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Top-cited Articles in Primary Aldosteronism: A Bibliometric Analysis

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Abstract: Background: The objective of this study was to identify the top 100 cited articles in primary aldosteronism, and examine their characteristics. Methods: Science Citation Index Expanded database was utilized to search for the top 100 cited articles published since 1900. Articles were evaluated for several characteristics, including the number of citations, authorship, country and institution of origin, publication year, journal, and study design. Results: The top 100 articles were cited between 88 and 762 times, with a median of 130. The articles were published between 1955 and 2012, with the majority of the primary aldosteronism publications (n=35) being published between 2000 and 2009. The biggest number of the top 100 cited articles (n=19) were published in the *Journal of Clinical Endocrinology Metabolism*, followed by *Hypertension* (n=9), *Annals of Internal Medicine* (n=6), and *Archives of Internal Medicine* (n=6). The United States and Italy had the most publications, whereas University of Michigan and University of Padua were the top two institutions. Observational studies were the most popular article type, followed by reviews and basic science. The impact factor of a journal was not correlated with the number of top-cited articles it published. Furthermore there was no correlation between the number of citations and the number of years since publication, authors, participating institutions, or countries involved. Conclusion: These findings will assist researchers in quickly identifying the most significant advances in the field of primary aldosteronism, as well as deciphering the characteristics of top-cited articles in this subject, and laying a basis for further research.

Keywords: Bibliometrics, Primary Aldosteronism, Citation Classics, Citation Analysis

1. Introduction

Primary aldosteronism syndrome is characterized by hypertension and is caused by the autonomous secretion of aldosterone from adrenocortical lesions. Primary aldosteronism is found in over 10% of hypertensive patients and is the most frequent cause of secondary hypertension [1]. Besides, it is associated with hypokalemia, renal insufficiency, and cardiovascular diseases such as coronary artery disease, stroke, myocardial infarction, cardiomegaly, arrhythmia, among others [2, 3]. Numerous articles on primary aldosteronism have been published in the past decades, and the number continues to grow. Therefore, it is challenging for a medical researcher or clinician to obtain a general understanding of primary aldosteronism due to the abundance of articles. Classic papers (also known as top-cited articles) promote the development of any field of research. Consequently, there is an urgent need to assist researchers and clinicians in locating classic articles in the field of primary aldosteronism. However, identifying the classic papers on primary aldosteronism has received little attention.

Although the value of citation rate has been questioned, it has been widely used to assess the impact of a research article and identify major discoveries and challenges in a specific medical field [4]. The citation rate is a bibliometric analysis that investigates the frequency and pattern of citations of an article. The number of citations that an article receives is an important metric for assessing its impact in the scientific community [5]. The more citations an article has, the more valuable it is in its field. Recently, the top-cited articles were identified and analyzed in various medical fields, such as

urology, respiratory diseases, pain, hypospadiology, tuberculosis, hypertension, diabetes, orthodontics, digestive diseases, and dermatology [6-15]. However, similar identification and analyses in primary aldosteronism have yet to be performed. Therefore, this study aimed at identifying the top 100 cited articles in primary aldosteronism, and examine their characteristics using a bibliometric analysis.

2. Methods

There was no need for ethical approval because no patients were enrolled in this study. However, the study was conducted in accordance to the Preferred Reporting Items for Systematic Reviews and Meta-analysis (PRISMA) guidelines [16].

2.1 Study Design and Data Search

Science Citation Index Expanded (SCIE, 1900-2016) database was used to identify the top 100 cited articles in primary aldosteronism research. The following search terms were used: "Conns syndrome*" OR "Conn syndrome*" OR "Conn's syndrome*" OR hyperaldosteronism* OR aldosteronism* OR "primary adrenal hyperplasia*" OR "aldosterone-producing adenoma*" OR "aldosterone-producing carcinoma*" OR aldosteronoma*. The asterisk (*) was used as a wild card character in the search string. Results presented in this study were based on data collected over the internet on April 18, 2016. No language was restricted in this search.

2.2. Inclusion and Exclusion Criteria

The inclusion criteria were as follow: (1) papers focusing on primary aldosteronism as the main topic; (2) original articles and reviews. The following were the exclusion criteria: (1) articles focused on broad areas, with no emphasis on primary aldosteronism; (2) meeting abstracts, letters, editorial materials, corrections, book chapters, errata, discussions, or book reviews.

2.3. Identification and Assessment of the Top 100 Articles

The search results were ranked in descending order using the option "times cited". Two independent researchers reviewed the findings, to ensure that the articles focused on primary aldosteronism research, and determined the top 100 cited articles. Clinical studies on primary aldosteronism were included. However, articles that focused on secondary aldosteronism, hypertension, Cushing's syndrome, hypokalemia, and heart failure were excluded. Subsequently, two investigators re-examined the top 100 cited articles, and all researchers extracted data including number of citations, citation density, authorship (only considering the first author), number of authors, country and institution of origin, publication year, name of the journal, and study design.

Articles were grouped into six different categories according to study design and goal: (1) randomized controlled trial (RCT); (2) observational study including cohort studies, case-control studies, cross-sectional studies and case series; (3) basic science including bench-top laboratory research and research involving animal or cell models; (4) review; (5) meta-analysis or systematic review; (6) clinical guidelines. Additionally, the Oxford Centre for Evidence-based Medicine – Levels of Evidence (2009 edition) was chosen to assess the top-cited articles. Once a list of journal impact factors was obtained from the Journal Citation Report 2015, we studied the correlation between each journal's impact factor and the number of top 100 articles it published. Lastly, we investigated the correlation between the number of citations and other characteristics, including the number of years since publication, the number of authors, participating countries, and institutions involved.

2.4. Statistical Analyses

All data were analyzed using GraphPad Prism software (Version 6, GraphPad Software Inc. CA USA). Correlations were determined using nonparametric Spearman rank. All statistical tests were two-tailed and $P<0.05$ was considered statistically significant.

3. Results

3.1. Citations

Table 1 shows the characteristics of the top 100 cited articles in primary aldosteronism research in descending order of total citations. The median number of citations for the top 100 articles was 130 (ranging from 88 to 762). The total number of citations in SCIE was positively correlated with citation density (r=0.52, $P<0.05$). The most cited article (762 citations) studied genomic mutations in aldosterone synthase (11 beta-hydroxylase), which caused the main subtype of primary aldosteronism: glucocorticoid-remediable aldosteronism, published in 1992 by Lifton RP et al in *Nature* [17]. A guideline on detection, diagnosis, and treatment of primary aldosteronism, published in 2008 by Funder JW et al in *Journal of Clinical Endocrinology & Metabolism,* was the second most cited article (682 citations) but had the highest citation-density [1]. The third most cited study (624 citations) was a classic report on primary aldosteronism as a new clinical syndrome, published in 1955 by Conn JW et al in *Journal of Laboratory and Clinical Medicine* [18].

Table 1. *The top 100 cited articles in primary aldosteronism research.*

rank	article	study design	citations	citation density
1	Lifton RP, et al. A chimeric 11-beta-hydroxylase aldosterone synthase gene causes glucocorticoid-remediable aldosteronism and human hypertension. *Nature*. 1992; 355 (6357): 262-265	basic science	762	32
2	Funder JW, et al. Case detection, diagnosis, and treatment of patients with primary aldosteronism: an endocrine society clinical practice guideline. *Journal of Clinical Endocrinology & Metabolism*. 2008;	guideline	682	85

rank	article	study design	citations	citation density
	93 (9): 3266-3281			
3	Conn JW, et al. Presidential address. I. Painting background. Ii. Primary aldosteronism, a new clinical syndrome.. *Journal of Laboratory and Clinical Medicine*. 1955; 45 (1): 3-17	observational study	624	10
4	Milliez P, et al. Evidence for an increased rate of cardiovascular events in patients with primary aldosteronism. *Journal of the American College of Cardiology*. 2005; 45 (8): 1243-1248	observational study	543	49
5	Rossi GP, et al. A prospective study of the prevalence of primary aldosteronism in 1,125 hypertensive patients. *Journal of the American College of Cardiology*. 2006; 48 (11): 2293-2300	observational study	423	42
6	Conn JW, et al. Clinical characteristics of primary aldosteronism from an analysis of 145 cases. *American Journal of Surgery*. 1964; 107 (1): 159-172	review	393	8
7	Conn JW, et al. Suppression of plasma renin activity in primary aldosteronism - distinguishing primary from secondary aldosteronism in hypertensive disease. *JAMA*. 1964; 190 (3): 213-221	observational study	361	7
8	Gordon RD, et al. High-incidence of primary aldosteronism in 199 patients referred with hypertension. *Clinical and Experimental Pharmacology and Physiology*. 1994; 21 (4): 315-318	observational study	301	14
9	Weinberger MH, et al. Primary aldosteronism - diagnosis, localization, and treatment. *Annals of Internal Medicine*. 1979; 90 (3): 386-395	review	300	8
10	Calhoun DA, et al. Hyperaldosteronism among with resistant black and white subjects hypertension. *Hypertension*. 2002; 40 (6): 892-896	observational study	295	21
11	Choi M, et al. K+ channel mutations in adrenal aldosterone-producing adenomas and hereditary hypertension. *Science*. 2011; 331 (6018): 768-772	basic science	276	55
12	Fardella CE, et al. Primary hyperaldosteronism in essential hypertensives: prevalence, biochemical profile, and molecular biology. *Journal of Clinical Endocrinology & Metabolism*. 2000; 85 (5): 1863-1867	observational study	276	17
13	Hiramatsu K, et al. A screening-test to identify aldosterone-producing adenoma by measuring plasma-renin activity - results in hypertensive patients. *Archives of Internal Medicine*. 1981; 141 (12): 1589-1593	observational study	276	8
14	Bravo EL, et al. The changing clinical spectrum of primary aldosteronism. *American Journal of Medicine*. 1983; 74 (4): 641-651	observational study	239	7
15	Melby JC, et al. Diagnosis and localization of aldosterone-producing adenomas by adrenal-vein catheterization. *New England Journal of Medicine*. 1967; 277 (20): 1050-1056	observational study	239	5
16	Young WF, et al. Role for adrenal venous sampling in primary aldosteronism. *Surgery*. 2004; 136 (6): 1227-1233	observational study	235	20
17	Conn JW. Primary aldosteronism. *Journal of Laboratory and Clinical Medicine*. 1955; 45 (4): 661-664	observational study	234	4
18	Young WF. Normokalemic primary aldosteronism - a detectable cause of curable essential hypertension. *JAMA*. 1965; 193 (3): 200-206	observational study	233	5
19	Loh KC, et al. Primary aldosteronism: renaissance of a syndrome. *Clinical Endocrinology*. 2007; 66 (5): 607-618	review	222	25
20	Mosso L, et al. Prevalence of primary aldosteronism among asian hypertensive patients in singapore. *Journal of Clinical Endocrinology & Metabolism*. 2000; 85 (8): 2854-2859	observational study	214	13
21	Ganguly A, et al. Primary aldosteronism and hypertensive disease. *Hypertension*. 2003; 42 (2): 161-165	observational study	207	16
22	Mulatero P, et al. Control of plasma aldosterone in primary aldosteronism: distinction between adenoma and hyperplasia. *Journal of Clinical Endocrinology & Metabolism*. 1973; 37 (5): 765-775	observational study	194	5
23	Ganguly A, et al. Drug effects on aldosterone/plasma renin activity ratio in primary aldosteronism. *Hypertension*. 2002; 40 (6): 897-902	randomized controlled trial	193	14
24	Rossi GP, et al. Current concepts - primary aldosteronism. *New England Journal of Medicine*. 1998; 339 (25): 1828-1834	review	191	11
25	Conn JW. Renal damage in primary aldosteronism - results of the papy study. *Hypertension*. 2006; 48 (2): 232-238	observational study	189	19
26	Pascoe L, et al. Plasma renin activity in primary aldosteronism - importance in differential diagnosis + in research of essential hypertension. *JAMA*. 1964; 190 (3): 222-225	review	188	4
27	Young WF. Glucocorticoid-suppressible hyperaldosteronism results from hybrid genes created by unequal crossovers between cyp11b1 and cyp11b2. *PNAS*. 1992; 89 (17): 8327-8331	basic science	182	8
28	Blumenfeld JD, et al. Minireview: primary aldosteronism - changing concepts in diagnosis and treatment. *Endocrinology*. 2003; 144 (6): 2208-2213	review	181	14
29	Lim PO, et al. Diagnosis and treatment of primary hyperaldosteronism. *Annals of Internal Medicine*. 1994; 121 (11): 877-885	observational study	181	8
30	Streeten DHP, et al. High prevalence of primary aldosteronism in the tayside hypertension clinic population. *Journal of Human Hypertension*. 2000; 14 (5): 311-315	observational study	166	10
31	Rossi GP, et al. Reliability of screening methods for the diagnosis of primary aldosteronism. *American Journal of Medicine*. 1979; 67 (3): 403-413	observational study	164	4
32	Gallay BJ, et al. Remodeling of the left ventricle in primary aldosteronism due to conn's adenoma. *Circulation*. 1997; 95 (6): 1471-1478	observational study	161	8
33	Newton MA, et al. Screening for primary aldosteronism without discontinuing hypertensive medications: plasma aldosterone-renin ratio. *American Journal of Kidney Diseases*. 2001; 37 (4): 699-705	observational study	159	11
34	Rossi GP, et al. Effect of corticotropin on aldosterone excretion and plasma renin in normal subjects in essential hypertension and in primary aldosteronism. *Journal of Clinical Endocrinology & Metabolism*. 1968; 28 (7): 1006-1013	observational study	158	3

rank	article	study design	citations	citation density
35	Rossi GP, et al. Identification of the etiology of primary aldosteronism with adrenal vein sampling in patients with equivocal computed tomography and magnetic resonance findings: results in 104 consecutive cases. *Journal of Clinical Endocrinology & Metabolism*. 2001; 86 (3): 1083-1090	observational study	157	10
36	Young WF, et al. Changes in left ventricular anatomy and function in hypertension and primary aldosteronism. *Hypertension*. 1996; 27 (5): 1039-1045	observational study	156	8
37	Conn JW, et al. Primary aldosteronism - diagnosis and treatment. *Mayo Clinic Proceedings*. 1990; 65 (1): 96-110	review	154	6
38	Stowasser M, et al. Primary aldosteronism, a new clinical entity. *Annals of Internal Medicine*. 1956; 44 (1): 1-15	observational study	154	3
39	Sawka AM, et al. High rate of detection of primary aldosteronism, including surgically treatable forms, after 'non-selective' screening of hypertensive patients. *Journal of Hypertension*. 2003; 21 (11): 2149-2157	observational study	152	12
40	Fallo F, et al. Primary aldosteronism: factors associated with normalization of blood pressure after surgery. *Annals of Internal Medicine*. 2001; 135 (4): 258-261	observational study	151	10
41	Magill SB, et al. Prevalence and characteristics of the metabolic syndrome in primary aldosteronism. *Journal of Clinical Endocrinology & Metabolism*. 2006; 91 (2): 454-459	observational study	150	15
42	Conn JW, et al. Comparison of adrenal vein sampling and computed tomography in the differentiation of primary aldosteronism. *Journal of Clinical Endocrinology & Metabolism*. 2001; 86 (3): 1066-1071	observational study	149	10
43	Sechi LA, et al. Primary aldosteronism - photoscanning of tumors after administration of i-131-19-iodocholesterol. *Archives of Internal Medicine*. 1972; 129 (3): 417-425	observational study	145	3
44	Gordon RD, et al. Long-term renal outcomes in patients with primary aldosteronism. *JAMA*. 2006; 295 (22): 2638-2645	observational study	144	14
45	Lim PO, et al. Evidence that primary aldosteronism may not be uncommon - 12-percent incidence among antihypertensive drug trial volunteers. *Clinical and Experimental Pharmacology and Physiology*. 1993; 20 (5): 296-298	observational study	144	6
46	Kawamoto T, et al. Potentially high prevalence of primary aldosteronism in a primary-care population. *Lancet*. 1999; 353 (9146): 40	observational study	143	8
47	Douma S, et al. Cloning and expression of a cdna for human cytochrome-p-450aldo as related to primary aldosteronism. *Biochemical and Biophysical Research Communications*. 1990; 173 (1): 309-316	basic science	143	6
48	Milne MD, et al. Prevalence of primary hyperaldosteronism in resistant hypertension: a retrospective observational study. *Lancet*. 2008; 371 (9628): 1921-1926	observational study	142	18
49	Dunn PJ, et al. Primary aldosteronism. Quarterly Journal of Medicine. 1957; 26 (103): 317-33	observational study	138	2
50	Catena C, et al. Outpatient screening-tests for primary aldosteronism. *Australian and New Zealand Journal of Medicine*. 1976; 6 (2): 131-135	observational study	132	3
51	Fishman LM, et al. Long-term cardiac effects of adrenalectomy or mineralocorticoid antagonists in patients with primary aldosteronism. *Hypertension*. 2007; 50 (5): 911-918	observational study	127	14
52	Rich GM, et al. Incidence of primary aldosteronism uncomplicated essential hypertension - a prospective study with elevated aldosterone secretion and suppressed plasma renin activity used as diagnostic criteria. *JAMA*. 1968; 205 (7): 497-502	observational study	127	3
53	Ogishima T, et al. Glucocorticoid-remediable aldosteronism in a large kindred - clinical spectrum and diagnosis using a characteristic biochemical phenotype. *Annals of Internal Medicine*. 1992; 116 (10): 813-820	observational study	124	5
54	Conn JW, et al. Aldosterone synthase cytochrome-p-450 expressed in the adrenals of patients with primary aldosteronism. *Journal of Biological Chemistry*. 1991; 266 (17): 10731-10734	basic science	124	5
55	Irony I, et al. Correctable subsets of primary aldosteronism: primary adrenal hyperplasia and renin responsive adenoma. *American Journal of Hypertension*. 1990; 3 (7): 576-582	observational study	123	5
56	Biglieri EG, et al. Significance of elevated levels of plasma 18-hydroxycorticosterone in patients with primary aldosteronism. *Journal of Clinical Endocrinology & Metabolism*. 1979; 49 (1): 87-91	observational study	122	3
57	Rossi GP, et al. Excess aldosterone is associated with alterations of myocardial texture in primary aldosteronism. *Hypertension*. 2002; 40 (1): 23-27	observational study	117	8
58	Weinberger MH, et al. The diagnosis of primary aldosteronism and separation of 2 major subtypes. *Archives of Internal Medicine*. 1993; 153 (18): 2125-2129	observational study	116	5
59	Biglieri EG, et al. In vivo and in vitro studies of adrenal secretions in cushings syndrome and primary aldosteronism. *Journal of Clinical Investigation*. 1963; 42 (4): 516-524	observational study	115	2
60	GeorgeJM, et al. The syndrome of primary aldosteronism. *American Journal of Medicine*. 1970; 48 (3): 343-356	observational study	113	2
61	Conn JW. Aldosteronism and hypertension: primary aldosteronism versus hypertensive disease with secondary aldosteronism. *Archives of Internal Medicine*. 1961; 107 (6): 813-828	review	113	2
62	Kem DC, et al. Circadian-rhythm of plasma aldosterone concentration in patients with primary aldosteronism. *Journal of Clinical Investigation*. 1973; 52 (9): 2272-2277	observational study	112	3
63	Jonsson JR, et al. A new genetic test for familial hyperaldosteronism type-i aids in the detection of curable hypertension. *Biochemical and Biophysical Research Communications*. 1995; 207 (2): 565-571	basic science	111	5
64	Young WF, et al. Primary aldosteronism - diagnostic evaluation. *Endocrinology and Metabolism Clinics of North America*. 1988; 17 (2): 367-395	review	111	4
65	Catena C, et al. Insulin sensitivity in patients with primary aldosteronism: a follow-up study. *Journal of Clinical Endocrinology & Metabolism*. 2006; 91 (9): 3457-3463	observational study	109	11

rank	article	study design	citations	citation density
66	Doppman JL, et al. Distinction between hyperaldosteronism - due to bilateral hyperplasia and unilateral aldosteronoma - reliability of ct. *Radiology*. 1992; 184 (3): 677-682	observational study	107	4
67	Schambelan M, et al. Circadian-rhythm and effect of posture on plasma aldosterone concentration in primary aldosteronism. *Journal of Clinical Endocrinology & Metabolism*. 1976; 43 (1): 115-131	observational study	107	3
68	Gomezsanchez CE, et al. Elevated urinary excretion of 18-oxocortisol in glucocorticoid-suppressible aldosteronism. *Journal of Clinical Endocrinology & Metabolism*. 1984; 59 (5): 1022-1024	basic science	105	3
69	Nishimura M, et al. Cardiovascular complications in patients with primary aldosteronism. *American Journal of Kidney Diseases*. 1999; 33 (2): 261-266	observational study	104	6
70	Hogan MJ, et al. Location of aldosterone-producing adenomas with i-131-19-iodocholesterol. *New England Journal of Medicine*. 1976; 294 (8): 410-414	observational study	104	3
71	Pascoe L, et al. Glucocorticoid-suppressible hyperaldosteronism and adrenal-tumors occurring in a single french pedigree. *Journal of Clinical Investigation*. 1995; 96 (5): 2236-2246	basic science	102	5
72	Davis WW, et al. Bilateral adrenal hyperplasia as a cause of primary aldosteronism with hypertension hypokalemia and suppressed renin activity. *American Journal of Medicine*. 1967; 42 (4): 642-647	observational study	102	2
73	Montori VM, et al. Use of plasma aldosterone concentration-to-plasma renin activity ratio as a screening test for primary aldosteronism - a systematic review of the literature. *Endocrinology and Metabolism Clinics of North America*. 2002; 31 (3): 619-632	systematic review	101	7
74	Gordon RD. Primary aldosteronism. *Journal of Endocrinological Investigation*. 1995; 18 (7): 495-511	review	100	5
75	Yamaji T, et al. Plasma levels of atrial natriuretic peptide in primary aldosteronism and essential hypertension. *Journal of Clinical Endocrinology & Metabolism*. 1986; 63 (4): 815-818	observational study	100	3
76	Davies LA, et al. Task channel deletion in mice causes primary hyperaldosteronism. *PNAS*. 2008; 105 (6): 2203-2208	basic science	98	12
77	Mulatero P, et al. Diagnosis of primary aldosteronism: from screening to subtype differentiation. *Trends in Endocrinology and Metabolism*. 2005; 16 (3): 114-119	review	96	9
78	Celen O, et al. Factors influencing outcome of surgery for primary aldosteronism. *Archives of Surgery*. 1996; 131 (6): 646-650	observational study	95	5
79	Lyons DF, et al. Single dose captopril as a diagnostic test for primary aldosteronism. *Journal of Clinical Endocrinology & Metabolism*. 1983; 57 (5): 892-896	observational study	94	3
80	White EA, et al. Use of computed-tomography in diagnosing the cause of primary aldosteronism. *New England Journal of Medicine*. 1980; 303 (26): 1503-1507	observational study	94	3
81	Chu MD, et al. Isolation and identification of 18-hydroxycortisol from the urine of patients with primary aldosteronism. *Journal of Biological Chemistry*. 1982; 257 (5): 2218-2224	basic science	93	3
82	Phillips JL, et al. Predictive value of preoperative tests in discriminating bilateral adrenal hyperplasia from an aldosterone-producing adrenal adenoma. *Journal of Clinical Endocrinology & Metabolism*. 2000; 85 (12): 4526-4533	observational study	92	6
83	Rovner DR, et al. Nature of renal escape from sodium-retaining effect of aldosterone in primary aldosteronism and in normal subjects. *Journal of Clinical Endocrinology & Metabolism*. 1965; 25 (1): 53-64	observational study	92	2
84	Strauch B, et al. Prevalence of primary hyperaldosteronism in moderate to severe hypertension in the central europe region. *Journal of Human Hypertension*. 2003; 17 (5): 349-352	observational study	91	7
85	Holland OB, et al. Further evaluation of saline infusion for the diagnosis of primary aldosteronism. *Hypertension*. 1984; 6 (5): 717-723	observational study	91	3
86	Ferriss JB, et al. Clinical, biochemical and pathological features of low-renin (primary) hyper-aldosteronism. *American Heart Journal*. 1978; 95 (3): 375-388	review	91	2
87	Neville AM, et al. Pathology of primary aldosteronism. *Cancer*. 1966; 19 (12): 1854-1868	observational study	91	2
88	Giacchetti G, et al. Aldosterone as a key mediator of the cardiometabolic syndrome in primary aldosteronism: an observational study. *Journal of Hypertension*. 2007; 25 (1): 177-186	observational study	90	10
89	Stowasser M, et al. Diagnosis and management of primary aldosteronism. *Journal of the Renin-Angiotensin-Aldosterone System*. 2001; 2 (3): 156-169	review	90	6
90	Lim PO, et al. A review of the medical treatment of primary aldosteronism. *Journal of Hypertension*. 2001; 19 (3): 353-361	systematic review	90	6
91	Biglieri EG, et al. Postoperative studies of adrenal function in primary aldosteronism. *Journal of Clinical Endocrinology & Metabolism*. 1966; 26 (5): 553-558	observational study	90	2
92	Cain JP, et al. The regulation of aldosterone secretion in primary aldosteronism. *American Journal of Medicine*. 1972; 53 (5): 627-637	observational study	89	2
93	Conn JW, et al. Preoperative diagnosis of primary aldosteronism - including a comparison of operative findings and preoperative tumor localization by adrenal phlebography. *Archives of Internal Medicine*. 1969; 123 (2): 113-123	observational study	89	2
94	Jose A, et al. Plasma renin activity in diagnosis of primary aldosteronism - failure to distinguish primary aldosteronism from essential hypertension. *Archives of Internal Medicine*. 1969; 123 (2): 141-146	observational study	89	2
95	Boulkroun S, et al. Prevalence, clinical, and molecular correlates of kcnj5 mutations in primary aldosteronism. *Hypertension*. 2012; 59 (3): 592-598	basic science	88	22
96	Kempers MJE, et al. Systematic review: diagnostic procedures to differentiate unilateral from bilateral adrenal abnormality in primary aldosteronism. *Annals of Internal Medicine*. 2009; 151 (5): 329-337	systematic Review	88	13
97	Rossi GP, et al. Primary aldosteronism: cardiovascular, renal and metabolic implications. *Trends in Endocrinology and Metabolism*. 2008; 19 (3): 88-90	review	88	11

rank	article	study design	citations	citation density
98	Stowasser M, et al. Evidence for abnormal left ventricular structure and function in normotensive individuals with familial hyperaldosteronism type I. *Journal of Clinical Endocrinology & Metabolism*. 2005; 90 (9): 5070-5076	observational study	88	8
99	Takeda M, et al. Laparoscopic adrenalectomy for primary aldosteronism - report of initial 10 cases. *Surgery*. 1994; 115 (5): 621-625	observational study	88	4
100	Slaton PE, et al. Stimulation and suppression of aldosterone secretion in patients with an aldosterone-producing adenoma. *Journal of Clinical Endocrinology & Metabolism*. 1969; 29 (2): 239-250	observational study	88	2

3.2. Publication Year

The retrieved articles were published between 1955 and 2012. The top 100 cited articles were grouped by decade of publication as shown in Figure 1. The decade with the highest number of published articles was the 2000s (35 articles), followed by the 1990s (22 articles).

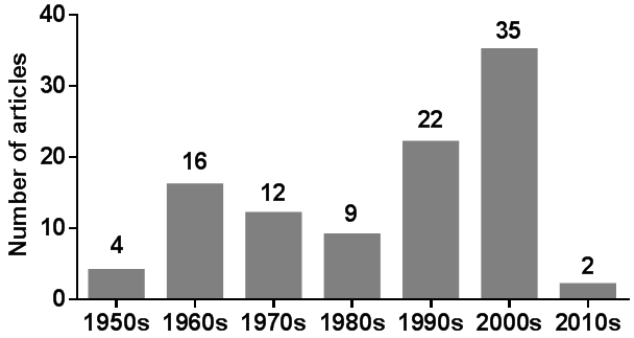

Figure 1. *Distribution of top 100 cited articles in primary aldosteronism by decade.*

3.3. Study Design and Level of Evidence of the Top-cited Articles

Observational studies had the most articles (70), followed by reviews (14), basic science (11), and systematic reviews (3) (Figure 2). Guideline and randomized controlled trial (RCT) were the least represented, each with only one article. In terms of level of evidence, levels 1a and 1b each had a single article, whereas levels 2a. 2b, 3b, 4 and 5, were represented by 3, 7, 17, 46 and 25 articles, respectively.

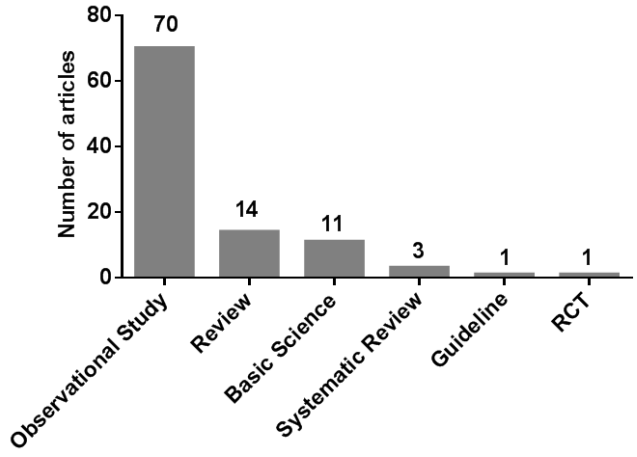

Figure 2. *Distribution of top 100 cited articles in primary aldosteronism by study design.*

3.4. Authors, Countries, and Institutions of Origin

We also analyzed the first author in each of the top 100 cited articles. Twelve authors published two or more of the most-cited articles (Table 2). Conn JW, the famous endocrinologist who authored ten classic articles and coined the term "primary aldosteronism" in 1955, was the leading author followed by Rossi GP and Young WF with seven and five classic articles, respectively.

Table 2. *Most common first authors of the top 100 cited articles in primary aldosteronism.*

Rank	Authors	Number of articles
1	Conn JW	10
2	Rossi GP	7
3	Young WF	5
4a	Biglieri EG	3
4b	Gordon RD	3
4c	Lim PO	3
4d	Stowasser M	3
5a	Catena C	2
5b	Ganguly A	2
5c	Mulatero P	2
5d	Pascoe L	2
5e	Weinberger MH	2

Table 3. *Countries of origin of the top 100 cited articles in primary aldosteronism.*

Rank	Country	Number of articles
1	USA	62
2	Italy	16
3	Australia	9
4	UK	8
5	Japan	6
6a	Chile	3
6b	France	3
7	Germany	2
8a	Argentina	1
8b	Brazil	1
8c	Czech Republic	1
8d	Greece	1
8e	Netherlands	1
8f	New Zealand	1
8g	Singapore	1
8h	Sweden	1

The top 100 cited articles originated from 16 countries (Table 3). Countries with the most articles were the United States of America (62), Italy (16), Australia (9), the United Kingdom (8), and Japan (6). Only 12 articles were completed through multinational collaborations, whereas the authors of each of the 88 articles were all from the same country.

Table 4. *Institutions of origin with 3 or more top 100 cited articles in primary aldosteronism.*

Rank	Institution	Number of articles	Country
1a	University of Michigan	11	USA
1b	University of Padua	11	Italy
2	Mayo Clinic	10	USA
3	University of California	8	USA
4	Greenslopes Hospital	6	Australia
5a	Indiana University	4	USA
5b	University of Texas	4	USA
5c	University of Turin	4	Italy
5d	University of Udine	4	Italy
6a	Catholic University of Chile	3	Chile
6b	Cornell University	3	USA
6c	Harvard University	3	USA
6d	Howard Hughes Medical Institute	3	USA
6e	Marche Polytechnic University	3	Italy
6f	National Cancer Institute	3	USA
6g	University of Dundee	3	UK
6h	University of Queensland	3	Australia

Seventeen institutions published three or more of the top 100 cited articles (Table 4). Out of the 17, nine (53%) institutions are located in the United States, whereas the other eight (47%) are from various countries: four institutions from Italy, two from Australia, and one each from the UK and Chile. The institutions with the highest number of articles were University of Michigan and University of Padua (n=11 each), followed by Mayo Clinic (n=10) and University of California (n=8).

3.5. Journals

The top 100 cited articles were published in 37 journals (Table 5). The majority of the articles were published in the *Journal of Clinical Endocrinology and Metabolism* (n=19), *Hypertension* (n=9), *Annals of Internal Medicine* (n=6), *Archives of Internal Medicine* (n=6), *American Journal of Medicine* (n=5), and *Journal of the American Medical Association (JAMA)* (n=4). The majority of the articles (42%, 42 articles) were published in the leading journals in endocriminology or hypertension, while 36 (36%) were published in the top medical journals. There was no correlation between the impact factor of a journal and the number of the top 100 cited articles it published (r=0.28, P>0.05).

Table 5. *Journals in which the top 100 most cited articles were published.*

Rank	Journals	Number of articles	Impact factor (2016)
1	*Journal of Clinical Endocrinology Metabolism*	19	5.531
2	*Hypertension*	9	6.294
3a	*Annals of Internal Medicine*	6	16.440
3b	*Archives of Internal Medicine*	6	14
4a	*American Journal of Medicine*	5	5.610
4b	*The Journal of the American Medical Association (JAMA)*	5	59.558
5	*New England Journal of Medicine*	4	37.684
6a	*Journal of Clinical Investigation*	3	12.575
6b	*Journal of Hypertension*	3	5.062
7a	*American Journal of Kidney Diseases*	2	6.269
7b	*Biochemical and Biophysical Research Communications*	2	2.371
7c	*Clinical and Experimental Pharmacology and Physiology*	2	2.004
7d	*Endocrinology and Metabolism Clinics of North America*	2	3.305
7e	*Journal of Biological Chemistry*	2	4.258
7f	*Journal of Human Hypertension*	2	2.833
7g	*Journal of Laboratory and Clinical Medicine*	2	
7h	*Journal of The American College of Cardiology*	2	17.759
7i	*Lancet*	2	44.002
7j	*Proceedings of the National Academy of Sciences (PNAS)*	2	9.423
7k	*Surgery*	2	3.309
7l	*Trends In Endocrinology and Metabolism*	2	8.964
8a	*American Heart Journal*	1	4.332
8b	*American Journal of Hypertension*	1	3.182
8c	*American Journal of Surgery*	1	2.403
8d	*Archives of Surgery*	1	5.661
8e	*Australian and New Zealand Journal of Medicine*	1	
8f	*Cancer*	1	5.649
8g	*Circulation*	1	17.047
8h	*Clinical Endocrinology*	1	3.487
8i	*Endocrinology*	1	4.159
8j	*Journal of Endocrinological Investigation*	1	1.994
8k	*Journal of The Renin Angiotensin Aldosterone System*	1	2.350
8l	*Mayo Clinic Proceedings*	1	5.920
8m	*Nature*	1	38.138
8n	*Quarterly Journal of Medicine*	1	
8o	*Radiology*	1	6.798
8p	*Science*	1	34.661

3.6. Investigation of Possible Factors Influencing Citations

To determine the factors influencing the number of citations of the most-cited articles, we investigated the relationships between the number of citations and the number of years since publication, the number of authors, the number of institutions or the number of countries involved. There was no correlation between the number of citations and the number of years since publication (*r=-0.01, P=0.96*), the number of authors (*r=0.05, P=0.65*), the number of institutions (*r=-0.04, P=0.71*) or the number of countries involved (*r=-0.05, P=0.59*) (Figure 3).

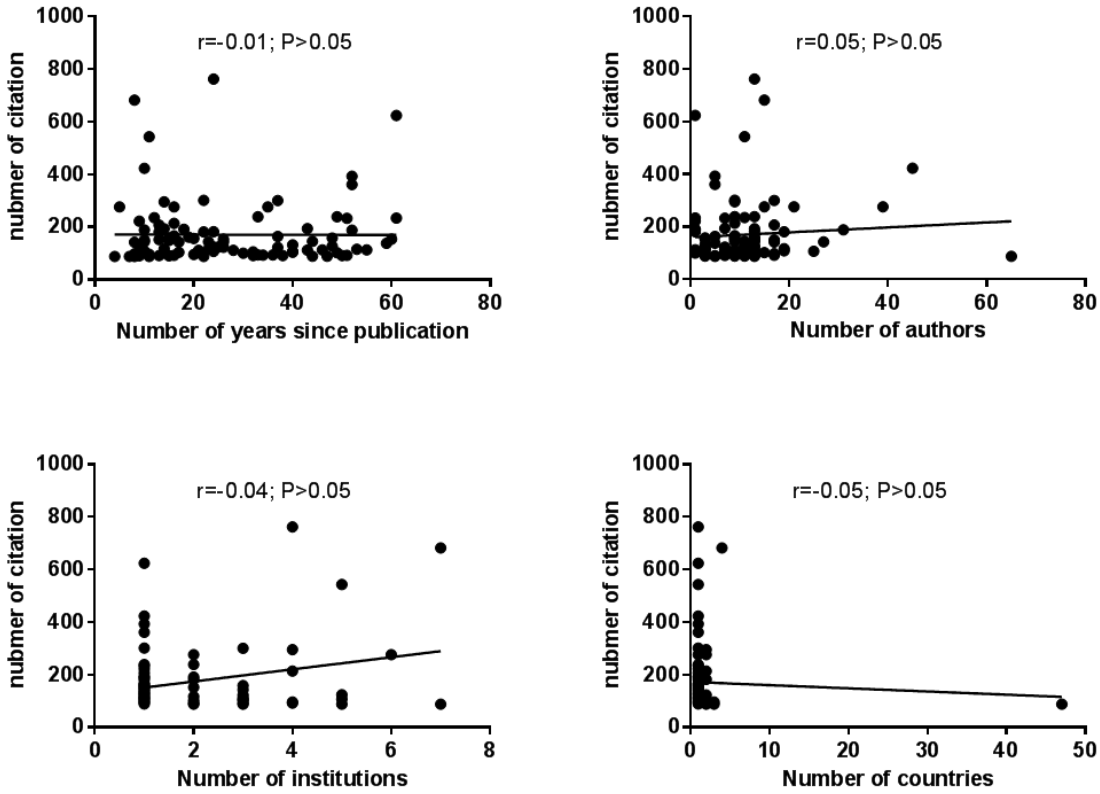

Figure 3. *Correlations between the number of citations and the number of years since publication (A), the number of authors (B), the number of institutions (C) or the number of countries involved (D).*

4. Discussion

In this study, we used bibliometric method to identify and characterize the top 100 cited articles in the field of primary aldosteronism. Identifying the top 100 cited publications is useful for the following reasons. Firstly, it highlights the landmark articles in the development of primary aldosteronism. Furthermore, it enables researchers or clinicians to get essential information about authors and institutions that have greatly contributed to these milestones and have subsequently steered the primary aldosteronism field. Lastly, knowing and understanding the key features of the most-cited articles will aid young researchers in publishing effectively [19].

The top 100 cited articles on primary aldosteronism were cited 88-762 times, which is remarkably lower than that of classic articles in other medical fields, such as hypertension (582-7248), diabetes (1121-10292), and tuberculosis (366-4443) [10-12]. Citations varied by specialty and were likely to be influenced by the number of researchers active in a specific medical field [14]. For example, hypertension, diabetes, and tuberculosis are the most common diseases and continue to increase rapidly worldwide. Consequently, more researchers are focusing on these areas rather than primary aldosteronism.

A proportion of the 100 most-cited articles in the field of primary aldosteronism were published recently, with 37 articles being published after 2000, which was similar to the findings of some bibliometric analyses [14, 20]. However, previous bibliometric-based studies indicated that articles might take at least 15 years to achieve a peak in citations [13, 21]. This disparity could be attributed to a number of factors. First, similar to digestive diseases, more articles emerged in the past 15 years and researchers in the field of primary aldosteronism tend to cite the most recent studies [14]. Furthermore, the number of citations showed no correlation with the number of years since publication. Finally, the time period varies with specialty since different journals and fields have diverse citation half-lives [22].

Although RCTs provided the highest-quality evidence for most clinical problems, only one RCT (level 1b) was found among the 100 most-cited articles in the field of primary aldosteronism. This is contrary to most other specialties, such as hypertension (n=24) and diabetes (n=29) [11, 12].

Consequently, further research is needed to provide more high-level evidence of clinical trials. Several possible reasons can explain the lack of RCTs in primary aldosteronism. First, it is difficult for primary aldosteronism to enroll abundant patients in comparison with hypertension and diabetes. Furthermore, RCTs are extremely expensive and time-consuming. Consequently, we discovered that observational studies accounted for the majority of the most-cited articles in the field of primary aldosteronism, implying that novel concepts were initially published as observational studies and could still be of interest to the scientific community.

Our study also found that the United States produced the majority of the top 100 cited articles. In addition, nine of the 17 leading institutions in primary aldosteronism articles were based in the United States. These results were similar to those reported in a variety of medical fields regarding to the origin of 100 most-cited articles [11, 12, 23, 24], demonstrating that USA was far ahead in medical research due to its large number of researchers and plentiful funding. Furthermore, American authors prefer to cite local articles, and American reviewers favor articles from their own country [21, 25, 26].

This study revealed that the top 100 cited articles were published in 37 journals. Forty-two articles (42%) were published in the top journals in endocriminology or hypertension. According to Bradford's law, citations are mostly obtained from a few core journals in the specialized field, whereas articles published in non-core journals have significantly fewer citations [27]. Thus, most of the top-cited articles appear in a few major, specialized medical journals. In this study, two specialized journals: *Journal of Clinical Endocrinology Metabolism* and *Hypertension,* published the highest number (n=28) of the 100 most-cited articles. However, many top-cited articles on primary aldosteronism were published in general medical journals with high impact factors, such as *Annals of Internal Medicine* (n=6), *Archives of Internal Medicine* (n=6), and *JAMA* (n=5).

The impact factor of a journal has been shown to be the strongest determinant of citations, and most of the top-cited articles were published in journals with high impact factors [28]. However, in line with some of the previous bibliometric analyses [29, 30], we found no significant correlation between the impact factor of a journal and the number of the top 100 cited articles in the field of primary aldosteronism. Nevertheless, certain bibliometric-based studies contradicted the aforementioned conclusions, suggesting that the tendency for top-cited articles to be published in general or specialized journals varies across different medical fields [20, 24]. These findings indicated the need for more accurate measures to assess the significance of specific research papers.

There were some limitations in this study. First, we only used a single medical database, Science Citation Index Expanded (SCIE). It is worth noting that SCIE did not index all journals at the time of the study, and certain journals that may be indexed in Google Scholar or Scopus databases were overlooked. Therefore, our results differed significantly from those obtained using various databases [31-33]. However, it is acceptable to use a single medical database to identify top-cited medical research articles—many published bibliometric analyses have used the SCIE database for this purpose [11, 32-35]. Furthermore, to prevent the "obliteration by incorporation" effect which has been demonstrated in the literature of other medical fields, we created the list of the top 100 cited articles based on the absolute amount of citations that articles received. This could preferentially favor older articles that have accumulated numerous citations over time [20, 24, 36, 37]. Other potential factors that affect citations such as journal and author self-citation, citations in textbooks, conferences and web-based literatures, omission bias may not be accurately determined [21, 38].

5. Conclusion

Despite the above mentioned shortcomings, this study showed the characteristics of the top-cited articles in the field of primary aldosteronism. The top-cited articles were mainly observational studies, and high-quality evidence-based articles were still rare. The majority of the top-cited articles were published in the *Journal of Clinical Endocrinology and Metabolism* and *Hypertension,* and were from American institutions. Our findings provide insight into the history and evolution of primary aldosteronism, and a foundation for future research. Given that only a single RCT article was identified in this study, more RCTs on the diagnosis and treatment of primary aldosteronism should be conducted in future to improve clinical practice. There were no Chinese researchers nor institution among the 100 top-cited articles. Therefore, Chinese researchers should publish high-impact papers to guide further study in this field.

Competing Interests

The authors declare that they have no competing interests.

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