, parallel-group, non-inferiority trial*	657	131.4 (17)	657
47	2013	A trial of imaging selection and endovascular treatment for ischemic stroke*	655	163.8 (13)	(655)
48	1997	Intracerebral hemorrhage after intravenous t-PA therapy for ischemic stroke	616	30.8 (61)	165
49	2004	Ultrasound-enhanced systemic thrombolysis for acute ischemic stroke	629	48.4 (38)	274
50	1991	The united-kingdom transient ischemic attack (UK-TIA) aspirin trial—final results	592	22.8 (87)	22
51	1996	Stroke severity in atrial fibrillation—The Framingham Study	621	29.6 (63)	86
52	2015	Stent-retriever thrombectomy after intravenous t-PA versus t-PA alone in stroke*†	780	390.0 (4)	(780)
53	1996	Hyperacute stroke: evaluation with combined multisection diffusion-weighted and hemodynamically weighted echo-planar MR imaging	562	26.8 (69)	293
54	2008	Effects of alteplase beyond 3 h after stroke in the echoplanar imaging thrombolytic evaluation trial (EPITHET): a placebo-controlled randomised trial*	600	66.7 (27)	398
55	2004	Change in stroke incidence, mortality, case-fatality, severity, and risk factors in Oxfordshire, UK from 1981 to 2004 (Oxford Vascular Study)	585	45.0 (41)	233
56	2013	Endovascular treatment for acute ischemic stroke*	589	147.3 (16)	(589)
57	2001	A clinical trial of estrogen-replacement therapy after ischemic stroke	564	35.3 (51)	307
58	1994	Nitric-oxide synthase inhibition and cerebrovascular regulation	548	23.8 (81)	336
59	1996	Body temperature in acute stroke: relation to stroke severity, infarct size, mortality, and outcome	553	26.3 (72)	163
60	2015	Thrombectomy within 8 hours after symptom onset in ischemic stroke*†	730	365.0 (5)	(730)
61	2011	Stenting versus aggressive medical therapy for intracranial arterial stenosis*	586	97.7 (22)	581
62	1991	Cerebral hemodynamics in ischemic cerebrovascular-disease	538	20.7 (90)	75
63	1995	Race ethnicity and determinants of intracranial atherosclerotic cerebral infarction—the Northern Manhattan Stroke Study	549	25.0 (77)	59
64	1985	Multicenter trial of hemodilution in ischemic stroke—background and study protocol	516	16.1 (96)	28
65	2001	Epidemiology of ischemic stroke subtypes according to toast criteria—incidence, recurrence, and long-term survival in ischemic stroke subtypes: a population-based study	564	35.3 (51)	81
66	2002	Effect of medical treatment in stroke patients with patent foramen ovale—patent foramen ovale in cryptogenic stroke study	540	36.0 (50)	190
67	1983	AICLA controlled trial of aspirin and dipyridamole in the secondary prevention of athero-thrombotic cerebral-ischemia	516	15.2 (97)	137
68	1981	Reversal of focal misery-perfusion syndrome by extra-intracranial arterial bypass in hemodynamic cerebral-ischemia—a case-study with o-15 positron emission tomography	522	14.5 (98)	63

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Supplementary Table 1. Continued

Rank	Year of Publication	Article Title	Number of Citations	Number of Annual Citations (Rank)	Number of Citations in Initial 5 Years of Publication
69	1970	Joint study of extracranial arterial occlusion .5. progress report of prognosis following surgery or nonsurgical treatment for transient cerebral ischemic attacks and cervical carotid artery lesions	509	10.8 (100)	52
70	2001	Cerebral sinovenous thrombosis in children.	522	32.6 (58)	128
71	1999	Baseline NIH stroke scale score strongly predicts outcome after stroke—a report of the Trial of Org 10172 in Acute Stroke Treatment (TOAST)	521	28.9 (64)	80
72	1998	The greater Cincinnati Northern Kentucky stroke study—preliminary first-ever and total incidence rates of stroke among blacks	507	26.7 (70)	169
73	1996	Lifetime cost of stroke in the United States	507	24.1 (79)	97
74	1995	Hydroxyurea for patients with essential thrombocythemia and a high-risk of thrombosis	506	23.0 (84)	104
75	1999	The North American Symptomatic Carotid Endarterectomy Trial—surgical results in 1415 patients	505	28.1 (67)	117
76	1982	Regional cerebral blood-flow and glucose-metabolism following transient forebrain ischemia	483	13.8 (99)	111
77	1996	Ischemia-induced neuronal apoptosis	487	23.2 (83)	217
78	2003	Effects of blood pressure lowering with perindopril and indapamide therapy on dementia and cognitive decline in patients with cerebrovascular disease	491	35.1 (53)	182
79	1991	North-American Symptomatic Carotid Endarterectomy Trial—methods, patient characteristics, and progress	480	18.5 (92)	23
80	1991	Cerebral-circulation and metabolism after severe traumatic brain injury—the elusive role of ischemia	473	18.2 (93)	81
81	1996	Stroke incidence, prevalence, and survival—secular trends in Rochester, Minnesota, through 1989	474	22.6 (88)	132
82	2001	Plasma concentration of C-reactive protein and risk of ischemic stroke and transient ischemic attack—The Framingham Study	475	29.7 (62)	180
83	2001	Why are stroke patients excluded from TPA therapy? An analysis of patient eligibility	460	28.8 (65)	97
84	2001	Risk factors for severe hemorrhagic transformation in ischemic stroke patients treated with recombinant tissue plasminogen activator—a secondary analysis of the European-Australasian acute stroke study (ECASS II)	459	28.7 (66)	92
85	2006	Time is brain—quantified*	484	44.0 (43)	129
86	1997	Enlargement of human cerebral ischemic lesion volumes measured by diffusion-weighted magnetic resonance imaging	444	22.2 (89)	198
87	2000	Intravenous tissue-type plasminogen activator for treatment of acute stroke—the standard treatment with alteplase to reverse stroke (STARS) study	444	26.1 (74)	182
88	2000	Use of tissue-type plasminogen activator for acute ischemic stroke—the Cleveland area experience	442	26.0 (75)	190

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Supplementary Table 1. Continued

Rank	Year of Publication	Article Title	Number of Citations	Number of Annual Citations (Rank)	Number of Citations in Initial 5 Years of Publication
89	2008	Aspirin and extended-release dipyridamole versus clopidogrel for recurrent stroke*	463	51.4 (36)	316
90	2007	Magnetic resonance imaging and computed tomography in emergency assessment of patients with suspected acute stroke: a prospective comparison*	459	45.9 (40)	256
91	2000	Thrombolytic reversal of acute human cerebral ischemic injury shown by diffusion/perfusion magnetic resonance imaging	441	25.9 (76)	208
92	1998	Early hemicraniectomy in patients with complete middle cerebral artery infarction	433	22.8 (85)	117
93	1994	Role of angiogenesis in patients with cerebral ischemic stroke	447	19.4 (91)	29
94	1998	Moderate hypothermia in the treatment of patients with severe middle cerebral artery infarction	433	22.8 (85)	178
95	1998	Impaired clearance of emboli (washout) is an important link between hypoperfusion, embolism, and ischemic stroke	441	23.2 (82)	65
96	2001	Risk factors, outcome, and treatment in subtypes of ischemic stroke—the German stroke data bank	446	27.9 (68)	73
97	1999	The ischemic penumbra—operationally defined by diffusion and perfusion MRI	433	24.1 (80)	162
98	2003	Influenza vaccination and reduction in hospitalizations for cardiac disease and stroke among the elderly	432	30.9 (60)	216
99	2004	Selecting patients with atrial fibrillation for anticoagulation—stroke risk stratification in patients taking aspirin	445	34.2 (55)	151
100	1991	Superiority of transesophageal echocardiography in detecting cardiac source of embolism in patients with cerebral-ischemia of uncertain etiology	420	16.2 (95)	160

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