Original paper

The top 100 cited articles in lung cancer – a bibliometric analysis

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Aim of the study: To analyze the 100 most cited lung cancer articles published in biomedical literature in the last 44 years. We pointed out developments in lung cancer and aimed to create convenient access for the researchers of this dynamic field.

Material and methods: We accessed the WoS database (accessed: 15.07.2019) using the keyword "lung cancer" between 1975 and 2019. The top 100 cited articles were analyzed by topic, journal, author, year, institution, level of evidence, adjusted citation index and also the correlations between citation, adjusted citation index, impact factor and length of time since publication.

Results: A total of 240,701 eligible articles were identified and we chose the top 100 articles cited in the field of lung cancer. The mean number of citations for these articles was 1879.82 ±1264.78. The most cited article was (times cited: 7751) a study by Lynch *et al. The New England Journal of Medicine* (NEJM) made the greatest contribution to the top 100 list with 32 articles, and the most cited article also originated from NEJM. The highest number of citations was seen in 2017 with 18,393 citations while the highest number of publications was seen in 2005 with 12 publications.

Conclusions: Oncology is a developing field and we have seen the evolution in this area through the treatment of lung cancer in recent years. The first 100 articles in our analysis not only reflect the landmark articles with the greatest impact on lung cancer research, but also acknowledge the most productive authors and institutions that have contributed to the list with their articles.

Key words: bibliometric study, citation, lung cancer.

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Introduction

Lung cancer is an important health problem with an increasing incidence. In most European countries, lung cancer has increased so dramatically that it may be considered one of the major health problems in the last century [1]. The most common causes of cancer-related death are cancers of the lung and bronchus (24%), prostate (10%) and colorectum (9%) in men, and lung and bronchus (23%), breast (15%), and colorectum (8%) in women [2]. Although lung cancer has long been characterized by late-stage diagnosis and poor survival, encouraging results have been achieved for lung cancer screening in high-risk populations in the last decade and there has been significant progress in systemic treatments for molecular subgroups of patients with advanced disease. Furthermore, within the last ten years, new molecular targets have emerged, next-generation drugs with more specific target effects have been introduced, and targeting specific resistant mutations is expected to advance the treatment of lung cancer by creating a chronic therapeutic pathway [3]. This bibliometric study demonstrates the development of lung cancer treatment over the years.

Bibliometric studies represent an important study type showing the trend topics in a given field. Numerous medical and surgical specialists have published the most cited articles in their specialties in the form of bibliometric analysis such as general surgery [4], anesthesiology [5], orthopedics [6], otolaryngology [7], radiology [8] and plastic surgery [9]. The first bibliometric analysis was penned by Garfield and published in JAMA in 1987 [10]. He also continued with new bibliometric studies in different fields of medical science.

The purpose of our study was to identify and analyze the 100 most cited lung cancer articles published in biomedical literature in the last 44 years. We determined the number of citations with ranking, average citations per year (ACY), citations and publications by year, publishing journal, institution and country of origin, the most common subject of frequently cited articles, authorship status of classical papers and correlation analyses between citation, ACY, Impact Factor (IF) and length of time since publication in years.

Material and methods

Study design

Study type: retrospective clinical study, Level of evidence: 3 or Group B (Scottish Intercollegiate Guidelines Network; SIGN) [11].

Data collection and inclusion criteria: In this paper reporting a bibliometric citation analysis, data were obtained from Thomson Reuters' WoS Core Collection database (Philadelphia, Pennsylvania, USA) and PubMed (US National Library of Medicine-National Institutes of Health). We accessed the WoS database (accessed: 15.07.2019) using the keyword "lung cancer" between 1975 and 2019. We identified 240,701 articles and conducted an analysis of the top 100 cited articles among these hits shown in Table 1 [12–111]. Articles not relevant to lung cancer were excluded from our study and we included original re-

Table 1. The top 100 cited articles in lung cancer

Rank	Article	Citations	ACY*
1	Lynch TJ, Bell D, Sordella R, et al. Activating mutations in the epidermal growth factor receptor underlying responsiveness of nonsmallcell lung cancer to gefitinib. N Engl J Med 2004; 350: 2129-2139	7751	484.44
2	Aaronson NK, Ahmedzai S, Bergman B, et al. The European Organization for Research and Treatment of Cancer QLQC30: a quality-of-life instrument for use in international clinical trials in oncology. J Natl Cancer Inst 1993; 85: 365-376	7190	266.30
3	Paez JG, Jänne PA, Lee JC, et al. EGFR mutations in lung cancer: correlation with clinical response to gefitinib therapy. Science 2004; 304: 1497-1500	6599	412.44
4	Mok TS, Wu YL, Thongprasert S, et al. Gefitinib or carboplatin-paclitaxel in pulmonary adenocarcinoma. N Engl J Med 2009; 361: 947-957	4907	446.09
5	Shepherd FA, Rodrigues Pereira J, Ciuleanu T, et al. Erlotinib in previously treated nonsmallcell lung cancer. N Engl J Med 2005; 353: 123-132	4163	277.53
6	Sandler A, Gray R, Perry MC, et al. Paclitaxel-carboplatin alone or with bevacizumab for non-small-cell lung cancer. N Engl J Med 2006; 355: 2542-2550	4076	291.14
7	Schiller JH, Harrington D, Belani CP, et al. Comparison of four chemotherapy regimens for advanced non-small-cell lung cancer. N Engl J Med 2002; 346: 92-98	3672	204
8	Mountain CF. Revisions in the International System for Staging Lung Cancer. Chest 1997; 111: 1710-1717	3663	159.26
9	National Lung Screening Trial Research Team, Aberle DR, Adams AM, et al. Reduced lung-cancer mortality with lowdose computed tomographic screening. N Engl J Med 2011; 365: 395-409	3539	393.22
10	Maemondo M, Inoue A, Kobayashi K, et al. Gefitinib or chemotherapy for non-small-cell lung cancer with mutated EGFR. N Engl J Med. 2010; 362: 2380-2388	3077	307.7
11	Temel JS, Greer JA, Muzikansky A, et al. Early palliative care for patients with metastatic non-small-cell lung cancer. N Engl J Med 2010; 363: 733-742	3042	304.2
12	Engelman JA, Zejnullahu K, Mitsudomi T, et al. MET amplification leads to gefitinib resistance in lung cancer by activating ERBB3 signaling. Science 2007; 316: 1039-1043	3000	230.77
13	Brahmer J, Reckamp KL, Baas P, et al. Nivolumab versus Docetaxel in Advanced Squamous-Cell Non-Small-Cell Lung Cancer. N Engl J Med 2015; 373: 123-135	2966	593.2
14	Soda M, Choi YL, Enomoto M, et al. Identification of the transforming EML4-ALK fusion gene in non-small-cell lung cancer. Nature 2007; 448: 561-566	2960	227.69
15	Kwak EL, Bang YJ, Camidge DR, et al. Anaplastic lymphoma kinase inhibition in non-small-cell lung cancer. N Engl J Med 2010; 363: 1693-1703	2910	291
16	Borghaei H, Paz-Ares L, Horn L, et al. Nivolumab versus Docetaxel in Advanced Nonsquamous Non-Small-Cell Lung Cancer. Engl J Med 2015; 373: 1627-1639	2907	581.40
17	Rosell R, Carcereny E, Gervais R, et al. Erlotinib versus standard chemotherapy as first-line treatment for European patients with advanced EGFR mutation-positive non-small-cell lung cancer (EURTAC): a multicentre, open-label, randomised phase 3 trial. Lancet Oncol 2012; 13: 239-246	2804	350.5
18	Cole SP, Bhardwaj G, Gerlach JH, et al. Overexpression of a transporter gene in a multidrug-resistant human lung cancer cell line. Science 1992; 258: 1650-1654	2786	99.50
19	Kobayashi S, Boggon TJ, Dayaram T, et al. EGFR mutation and resistance of non-small-cell lung cancer to gefitinib. N Engl J Med 2005; 352: 786-792	2549	169.93
20	Rizvi NA, Hellmann MD, Snyder A, et al. Cancer immunology. Mutational landscape determines sensitivity to PD-1 blockade in non-small cell lung cancer. Science 2015; 348: 124-128	2501	500.2
21	Non-small Cell Lung Cancer Collaborative Group. Chemotherapy in non-small cell lung cancer: a meta-analysis using updated data on individual patients from 52 randomised clinical trials. BMJ 1995; 311: 899-909	2474	98.96
22	Mitsudomi T, Morita S, Yatabe Y, et al. Gefitinib versus cisplatin plus docetaxel in patients with non-small-cell lung cancer harbouring mutations of the epidermal growth factor receptor (WJTOG3405): an open label, randomised phase 3 trial. Lancet Oncol 2010; 11: 121-128.	2447	244.7
23	Travis WD, Brambilla E, Noguchi M, et al. International association for the study of lung cancer/american thoracic society/european respiratory society international multidisciplinary classification of lung adenocarcinoma. J Thorac Oncol 2011; 6: 244-285	2309	256.6
24	Fukuoka M, Yano S, Giaccone G, et al. Multi-institutional randomized phase II trial of gefitinib for previously treated patients with advanced non-small-cell lung cancer (The IDEAL 1 Trial). J Clin Oncol 2003; 21: 2237-2246	2256	132.71
25	Zhou C, Wu YL, Chen G, et al. Erlotinib versus chemotherapy as firstline treatment for patients with advanced EGFR mutation-positive non-small-cell lung cancer (OPTIMAL, CTONG0802): a multicentre, open-label, randomised, phase 3 study. Lancet Oncol 2011; 12: 735-742	2227	247.44

Table 1. Cont.

26	Yanaihara N, Caplen N, Bowman E, et al. Unique microRNA molecular profiles in lung cancer diagnosis and prognosis. Cancer Cell 2006; 9: 189-198	2201	157.21
27	Goldstraw P, Crowley J, Chansky K, et al. The IASLC Lung Cancer Staging Project: proposals for the revision of the TNM stage groupings in the forthcoming (seventh) edition of the TNM Classification of malignant tumours. J Thorac Oncol 2007; 2: 706-714	2185	168.08
28	Garon EB, Rizvi NA, Hui R, et al. Pembrolizumab for the treatment of non-small-cell lung cancer. N Engl J Med 2015; 372: 2018-2028	2127	425.4
29	Scagliotti GV, Parikh P, von Pawel J, et al. Phase III study comparing cisplatin plus gemcitabine with cisplatin plus pemetrexed in chemotherapy-naive patients with advanced-stage non-small-cell lung cancer. J Clin Oncol 2008; 26: 3543-3551	2108	175.67
30	Pao W, Miller VA, Politi KA, et al. Acquired resistance of lung adenocarcinomas to gefitinib or erlotinib is associated with a second mutation in the EGFR kinase domain. PLoS Med 2005; 2: e73	2073	138.2
31	Kris MG, Natale RB, Herbst RS, et al. Efficacy of gefitinib, an inhibitor of the epidermal growth factor receptor tyrosine kinase, in symptomatic patients with non-small cell lung cancer: a randomized trial. JAMA 2003; 290: 2149-2158	1998	117.53
32	Reck M, Rodríguez-Abreu D, Robinson AG, et al. Pembrolizumab versus Chemotherapy for PD-L1-Positive Non-Small-Cell Lung Cancer. N Engl J Med 2016; 375: 1823-1833	1970	492.5
33	Shaw AT, Kim DW, Nakagawa K, et al. Crizotinib versus chemotherapy in advanced ALK-positive lung cancer. N Engl J Med 2013; 368: 2385-2394	1906	272.29
34	Cancer Genome Atlas Research Network. Comprehensive genomic characterization of squamous cell lung cancers. Nature 2012; 489: 519-525	1806	225.75
35	Hanna N, Shepherd FA, Fossella FV, et al. Randomized phase III trial of pemetrexed versus docetaxel in patients with non-small-cell lung cancer previously treated with chemotherapy. J Clin Oncol 2004; 22: 1589-1597	1773	110.81
36	Takamizawa J, Konishi H, Yanagisawa K, et al. Reduced expression of the let-7 microRNAs in human lung cancers in association with shortened postoperative survival. Cancer Res 2004; 64: 3753-3756	1729	108.06
37	Sharma SV, Bell DW, Settleman J, Haber DA. Epidermal growth factor receptor mutations in lung cancer. Nat Rev Cancer 2007; 7: 169-181	1722	132.46
38	Herbst RS, Baas P, Kim DW, et al. Pembrolizumab versus docetaxel for previously treated, PD-L1- positive, advanced non-small-cell lung cancer (KEYNOTE-010): a randomised controlled trial. Lancet 2016; 387: 1540-1550	1705	426.5
39	Henschke CI, McCauley DI, Yankelevitz DF, et al. Early Lung Cancer Action Project: overall design and findings from baseline screening. Lancet 1999; 354: 99-105	1665	79.29
40	Bhattacharjee A, Richards WG, Staunton J, et al. Classification of human lung carcinomas by mRNA expression profiling reveals distinct adenocarcinoma subclasses. Proc Natl Acad Sci U S A 2001; 98: 13790-13795	1645	86.58
41	Sequist LV, Waltman BA, Dias-Santagata D, et al. Genotypic and histological evolution of lung cancers acquiring resistance to EGFR inhibitors. Sci Transl Med 2011; 3: 75ra26	1636	181.78
42	Thatcher N, Chang A, Parikh P, et al. Gefitinib plus best supportive care in previously treated patients with refractory advanced non-small-cell lung cancer: results from a randomised, placebo-controlled, multicentre study (Iressa Survival Evaluation in Lung Cancer). Lancet 2005; 366: 1527-1537	1628	108.53
43	Shigematsu H, Lin L, Takahashi T, et al. Clinical and biological features associated with epidermal growth factor receptor gene mutations in lung cancers. J Natl Cancer Inst 2005; 97: 339-346	1607	107.13
44	Shepherd FA, Dancey J, Ramlau R, et al. Prospective randomized trial of docetaxel versus best supportive care in patients with non-small-cell lung cancer previously treated with platinum-based chemotherapy. J Clin Oncol 2000; 18: 2095-2103	1551	77.55
45	Murren JR, Buzaid AC, Hait WN. Critical analysis of neoadjuvant therapy for Stage IIIa non-small cell lung cancer. Am Rev Respir Dis 1991; 143: 889-894.	1509	52.03
46	Mountain CF. A new international staging system for lung cancer. Chest 1986; 89: 225S-233S	1509	44.38
47	Rosell R, Moran T, Queralt C, et al. Screening for epidermal growth factor receptor mutations in lung cancer. N Engl J Med 2009; 361: 958-967	1483	34.82
48	Arriagada R, Bergman B, Dunant A, Le Chevalier T, Pignon JP, Vansteenkiste J; International Adjuvant Lung Cancer Trial Collaborative Group. Cisplatin-based adjuvant chemotherapy in patients with completely resected non-small-cell lung cancer. N Engl J Med 2004; 350: 351-360	1471	91.94
49	Herbst RS, Heymach JV, Lippman SM. Lung cancer. N Engl J Med 2008; 359: 1367-1380	1451	120.92
50	Rikova K, Guo A, Zeng Q, et al. Global survey of phosphotyrosine signaling identifies oncogenic kinases in lung cancer. Cell 2007; 131: 1190-1203	1436	110.46

Table 1. Cont.

51	Johnson DH, Fehrenbacher L, Novotny WF, et al. Randomized phase II trial comparing bevacizumab plus carboplatin and paclitaxel with carboplatin and paclitaxel alone in previously untreated locally advanced or metastatic non-small-cell lung cancer. J Clin Oncol 2004; 22: 2184-2191	1428	89.25
52	Tsao MS, Sakurada A, Cutz JC, et al. Erlotinib in lung cancer - molecular and clinical predictors of outcome. N Engl J Med 2005; 353: 133-144	1423	94.87
53	Kim CF, Jackson EL, Woolfenden AE, et al. Identification of bronchioalveolar stem cells in normal lung and lung cancer. Cell 2005; 121: 823-835	1355	90.33
54	Timmerman R, Paulus R, Galvin J, et al. Stereotactic body radiation therapy for inoperable early stage lung cancer. JAMA 2010; 303: 1070-1076	1337	133.7
55	Giaccone G, Herbst RS, Manegold C, et al. Gefitinib in combination with gemcitabine and cisplatin in advanced non-small-cell lung cancer: a phase III trial – INTACT 1. J Clin Oncol 2004; 22: 777-784	1333	83.31
56	Herbst RS, Giaccone G, Schiller JH, et al. Gefitinib in combination with paclitaxel and carboplatin in advanced non-small-cell lung cancer: a phase III trial – INTACT 2. J Clin Oncol 2004; 22: 785-794	1314	82.13
57	Solomon BJ, Mok T, Kim DW, et al. First-line crizotinib versus chemotherapy in ALK-positive lung cancer. N Engl J Med 2014; 371: 2167-2177	1301	216.83
58	Denissenko MF, Pao A, Tang M, Pfeifer GP. Preferential formation of benzo[a]pyrene adducts at lung cancer mutational hotspots in P53. Science 1996; 274: 430-432	1294	53.92
59	Olaussen KA, Dunant A, Fouret P, et al. DNA repair by ERCC1 in non-small-cell lung cancer and cisplatinbased adjuvant chemotherapy. N Engl J Med 2006; 355: 983-991	1290	92.14
60	Hecht SS. Tobacco smoke carcinogens and lung cancer. J Natl Cancer Inst 1999; 91: 1194-1210	1288	61.33
61	Molina JR, Yang P, Cassivi SD, Schild SE, Adjei AA. Non-small cell lung cancer: epidemiology, risk factors, treatment, and survivorship. Mayo Clin Proc 2008; 83: 584-594	1280	106.67
62	Cuttitta F, Carney DN, Mulshine J, et al. Bombesin-like peptides can function as autocrine growth factors in human small-cell lung cancer. Nature 1985; 316: 823-826	1280	36.57
63	Cappuzzo F, Hirsch FR, Rossi E, et al. Epidermal growth factor receptor gene and protein and gefitinib sensitivity in non-small-cell lung cancer. J Natl Cancer Inst 2005; 97: 643-655	1278	85.2
64	Sordella R, Bell DW, Haber DA, Settleman J. Gefitinib-sensitizing EGFR mutations in lung cancer activate antiapoptotic pathways. Science 2004; 305: 1163-1167	1213	75.81
65	Winton T, Livingston R, Johnson D, et al. Vinorelbine plus cisplatin vs. observation in resected non-small-cell lung cancer. N Engl J Med 2005; 352: 2589-2597	1202	80.13
66	Takahashi T, Nau MM, Chiba I, et al. p53: a frequent target for genetic abnormalities in lung cancer. Science 1989; 246: 491-494	1194	38.52
67	Maheswaran S, Sequist LV, Nagrath S, et al. Detection of mutations in EGFR in circulating lung-cancer cells. N Engl J Med 2008; 359: 366-377	1158	96.5
68	Iggo R, Gatter K, Bartek J, Lane D, Harris AL. Increased expression of mutant forms of p53 oncogene in primary lung cancer. Lancet 1990; 335: 675-679	1155	38.5
69	Ji P, Diederichs S, Wang W, et al. MALAT-1, a novel noncoding RNA, and thymosin beta4 predict metastasis and survival in early-stage non-small cell lung cancer. Oncogene 2003; 22: 8031-8041	1143	67.24
70	Shaw AT, Yeap BY, Mino-Kenudson M, et al. Clinical features and outcome of patients with non-small-cell lung cancer who harbor EML4-ALK. J Clin Oncol 2009; 27: 4247-4253	1140	103.64
71	Crawford J, Ozer H, Stoller R, et al. Reduction by granulocyte colony-stimulating factor of fever and neutropenia induced by chemotherapy in patients with small-cell lung cancer. N Engl J Med 1991; 325: 164-170	1140	39.31
72	Hayashita Y, Osada H, Tatematsu Y, et al. A polycistronic microRNA cluster, miR-17-92, is overexpressed in human lung cancers and enhances cell proliferation. Cancer Res 2005; 65: 9628-9632	1112	74.13
73	Herbst RS, Prager D, Hermann R, et al. TRIBUTE: a phase III trial of erlotinib hydrochloride (OSI-774) combined with carboplatin and paclitaxel chemotherapy in advanced non-small-cell lung cancer. J Clin Oncol 2005; 23: 5892-5899	1106	73.73
74	Eberhard DA, Johnson BE, Amler LC, et al. Mutations in the epidermal growth factor receptor and in KRAS are predictive and prognostic indicators in patients with non-small-cell lung cancer treated with chemotherapy alone and in combination with erlotinib. J Clin Oncol 2005; 23: 5900-5909	1099	73.27
75	Eramo A, Lotti F, Sette G, et al. Identification and expansion of the tumorigenic lung cancer stem cell population. Cell Death Differ 2008; 15: 504-514	1080	90
76	Fabbri M, Garzon R, Cimmino A, et al. MicroRNA-29 family reverts aberrant methylation in lung cancer by targeting DNA methyltransferases 3A and 3B. Proc Natl Acad Sci U S A 2007; 104: 15805-15810	1071	82.38

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77	Yun CH, Mengwasser KE, Toms AV, et al. The T790M mutation in EGFR kinase causes drug resistance by increasing the affinity for ATP. Proc Natl Acad Sci U S A 2008; 105: 2070-2075	1054	87.83
78	Schaake-Koning C, van den Bogaert W, Dalesio O, et al. Effects of concomitant cisplatin and radiotherapy on inoperable non-small-cell lung cancer. N Engl J Med 1992; 326: 524-530	1047	37.39
79	Furuse K, Fukuoka M, Kawahara M, et al. Phase III study of concurrent versus sequential thoracic radiotherapy in combination with mitomycin, vindesine, and cisplatin in unresectable stage III non-small-cell lung cancer. J Clin Oncol 1999; 17: 2692-2699	1046	49.81
80	International Early Lung Cancer Action Program Investigators, Henschke CI, Yankelevitz DF, Libby DM, et al. Survival of patients with stage I lung cancer detected on CT screening. N Engl J Med 2006; 355: 1763-1771.	1030	73.57
81	Pignon JP, Tribodet H, Scagliotti GV, et al. Lung adjuvant cisplatin evaluation: a pooled analysis by the LACE Collaborative Group. J Clin Oncol 2008; 26: 3552-3559	1022	85.17
82	Reck M, von Pawel J, Zatloukal P, et al. Phase III trial of cisplatin plus gemcitabine with either placebo or bevacizumab as first-line therapy for nonsquamous non-small-cell lung cancer: AVAil. J Clin Oncol 2009; 27: 1227-1234	1015	92.27
83	Jackson EL, Willis N, Mercer K, et al. Analysis of lung tumor initiation and progression using conditional expression of oncogenic K-ras. Genes Dev 2001; 15: 3243-3248	1008	53.05
84	Pirker R, Pereira JR, Szczesna A, et al. Cetuximab plus chemotherapy in patients with advanced nonsmall-cell lung cancer (FLEX): an open-label randomised phase III trial. Lancet 2009; 373: 1525-1531	1002	91.09
85	Kim ES, Hirsh V, Mok T, et al. Gefitinib versus docetaxel in previously treated non-small-cell lung cancer (INTEREST): a randomised phase III trial. Lancet 2008; 372: 1809-1818	987	82.25
86	Govindan R, Page N, Morgensztern D, et al. Changing epidemiology of small-cell lung cancer in the United States over the last 30 years: analysis of the surveillance, epidemiologic, and end results database. J Clin Oncol 2006; 24: 4539-4544	981	70.07
87	Jänne PA, Yang JC, Kim DW, et al. AZD9291 in EGFR inhibitor-resistant non-small-cell lung cancer. N Engl J Med 2015; 372: 1689-1699	977	195.4
88	Fossella FV, DeVore R, Kerr RN, et al. Randomized phase III trial of docetaxel versus vinorelbine or ifosfamide in patients with advanced non-small-cell lung cancer previously treated with platinum-containing chemotherapy regimens. The TAX 320 Non-Small Cell Lung Cancer Study Group. J Clin Oncol 2000; 18: 2354-2362	975	48.75
89	Pfister DG, Johnson DH, Azzoli CG, et al. American Society of Clinical Oncology treatment of unresectable non-small-cell lung cancer guideline: update 2003. J Clin Oncol 2004; 22: 330-353	967	60.44
90	Lardinois D, Weder W, Hany TF, et al. Staging of non-small-cell lung cancer with integrated positronemission tomography and computed tomography. N Engl J Med 2003; 348: 2500-2507	963	56.65
91	Dillman RO, Seagren SL, Propert KJ, et al. A randomized trial of induction chemotherapy plus high-dose radiation versus radiation alone in stage III non-small-cell lung cancer. N Engl J Med 1990; 323: 940-945	961	32.03
92	Mountain CF, Dresler CM. Regional lymph node classification for lung cancer staging. Chest 1997; 111: 1718-1723	952	41.39
93	Aupérin A, Arriagada R, Pignon JP, et al. Prophylactic cranial irradiation for patients with small-cell lung cancer in complete remission. Prophylactic Cranial Irradiation Overview Collaborative Group. N Engl J Med 1999; 341: 476-484	933	44.43
94	Rosell R, Gómez-Codina J, Camps C, et al. A randomized trial comparing preoperative chemotherapy plus surgery with surgery alone in patients with non-small-cell lung cancer. N Engl J Med 1994; 330: 153-158	927	35.65
95	Rittmeyer A, Barlesi F, Waterkamp D, et al. Atezolizumab versus docetaxel in patients with previously treated non-small-cell lung cancer (OAK): a phase 3, open-label, multicentre randomised controlled trial. Lancet 2017; 389: 255-265	926	308.67
96	Douillard JY, Rosell R, De Lena M, et al. Adjuvant vinorelbine plus cisplatin versus observation in patients with completely resected stage IB-IIIA non-small-cell lung cancer (Adjuvant Navelbine International Trialist Association [ANITA]): a randomised controlled trial. Lancet Oncol 2006; 7: 719-727	925	66.07
97	Kosaka T, Yatabe Y, Endoh H, Kuwano H, Takahashi T, Mitsudomi T. Mutations of the epidermal growth factor receptor gene in lung cancer: biological and clinical implications. Cancer Res 2004; 64: 8919-8923	927	57.56
98	Cappuzzo F, Ciuleanu T, Stelmakh L, et al. Erlotinib as maintenance treatment in advanced non-small-cell lung cancer: a multicentre, randomised, placebo-controlled phase 3 study. Lancet Oncol 2010; 11: 521-529	894	89.4
99	Pignon JP, Arriagada R, Ihde DC, et al. A meta-analysis of thoracic radiotherapy for small-cell lung cancer. N Engl J Med 1992; 327: 1618-1624	891	31.82
100	Imielinski M, Berger AH, Hammerman PS, et al. Mapping the hallmarks of lung adenocarcinoma with massively parallel sequencing. Cell 2012; 150: 1107-1120	889	111.13

ACY – average citations per year

Table 2. Type of treatment and level of evidence of the treatment based clinical articles (n = 59)

Treatment	Level 1	Level 2	Level 3	Level 4
EGFR mutations	17	–	6	–
Chemotherapy	19	–	–	1
Palliative care	1	–	–	–
Immunotherapy	5	1	1	–
ALK mutations	2	–	1	–
Radiotherapy	3	1	1	–

EGFR – epidermal growth factor receptor, ALK – anaplastic lymphoma kinase

search articles, editorials, correspondences, review articles and case reports. We also utilized the PubMed database to obtain additional data related to the study. Two of the authors (NSS and EC) independently identified T100 with consensus. The difference in time since publication among the top 100 articles may cause a bias as older articles may be more likely to have obtained more citations owing to a longer citable period. The Web of Science, Citation Report feature displays bar charts for the number of items published each year and calculates the average number of citations per year per publication. Due to this bias, we used the ACY for each article.

Statistical analysis

A commercial software (SPSS version 16.0, SPSS, Chicago IL, USA) was used for the statistical analysis. The Kolmogorov-Smirnov test was used to analyze the normal distribution of data. Spearman's correlation was used to evaluate the associations between citation, ACY, IF and length of time since publication. A p-value < 0.05 was accepted as statistically significant.

Ethical statement

All authors declare that the study was conducted according to the principles of the World Medical Association Declaration of Helsinki: Ethical Principles for Medical Research Involving Human Subjects. This study did not require approval from an ethics committee as it was designed as a bibliometric analysis or citation analysis of existing published classical studies.

Results

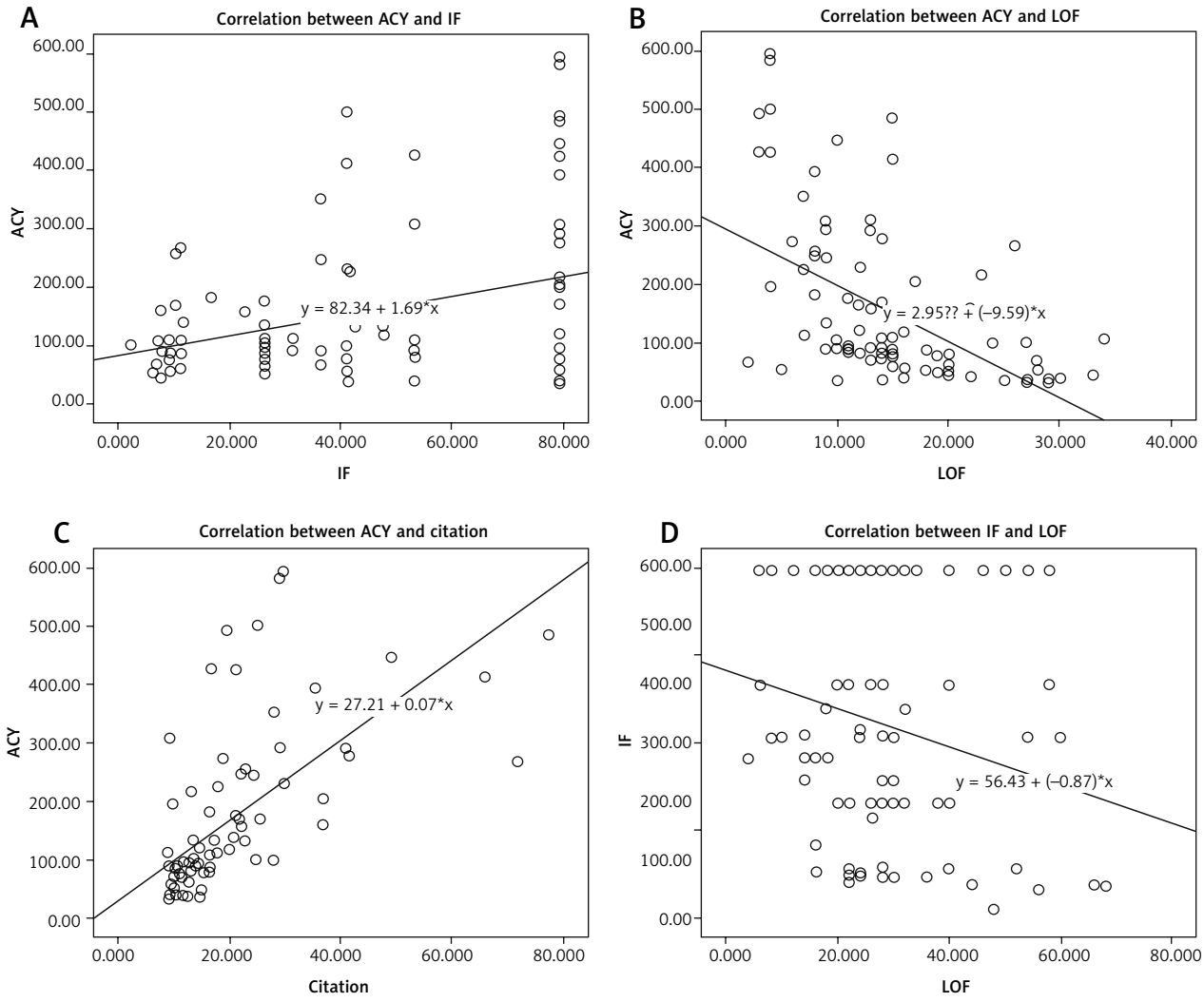
We identified 240,701 articles from 1975 to 2019. The language was English for all articles. The 100 most cited articles in lung cancer are listed in Table 1, arranged in descending order according to the number of times cited. The number of citations ranged from 7751 to 889, and the mean number of citations per article was 1879.82 ±1264.78 (range: 7751–889). We found that the most cited article (times cited: 7751) on lung cancer was a study by Lynch *et al.* with the following title: "Activating mutations in the epidermal growth factor receptor underlying responsiveness of nonsmallcell lung cancer to gefitinib" published in N Engl J Med 2004; 350: 2129-1239. The least cited article (times cited: 889) on lung cancer was penned by Imielinski *et al.* with the following title: "Mapping the hallmarks of lung adenocarcinoma with massively parallel sequencing" and published in Cell 2012; 150: 1107-1120. Additionally, we determined that there were 84 articles that got more than 1000 citations and the article with the highest ACY was the article that ranked 16 in the T100 list. The article with the highest ACY was a randomized phase 3 trial by Borghaei *et al.*, titled "Nivolumab versus docetaxel in advanced non-squamous non-smallcell lung cancer" and published in N Engl J Med 2015; 373: 1627-1639. The highest number of citations was seen in 2017 with 18,393 citations while the highest number of publications was seen in 2005 with 12 publications.

The oldest article was a review published in Nature 1985; 316: 823-826 titled "Bombesin-like peptides can function as autocrine growth factors in human small-cell lung cancer" by Cuttitta *et al.* with 1280 citations and ACY 36.57 ACY. The newest study in the T100 list was a phase 3 trial conducted by Rittmeyer *et al.* published in Lancet 2017; 389: 255-265 with the following title: "Atezolizumab versus docetaxel in patients with previously treated non-small-cell lung cancer

Table 3. List of journals with published articles

Journal	Number of articles	Impact Factor*	Quartile score**
New England Journal of Medicine (NEJM)	32	79.258	Q1
Journal of Clinical Oncology	16	26.303	Q1
Lancet	7	53.254	Q1
Science	7	41.058	Q1
Lancet Oncology	5	36. 418	Q1
Journal of the National Cancer Institute (JNCI)	4	11.238	Q1
Cancer Research	3	9.13	Q1
Cell	3	31.398	Q1
Chest	3	7.652	Q1
Nature	3	41.577	Q1
Proceedings of the National Academy of Sciences of the United States of America	3	9.504	Q1
Journal of the American Medical Association (JAMA)	2	47.661	Q1
Journal of Thoracic Oncology	2	10.336	Q1
American Review of Respiratory Disease	1	6.27	Q1
British Medical Journal (BMJ)	1	2.12	Q1
Cancer Cell	1	22.844	Q1
Cell Death & Differentiation	1	8.000	Q1
Genes & Development	1	9.462	Q1
Mayo Clinic Proceedings	1	7.199	Q1
Nature Reviews Cancer	1	42.784	Q1
Oncogene	1	6.854	Q1
PLOS Medicine	1	11.675	Q1
Science Translational Medicine	1	16.710	Q1

** 2017 Journal Citation Reports (Clarivate Analytics), ** 2019 SCImago Journal and Country Rank*



ACY – average citation per year, IF – impact factor, LOF – length of time since publication

Fig. 1. Correlation analysis for the citation numbers, ACY, IF, length of time since publication parameters

(OAK): a phase 3, open-label, multicentre randomised controlled trial", with 926 citations and ACY 308.67.

In the T100 list, 82 were clinical studies and 18 were experimental studies. The 82 clinical articles included 42 randomized controlled studies, 8 review articles, 4 meta-analyses, 2 case reports and other clinical studies. Fifty-nine of these 82 clinical articles were treatment-based studies. The treatment-based studies are classified in Table 2 according to the level of evidence.

While 32 of these articles were published in NEJM, 16 were published in the *Journal of Clinical Oncology*, 7 in *The Lancet*, 7 in *Science*, etc. (Table 3).

All of the T100 articles were published across 23 different journals. Eighty-five of the T100 articles were published in 14 journals that had IF ≥ 10.336. We determined that the mean IF of these 23 journals was 23.42 ±19.90 (range: 79.26–2.12) (according to Clarivate Analytics, 2017). The "Quartile Score" category was Q1 for all the journals (according to SCImago Journal and Country Rank, 2019). Most of the articles were published in NEJM, and NEJM was also the journal with the highest IF. The correlation analysis for the number of citations, ACY, IF and length of time since publication parameters in the T100 list revealed a positive correlation between citation and ACY (r = 0.744, p = 0.00) and between ACY and IF (r = 0.236, p = 0.018), whereas a negative correlation was observed between ACY and length of time since publication (r = –0.562, p = 0.00) and between IF and length of time since publication (r = –0.266, p = 0.008). There was no correlation between citation and length of time since publication or between citation and IF (Fig. 1).

According to the geographic origin of the T100 list, the USA (n = 74) was the most contributing country, followed by Japan and Canada (Table 4). We determined that the most commonly listed institution was the University of Harvard (USA), which was listed 27 times in the top 100 cited articles (Table 5). Moreover, 11/19 of the institutions that published eight or more publications were found to be in USA.

It was seen that 3 authors were the first author in more than one article in the T100 list's top 12 authors (Table 6). Herbst RS contributed to 8 articles and was the first author in 4 of them. Janne PA, Johnson BE and Johnson DH

Table 4. Geographic origin of the top 100 articles

Country	Number of articles
United States of America	74
Japan	20
Canada	19
Germany	19
Italy	19
England	18
Spain	18
France	18
Netherlands	10
South Korea	10
Poland	9
Australia	9
Brazil	8
China	7
Switzerland	6
Belgium	5
Chile	5
Russia	5
Taiwan	5
Denmark	4

Table 5. Institutions of origin with 8 or more of the top 100 cited articles

Rank	Institution	Number*
1	Harvard University	27
2	VA Boston Healthcare System	26
3	Dana Farber Cancer Institute	17
4	University of Texas System	17
5	Memorial Sloan Kettering Cancer Center	16
6	University of California System	16
7	UT MD Anderson Cancer Center	16
8	Massachusetts General Hospital	15
9	Unicancer	15
10	Vanderbilt University	15
11	University of Toronto	10
12	Princess Margaret Cancer Centre	9
13	Ruprecht Karls University Heidelberg	9
14	University Health Network Toronto	9
15	Astrazeneca	8
16	Gustave Roussy	8
17	National Institutes of Health NIH USA	8
18	Samsung Medical Center	8
19	Sungkyunkwan University	8
20	University of California Los Angeles	8

** Number of times listed of highest ranking 20 institutions in the top 100 cited articles.*

Table 6. The most common authors with 6 or more in the top 100 cited articles

Author	Number of top 100 articles		
	Author	First author	Co-author
Herbst RS	8	4	4
Janne PA	8	1	7
Johnson BE	8	–	8
Johnson DH	8	1	7
Lynch TJ	7	1	6
Rosell R	7	3	4
Takahashi T	7	1	6
Von Pawel J	7	–	7
Felip E	6	–	6
Meyerson M	6	–	6
Settleman J	6	–	6
Shepherd FA	6	2	4

also contributed to 8 articles. However, Herbst RS had the highest number of articles as first author. The "Web of Science" category analysis of the T100 in the field of the lung cancer revealed that these articles ranked under general internal medicine (n = 47), oncology (n = 33), multidisciplinary sciences (n = 13), cell biology (n = 8) and respiratory system (n = 6) as the most featured branches.

Discussion

Lung cancer is the major cause of cancer-related deaths worldwide. There are two main types of this cancer: small-cell lung cancer (SCLC) and non-small cell lung cancer (NSCLC). NSCLC accounts for 80% of all lung cancers. Despite the advances in surgical methods and advances in radiotherapy and chemotherapy, non-small-cell lung cancer continues to account for the majority of lung cancers and is associated with a 5-year survival rate of 15% [112].

There have been significant advances in the treatment of lung cancer in the last 40 years, and this is reflected in the scientific literature. A better understanding of disease progression coupled with targeted immunological therapies has led to increased survival rates.

We found that in our top 100, 28% of the articles were less than 10 years old while 72% of them were older than 10 years. Articles with a higher number of citations are indeed expected to be older. Year of publication and number of citations for an article are closely linked, and the number of citations grows over time. Needless to say, citation is an important metric, which shows the quality and attractiveness of an article; however, a certain amount of time should be allowed to pass after the publication of an article for it to reach a higher number of citations. For that reason, number of citations alone is inadequate to determine the quality of an article. In this study, ACY was used to eliminate the time bias when evaluating older articles against newer articles. Of the T100, 18% were comparative studies, and there were 2 case reports in the T100 list. The two case reports were published in 2005. One of them was published in NEJM (times cited: 2549), and the other in Plos Med (times cited: 2073). Both were about EGFR mutations. It is noteworthy that a case report receives such

a high number of citations. This may be due to the fact that EGFR mutations were popular in the 2000s. In the T100, 29% of the articles were noted to concern erlotinib (anti-EGFR), gefitinib (anti-EGFR) and EGFR mutations. The 1st study with the highest number of citations was a study related to EGFR mutations, showing that EGFR mutations play an important role in the development stages of lung cancer treatments.

Immunotherapy has become one of the most promising treatments for several human cancers. In fact, James P. Allison and Tasuku Honjo were awarded with the Nobel Prize in medicine for their research on immune checkpoint blockade [113, 114]. As a result, the immune check-point inhibitor (ICPI) may be regarded as an immunotherapy modality that started a new era in cancer treatment and remains a new trend topic. Especially in advanced non-small cell lung cancer (NSCLC), significant improvement has been observed in survival results with anti-PD-1 and PDL-1 drugs compared to chemotherapy. That shows the changing trends in cancer immunotherapy during the last decade. We can also see studies on immunotherapy in the T100 list. The most cited immunotherapy-related study in T100 was published in 2015 and received 2966 citations (ACY 593.2). It was published in N Engl J Med 2015; 373: 123-135 by Brahmer *et al.* with the following title: "Nivolumab versus docetaxel in advanced squamouscell non-smallcell lung cancer". This study currently remains a new study of only 4 years old, and despite being a very young article, the number of citations it has received shows that the study in question involves a very important innovation. Moreover, this article has the highest ACY score in the T100 list. This shows that scientists are currently focused on immunotherapy. There are only 7 studies about immunotherapy in the T100, and the newest article in the T100 was published in Lancet 2017; 389: 255-265 by Rittmeyer, titled "Atezolizumab versus docetaxel in patients with previously treated non-small-cell lung cancer (OAK): a phase 3, open-label, multicentre randomised controlled trial". It is only a 2-year-old article; however, it has 926 citations with an ACY score of 308.67. When we list the articles based on ACY scores in descending order, the first 4 articles are immunotherapy-related and recent articles.

The correlation analysis showed a positive correlation between citation and ACY and between ACY and IF, whereas a negative correlation was found between ACY and length of time since publication and between IF and length of time since publication. This indicates that articles with high ACY scores have been published in journals with a high IF. Furthermore, younger articles have higher ACY scores and have been published in journals with a higher IF.

When we looked at the T100 list, another point of interest also caught our attention: there were very few articles related to small-cell lung cancer (SCLC). Only 3 articles were on small-cell lung cancer [115–117]. This either means that there has not been any significant advance in SCLC or scientists are less interested in this topic.

Conclusions

To the best of our knowledge, this is the first report of a citation analysis of lung cancer in the English literature. The first 100 articles in our analysis not only identify landmark articles that have the greatest impact on lung cancer research, but also acknowledge the most productive authors and institutions that contributed to the list with their articles. Oncology is a developing field in science, and we have seen its evolution through the treatment of lung cancer over the years. Briefly, bibliometric analyses for different medical disciplines and sub-specialties demonstrate the improvements in a given field from a nominative perspective. The present bibliometric citation analysis on lung cancer has covered several scientific fields, and we believe it enables the systematic identification of true landmark publications as well as the distribution of citations of these publications by year, main topic, institution, scientific journal, level of evidence, and correlation analysis, thereby providing a substantial contribution for oncological research.

The authors declare no conflict of interest.

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