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The top 100 most impactful articles and recent trends in nasopharyngeal carcinoma from 1970 to 2018: a bibliometric analysis

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Abstract

Objective: To identify the top 100 most impactful articles in nasopharyngeal carcinoma (NPC).
Methods: Articles on NPC from 1970 to 2018 were retrieved from the Web of Science (WoS). These articles were ranked in descending order based on the number of times they were cited, and all titles and abstracts were screened to identify the top 100 most-cited articles.
Results: The earliest and most recent articles were published in 1971 and 2016, respectively. The most prolific decade was the 2000s, with 51 articles published. The highest citation count reached 1223 and the lowest was 155. Thirty-four journals contributed to the 100 articles, with the *International Journal of Radiation Oncology Biology Physics* contributing the most articles (n=16). Notable contribution origins were Hong Kong (n=34), the United States (n=26), and China (mainland, n=12). The top three contributors were Chan ATC, Lee AWM, and Lo KW who were from Hong Kong. The types of articles included basic research (n=50), clinical research (n=36), and reviews (n=14).

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Conclusions: This study identified the top 100 most impactful articles in NPC and stressed the multidisciplinary and multimodal nature of NPC management. Understanding historical articles may guide future NPC study.

Keywords
Bibliometric, citation analysis, Web of Science, radiotherapy, chemotherapy, nasopharyngeal carcinoma

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Introduction

Over the past decades, the mortality rate associated with nasopharyngeal carcinoma (NPC) has decreased,[1] reflecting years of research that was focused on innovative techniques for controlling and managing NPC. However, an abundance of NPC literature involving different researchers, countries, specialties, and scientific journals has emerged and it is difficult to identify the important papers.

Citation analysis is a bibliometric analysis method[2] that evaluates the influence and importance of an article in a certain field by analyzing the citation count.[3] It is also an affirmation to authors, institutions, and countries that have made important contributions. This method has been frequently applied and widely recognized in various disciplines, such as orthopedics,[4] neurosurgery,[5] ophthalmology,[6] and otolaryngology.[7,8] However, few articles have analyzed the highly cited NPC papers. Therefore, we aimed to identify the top 100 most-cited NPC articles from 1970 to 2018 using citation analysis.

In addition, recently published papers may not have sufficient citations mainly because of the time-dependent citation analysis.[9] For example, none of the clinical articles published from 2013 to 2018 were in our top 100 most-cited list. Therefore, to more comprehensively reveal the NPC development trend and research focus, we also conducted a corresponding analysis to identify the top 10 clinical research articles from 2013 to 2018.

Methods

Search strategy

We searched "TI = (nasopharyngeal carcinoma* OR nasopharyngeal cancer* OR nasopharyngeal neoplasm* OR nasopharyngeal tumor*)" on the Web of Science (WoS). The articles ranged from January 1970 to August 2018 and the document types were original articles and reviews. The retrieved articles were ranked from highest to lowest based on the number of citations. Two researchers reviewed and screened the title and abstract of the articles. If necessary, some studies with mixed NPC factors, such as head and neck cancer and Burkitt lymphoma, were excluded. Because no human subjects were enrolled, ethics approval was not required for this study.

Data extraction

After filtering the articles, we extracted the contents including the title of each article, the number of citations, the source journal,

the first author, and the research institute and its country. Next, based on the type of article, the literature records were further divided into basic research, clinical research, and review. We extracted the type of study and the clinical evidence.

Statistical analysis

Data were analyzed using IBM SPSS 22.0 package (IBM Corp., Armonk, NY, USA). Descriptive statistics are presented as the count or percentage of the parameters. This study did not involve statistically significant differences.

Results

Our literature search yielded 17,116 articles between 1970 and 2018, and the top 100 articles on AR were identified based on the number of times they were cited (Table 1).

There were 6675 articles between 2013 and 2018, and the top 10 most-cited clinical research papers were identified (Table 2).

Number of articles published

The Top 100 articles were mostly published from 1971 to 2016 (Figure 1). Among them, the greatest number of articles was published in the 2000s (n=51), followed by 1990s (n=24). The number of articles in the 2010s was equal to that in the 1980s (n=10) and the 1970s had the fewest articles (n=5).

Number of articles cited

In these articles, the highest and lowest citation counts were 1223 and 155, respectively. The average citation count for a single article in the 1970s, 1980s, 1990s, 2000s, and 2010s was 293.2, 239.0, 271.2, 274.5, and 195.3, respectively.

Published journals

The 100 most influential papers were published in 34 journals. Among these journals, those with more than one article published and their impact factor are presented in Table 3. The top three journals were *International Journal of Radiation Oncology Biology Physics* (n=16), *Journal of Clinical Oncology* (n=14), and *Cancer Research* (n=11).

Origins

These articles were mainly from 12 countries/regions (Figure 2). Among these countries/regions, the top three were Hong Kong (n=34), USA (n=26), and China (China mainland, n=12). The second tier of countries/regions were Britain (n=7), France (n=5), Taiwan (n=5), Sweden (n=3), and Singapore (n=3). An equal number of articles originated from Canada, Germany, Italy, and the Netherlands (n=1 each).

First authors

There were 81 first authors who had contributed to these articles. Nine of the first authors had published more than one article. The top three authors were Chan ATC (n=6), Lee AWM (n=4), and Lo KW (n=4). They were followed by Kam MKM and Lo YMD (n=3 each) and by Lin JC, Pathmanathan R, Raab-Traub N, and Yu MC (n=2 each).

Institutions

These articles came from 55 institutions. There were 15 institutions with more than one published article (Table 4). Among them, the top three were the Prince of Wales Hospital (n=13), Sun Yat-Sen University Cancer Center (n=8), and Queen Elizabeth Hospital (n=5).

Table 1. The top 100 most impactful articles on NPC.

Rank	Title	Journal	Year	First Author	Institute	Citation	Class
1	Chemoradiotherapy versus radiotherapy in patients with advanced nasopharyngeal cancer: Phase III randomized intergroup study 0099	Journal of Clinical Oncology	1998	Al-Sarraf M	Providence Cancer Center	1223	2
2	Nasopharyngeal carcinoma	Lancet	2005	Wei WI	Queen Mary Hospital	724	Review
3	Intensity-modulated radiotherapy in the treatment of nasopharyngeal carcinoma: An update of the UCSF experience	International Journal of Radiation Oncology Biology Physics	2002	Lee N	University of California–San Francisco	638	4
4	The enigmatic epidemiology of nasopharyngeal carcinoma	Cancer Epidemiology Biomarkers and Prevention	2006	Chang ET	Northern California Cancer Center	604	Review
5	Epidemiology of nasopharyngeal carcinoma	Seminars in Cancer Biology	2002	Yu MC	Norris Comprehensive Cancer Center	517	Review
6	Epstein-Barr virus-specific IgA serum antibodies as an outstanding feature of nasopharyngeal carcinoma	International Journal of Cancer	1976	Henle G	the Children's Hospital of Philadelphia and School of Medicine	491	Technique
7	Retrospective analysis of 5037 patients with nasopharyngeal carcinoma treated during 1976-1985 - overall survival and patterns of failure	International Journal of Radiation Oncology Biology Physics	1992	Lee AWM	Queen Elizabeth Hospital	446	4

(continued)

Table 1. Continued.

Rank	Title	Journal	Year	First Author	Institute	Citation	Class
8	Phase III study of concurrent chemoradiotherapy versus radiotherapy alone for advanced nasopharyngeal carcinoma: Positive effect on overall and progression-free survival	Journal of Clinical Oncology	2003	Lin JC	Taichung Veterans General Hospital	431	2
9	Expression of Epstein-Barr virus-encoded proteins in nasopharyngeal carcinoma	International Journal of Cancer	1988	Fahraeus R	Karolinska Institute	414	Technique
10	EB viral genomes in epithelial nasopharyngeal carcinoma cells	Nature-New Biology	1973	Wolf H	University of Erlangen Nuremberg	413	Technique
11	Epstein-Barr virus gene-expression in nasopharyngeal carcinoma	Journal of General Virology	1988	Young LS	University of Birmingham	411	Technique
12	Quantitative analysis of cell-free Epstein-Barr virus DNA in plasma of patients with Nasopharyngeal carcinoma	Cancer Research	1999	Lo YMD	The Chinese University of Hong Kong	407	Technique
13	Xerostomia and quality of life after intensity-modulated radiotherapy vs. conventional radiotherapy for early-stage nasopharyngeal carcinoma: Initial report on a randomized controlled clinical trial	International Journal of Radiation Oncology Biology Physics	2006	Pow Edmond HN	University of Hong Kong	392	2

(continued)

Table 1. Continued.

Rank	Title	Journal	Year	First Author	Institute	Citation	Class
14	Prospective randomized study of intensity-modulated radiotherapy on salivary gland function in early-stage nasopharyngeal carcinoma patients	Journal of Clinical Oncology	2007	Kam MKM	Prince of Wales Hospital	386	2
15	Epstein-Barr-virus latent gene-transcription in nasopharyngeal carcinoma-cells - coexpression of EBNA1, LMP1, and LMP2 transcripts	Journal of Virology	1992	Brooks L	University of Binningham	383	Technique
16	Clonal proliferations of cells infected with Epstein-Barr virus in preinvasive lesions related to nasopharyngeal carcinoma	New England Journal of Medicine	1995	Pathmanathan R	University of North Carolina	377	Technique
17	Quantification of plasma Epstein-Barr virus DNA in patients with advanced nasopharyngeal carcinoma	New England Journal of Medicine	2004	Lin JC	Taichung Veterans General Hospital	375	Technique
18	Chemotherapy in locally advanced nasopharyngeal carcinoma: An individual patient data meta-analysis of eight randomized trials and 1753 patients	International Journal of Radiation Oncology Biology Physics	2006	Baujat B	Institut Gustave Roussy	367	1

(continued)

Table 1. Continued.

Rank	Title	Journal	Year	First Author	Institute	Citation	Class
19	Randomized trial of radiotherapy versus concurrent chemoradiotherapy followed by adjuvant chemotherapy in patients with American Joint Committee on Cancer/International Union against Cancer stage III and IV Nasopharyngeal Cancer of the Endemic Variety	Journal of Clinical Oncology	2005	Wee J	National University of Singapore	356	2
20	Epstein-Barr virus in the pathogenesis of NPC	Seminars in Cancer Biology	2002	Raab-Traub N	Lineberger Comprehensive Cancer Center	346	Review
21	Focus on nasopharyngeal carcinoma	Cancer Cell	2004	Lo KW	Prince of Wales Hospital	335	Review
22	Treatment results for nasopharyngeal carcinoma in the modern era: The Hong Kong experience	International Journal of Radiation Oncology Biology Physics	2005	Lee AWM	Pamela Youde Nethersole Eastern Hospital	325	4
23	Treatment of nasopharyngeal carcinoma with intensity-modulated radiotherapy: The Hong Kong experience	International Journal of Radiation Oncology Biology Physics	2004	Kam MKM	Prince of Wales Hospital	313	4
24	MicroRNA 29c is down-regulated in nasopharyngeal carcinomas, up-regulating mRNAs encoding extracellular matrix proteins	Proceedings of the National Academy of Sciences of the United States of America	2008	Sengupta Srikumar	National Cancer Institute	297	Technique

(continued)

Table 1. Continued.

Rank	Title	Journal	Year	First Author	Institute	Citation	Class
25	How does intensity-modulated radiotherapy versus conventional two-dimensional radiotherapy influence the treatment results in nasopharyngeal carcinoma patients?	International Journal of Radiation Oncology Biology Physics	2011	Lai SZ	Sun Yat-Sen University Cancer Center	285	4
26	Intensity-modulated radiation therapy (IMRT) for nasopharynx cancer: Update of the memorial Sloan-Kettering experience	International Journal of Radiation Oncology Biology Physics	2006	Wolden SL	Memorial Sloan-Kettering Cancer Center	282	4
27	Intensity-modulated radiation therapy with or without chemotherapy for nasopharyngeal carcinoma: Radiation therapy oncology group phase II trial 0225	Journal of Clinical Oncology	2009	Lee Nancy	Memorial Sloan-Kettering Cancer Center	280	3
28	Concurrent chemotherapy-radiotherapy compared with radiotherapy alone in locoregionally advanced nasopharyngeal carcinoma: Progression-free survival analysis of a phase III randomized trial	Journal of Clinical Oncology	2002	Chan ATC	Prince of Wales Hospital	278	2
29	Identification of cancer stem cell-like side population cells in human nasopharyngeal carcinoma cell line	Cancer Research	2007	Wang J	Sun Yat-Sen University Cancer Center	262	Technique

(continued)

Table 1. Continued.

Rank	Title	Journal	Year	First Author	Institute	Citation	Class
30	Overall survival after concurrent cisplatin-radiotherapy compared with radiotherapy alone in locoregionally advanced nasopharyngeal carcinoma	Journal of the National Cancer Institute	2005	Chan ATC	Prince of Wales Hospital	262	2
31	Bmi-1 is a novel molecular marker of nasopharyngeal carcinoma progression and immortalizes primary human nasopharyngeal epithelial cells	Cancer Research	2006	Song LB	Sun Yat-sen University Cancer Center	256	Technique
32	Preliminary results of a randomized study on therapeutic gain by concurrent chemotherapy for regionally-advanced nasopharyngeal carcinoma: NPC-9901 trial by the Hong Kong nasopharyngeal cancer study group	Journal of Clinical Oncology	2005	Lee AWM	Pamela Youde Nethersole Eastern Hospital	256	2
33	Nasopharyngeal carcinoma cell line (C666-1) consistently harbouring Epstein-Barr virus	International Journal of Cancer	1999	Cheung ST	Prince of Wales Hospital	249	Technique
34	Mir-26a inhibits cell growth and tumorigenesis of nasopharyngeal carcinoma through repression of ezh2	Cancer Research	2011	Lu J	Nanfang Hospital	247	Technique
35	Serologic markers of Epstein-Barr virus infection and nasopharyngeal carcinoma in Taiwanese men	New England Journal of Medicine	2001	Chien YC	National Taiwan University	243	Technique

(continued)

Table 1. Continued.

Rank	Title	Journal	Year	First Author	Institute	Citation	Class
36	High frequency of promoter hypermethylation of rassf1a in nasopharyngeal carcinoma	Cancer Research	2001	Lo KW	Prince of Wales Hospital	242	Technique
37	Results of a prospective randomized trial comparing neoadjuvant chemotherapy plus radiotherapy with radiotherapy alone in patients with locoregionally advanced nasopharyngeal carcinoma	Journal of Clinical Oncology	2001	Ma J	Sun Yat-Sen University Cancer Center	242	2
38	Quantitative and temporal correlation between circulating cell-free Epstein-Barr virus DNA and tumor recurrence in nasopharyngeal carcinoma	Cancer Research	1999	Lo YMD	The Chinese University of Hong Kong	241	Technique
39	Abundant expression of eber1 small nuclear-RNA in nasopharyngeal carcinoma - a morphologically distinctive target for detection of Epstein-Barr virus in formalin-fixed paraffin-embedded carcinoma specimens	American Journal of Pathology	1991	Wu TC	Johns Hopkins School of Medicine	240	Technique
40	The additional value of chemotherapy to radiotherapy in locally advanced nasopharyngeal carcinoma: A meta-analysis of the published literature	Journal of Clinical Oncology	2004	Langendijk JA	University Hospital Vrije Universiteit	235	1

(continued)

Table 1. Continued.

Rank	Title	Journal	Year	First Author	Institute	Citation	Class
41	Norepinephrine up-regulates the expression of vascular endothelial growth factor, matrix metalloproteinase (MMP)-2, and MMP-9 in nasopharyngeal carcinoma tumor cells	Cancer Research	2006	Yang Eric V.	The Ohio State University Medical Center	234	Technique
42	Nasopharyngeal carcinoma: Molecular biomarker discovery and progress	Molecular Cancer	2007	Cho William Chi-shing	Queen Elizabeth Hospital	230	Review
43	Coexpression of hypoxia-inducible factors 1 alpha and 2 alpha, carbonic anhydrase ix, and vascular endothelial growth factor in nasopharyngeal carcinoma and relationship to survival	Clinical Cancer Research	2002	Hui EP	Prince of Wales Hospital	230	Technique
44	Treatment of nasopharyngeal carcinoma with Epstein-Barr virus-specific T lymphocytes	Blood	2005	Straathof KCM	Baylor College of Medicine	226	4
45	Nasopharyngeal carcinoma	Annals of Oncology	2002	Chan ATC	Prince of Wales Hospital	226	Review
46	The differentiated form of nasopharyngeal carcinoma contains Epstein-Barr virus-DNA	International Journal of Cancer	1987	Raab-Traub N	Lineberger Cancer Research Center	223	Technique
47	Randomized phase II trial of concurrent cisplatin-radiotherapy with or without neoadjuvant docetaxel and cisplatin in advanced nasopharyngeal carcinoma	Journal of Clinical Oncology	2009	Hui Edwin P	Prince of Wales Hospital	221	2

(continued)

Table 1. Continued.

Rank	Title	Journal	Year	First Author	Institute	Citation	Class
48	Isolation and sequencing of the Epstein-Barr virus bnlf-1 gene (LMP1) from a Chinese nasopharyngeal carcinoma	Journal of General Virology	1991	Hu LF	Karolinska Institute	219	Technique
49	Modulation of lmp1 protein expression by EBV-encoded microRNAs	Proceedings of The National Academy of Sciences of the United States of America	2007	Lo Angela KF	Sidney Kimmel Cancer Center	214	Technique
50	An unusualvirus in cultures from a human nasopharyngeal carcinoma	Journal of the National Cancer Institute	1971	Achong BG	University of Bristol Medical School	213	Technique
51	The infratemporal fossa approach for nasopharyngeal tumors	Laryngoscope	1983	Fisch U	University of Zurich Kantonsspital	211	4
52	Plasma Epstein-Barr virus DNA and residual disease after radiotherapy for undifferentiated nasopharyngeal carcinoma	Journal of the National Cancer Institute	2002	Chan ATC	Prince of Wales Hospital	208	Technique
53	Cantonese-style salted fish as a cause of nasopharyngeal carcinoma - report of a case-control study in Hong-Kong	Cancer Research	1986	Yu MC	University of Southern California	207	Technique
54	Bcl-2 proto-oncogene expression in Epstein-Barr virus-associated nasopharyngeal carcinoma	International Journal of Cancer	1993	Lu QL	Imperial Cancer Research Fund	205	Technique
55	Comparison of treatment plans involving intensity-modulated radiotherapy for nasopharyngeal carcinoma	International Journal of Radiation Oncology Biology Physics	2000	Xia P	University of California	201	4

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Table 1. Continued.

Rank	Title	Journal	Year	First Author	Institute	Citation	Class
56	MicroRNA deregulation and pathway alterations in nasopharyngeal carcinoma	British Journal of Cancer	2009	Chen HC	Chang Gung University	200	Technique
57	A prospective randomized study of chemotherapy adjunctive to definitive radiotherapy in advanced nasopharyngeal carcinoma	International Journal of Radiation Oncology Biology Physics	1995	Chan ATC	Prince of Wales Hospital	200	2
58	A genome-wide association study of nasopharyngeal carcinoma identifies three new susceptibility loci	Nature Genetics	2010	Bei JX	Sun Yat-sen University Cancer Center	199	Technique
59	Concurrent chemoradiotherapy plus adjuvant chemotherapy versus concurrent chemoradiotherapy alone in patients with locoregionally advanced nasopharyngeal carcinoma: A phase 3 multicentre randomised controlled trial	Lancet Oncology	2012	Chen L	Sun Yat-sen University Cancer Center	198	2
60	Preliminary report of the Asian-Oceanian clinical oncology association randomized trial comparing cisplatin and epirubicin followed by radiotherapy versus radiotherapy alone in the treatment of patients with locoregionally advanced nasopharyngeal carcinoma	Cancer	1998	Chua DTT	Queen Mary Hospital	198	2

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Table 1. Continued.

Rank	Title	Journal	Year	First Author	Institute	Citation	Class
61	Reirradiation of recurrent nasopharyngeal carcinoma - treatment techniques and results	International Journal of Radiation Oncology Biology Physics	1987	Wang CC	Massachusetts General Hospital Cancer Center	198	4
62	Adjuvant chemotherapy with vincristine, cyclophosphamide, and doxorubicin after radiotherapy in local-regional nasopharyngeal cancer - results of a 4-year multicenter randomized study	Journal of Clinical Oncology	1988	Rossi A	Istituto Nazionale Tumori	197	2
63	Induction of cyclooxygenase-2 by Epstein-Barr virus latent membrane protein 1 is involved in vascular endothelial growth factor production in nasopharyngeal carcinoma cells	Proceedings of The National Academy of Sciences of The United States of America	2001	Murono S	Lineberger Comprehensive Cancer Center	195	Technique
64	Molecular prognostication of nasopharyngeal carcinoma by quantitative analysis of circulating Epstein-Barr virus DNA	Cancer Research	2000	Lo YMD	The Chinese University of Hong Kong	195	Technique
65	Preliminary results of a randomized trial comparing neoadjuvant chemotherapy (cisplatin, epirubicin, bleomycin) plus radiotherapy vs radiotherapy alone in stage IV ($\geq$n2, m0) undifferentiated nasopharyngeal carcinoma: a positive effect on progression-free survival	International Journal of Radiation Oncology Biology Physics	1996	Cvitkovic E	Institute Gustave Roussy	193	2

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Table 1. Continued.

Rank	Title	Journal	Year	First Author	Institute	Citation	Class
66	Deletions within the LMP1 oncogene of Epstein-Barr virus are clustered in Hodgkin's-disease and identical to those observed in nasopharyngeal carcinoma	Blood	1993	Knecht H	CHUV University Hospital	190	Technique
67	Carcinoma of the nasopharynx treated by radiotherapy alone: Determinants of local and regional control	International Journal of Radiation Oncology Biology Physics	1997	Sanguineti G	M.D. Anderson Cancer Center	187	4
68	Linkage of a nasopharyngeal carcinoma susceptibility locus to the HLA region	Nature	1990	Lu SJ	People's Regional Hospital	186	Technique
69	Analysis of 1379 patients with nasopharyngeal carcinoma treated by radiation	Cancer	1988	Qin DX	Chinese Academy of Medical Sciences	186	Technique
70	Histo-pathology of nasopharyngeal carcinoma - correlations with epidemiology, survival rates and other biological characteristics	Cancer	1979	Shanmugaratnam K	University of Singapore	186	Technique
71	Nasopharyngeal cancer detection based on blood plasma surface-enhanced Raman spectroscopy and multivariate analysis	Biosensors & Bioelectronics	2010	Feng SY	Fujian Normal University	184	Technique
72	Intensity-modulated radiotherapy in nasopharyngeal carcinoma: Dosimetric advantage over conventional plans and feasibility of dose escalation	International Journal of Radiation Oncology Biology Physics	2003	Kam MKM	Prince of Wales Hospital	184	4

(continued)

Table 1. Continued.

Rank	Title	Journal	Year	First Author	Institute	Citation	Class
73	Blood diffusion and th1-suppressive effects of galectin-9-containing exosomes released by Epstein-Barr virus-infected nasopharyngeal carcinoma cells	Blood	2009	Klibi Jihene	Universite Paris-Sud	183	Technique
74	miR-218 suppresses nasopharyngeal cancer progression through downregulation of survivin and the SLIT2-ROBO1 pathway	Cancer Research	2011	Alajez Nehad M	Ontario Cancer Institute	182	Technique
75	Cloning and characterization of the latent membrane-protein (LMP) of a specific Epstein-Barr virus variant derived from the nasopharyngeal carcinoma in the Taiwanese population	Oncogene	1992	Chen ML	Chang-Gung Medical College	182	Technique
76	Establishment and characterization of 3 transplantable EBV-containing nasopharyngeal carcinomas	International Journal of Cancer	1988	Busson P	Institut Gustave Roussy	182	Technique
77	Nasopharyngeal carcinoma - review of the molecular mechanisms of tumorigenesis	Head and Neck-Journal for the Sciences and Specialties of the Head and Neck	2008	Chou Josephine	University of California	180	Review

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Table 1. Continued.

Rank	Title	Journal	Year	First Author	Institute	Citation	Class
78	A prospective, randomized study comparing outcomes and toxicities of intensity-modulated radiotherapy vs. conventional two-dimensional radiotherapy for the treatment of nasopharyngeal carcinoma	Radiotherapy and Oncology	2012	Peng G	Cancer Center of Union Hospital	179	2
79	Undifferentiated, nonkeratinizing, and squamous-cell carcinoma of the nasopharynx - variants of Epstein-Barr virus-infected neoplasia	American Journal of Pathology	1995	Pathmanathan R	Lineberger Comprehensive Cancer Center	178	Technique
80	Significant prognosticators after primary radiotherapy in 903 nondisseminated nasopharyngeal carcinoma evaluated by computer tomography	International Journal of Radiation Oncology Biology Physics	1996	Teo P	Prince of Wales Hospital	175	Technique
81	Nasopharyngeal carcinoma	Lancet	1997	Vokes EE	The University of Chicago	174	Review
82	Three-dimensional intensity-modulated radiotherapy in the treatment of nasopharyngeal carcinoma: The university of California-San Francisco experience	International Journal of Radiation Oncology Biology Physics	2000	Sultanem K	University of California	173	4
83	Etiology of nasopharyngeal carcinoma - a review	Epidemiologic Reviews	1993	Hildesheim A	National Cancer Institute	172	Review
84	Genome-wide scan for familial nasopharyngeal carcinoma reveals evidence of linkage to chromosome 4	Nature Genetics	2002	Feng BJ	Sun Yat-sen University Cancer Center	171	Technique

(continued)

Table 1. Continued.

Rank	Title	Journal	Year	First Author	Institute	Citation	Class
85	Nasopharyngeal carcinoma	Lancet	2016	Chua MLK	National Cancer Centre Singapore	167	Review
86	Genetic and epigenetic changes in nasopharyngeal carcinoma	Seminars in Cancer Biology	2002	Lo KW	Prince of Wales Hospital	166	Technique
87	Promoter hypermethylation of multiple genes in nasopharyngeal carcinoma	Clinical Cancer Research	2002	Kwong J	The Chinese University of Hong Kong	164	Technique
88	Concurrent and adjuvant chemotherapy for nasopharyngeal carcinoma: A factorial study	Journal of Clinical Oncology	2004	Kwong DLW	Queen Mary Hospital	163	2
89	Demonstration of Epstein-Barr virus-associated nuclear antigen in nasopharyngeal carcinoma cells from fresh biopsies	International Journal of Cancer	1974	Huang DP	Queen Elizabeth Hospital	163	Technique
90	Hypermethylation of the p16 gene in nasopharyngeal carcinoma	Cancer Research	1996	Lo KW	Prince of Wales Hospital	162	Technique
91	Nasopharyngeal cancer - epidemiology, staging, and treatment	Seminars in Oncology	1994	Fandi A	Institute Gustave Roussy	162	Review
92	2 Epithelial tumor-cell lines (HNE-1 and HONE-1) latently infected with Epstein-Barr virus that were derived from nasopharyngeal carcinomas	Proceedings of the National Academy of Sciences of the United States of America	1989	Glaser R	The Ohio State University Medical Center	161	Technique
93	High level expression of delta n-p63: A mechanism for the inactivation of p53 in undifferentiated nasopharyngeal carcinoma (NPC)?	Oncogene	2000	Crook T	Imperial College of Science, Technology and Medicine	160	Technique

(continued)

Table 1. Continued.

Rank	Title	Journal	Year	First Author	Institute	Citation	Class
94	Prognostic factors of nasopharyngeal carcinoma - a review of 759 patients	British Journal of Radiology	1990	Sham JST	Queen Mary Hospital	160	Review
95	Identification of serum amyloid a protein as a potentially useful biomarker to monitor relapse of nasopharyngeal cancer by serum proteomic profiling	Clinical Cancer Research	2004	Cho WCS	Queen Elizabeth Hospital	159	Technique
96	Plasma Epstein-Barr viral deoxyribonucleic acid quantitation complements tumor-node-metastasis staging prognostication in nasopharyngeal carcinoma	Journal of Clinical Oncology	2006	Leung SF	Sir YK Pao Centre for Cancer	158	Technique
97	Multicenter, phase II study of cetuximab in combination with carboplatin in patients with recurrent or metastatic nasopharyngeal carcinoma	Journal of Clinical Oncology	2005	Chan ATC	Prince of Wales Hospital	158	4
98	Prognostic value of a microRNA signature in nasopharyngeal carcinoma: A microRNA expression analysis	Lancet Oncology	2012	Liu N	Sun Yat-sen University Cancer Center	157	Technique
99	Randomized trial of radiotherapy plus concurrent-adjuvant chemotherapy vs radiotherapy alone for regionally advanced nasopharyngeal carcinoma	JNCI-Journal of the National Cancer Institute	2010	Lee AWM	Pamela Youde Nethersole Eastern Hospital	155	2
100	The aetiology of nasopharyngeal carcinoma	Clinical Otolaryngology	2001	McDermott AL	Queen Elizabeth Hospital	155	Review

Table 2. The top 10 most impactful clinical research articles on NPC from 2013 to 2018.

Rank	Title	Journal	Year	First Author	Institute	Citation	Class
1	Long-term outcomes of intensity-modulated radiotherapy for 868 patients with nasopharyngeal carcinoma: An analysis of survival and treatment toxicities	Radiotherapy and Oncology	2014	Sun XM	Sun Yat-sen University Cancer Center	135	4
2	Chemotherapy and radiotherapy in nasopharyngeal carcinoma: An update of the MAC-NPC meta-analysis	Lancet Oncology	2015	Blanchard P	Paris-Saclay University	130	1
3	Induction chemotherapy plus concurrent chemoradiotherapy versus concurrent chemoradiotherapy alone in locoregionally advanced nasopharyngeal carcinoma: A phase 3, multicentre, randomised controlled trial	Lancet Oncology	2016	Sun Y	Sun Yat-sen University Cancer Centre	84	2
4	Concurrent chemo-radiation with or without induction gemcitabine, carboplatin, and paclitaxel: A randomized, phase 2/3 trial in locally advanced nasopharyngeal carcinoma	International Journal of Radiation Oncology Biology Physics	2015	Tan T	National Cancer Centre Singapore	71	2
5	Adoptive T-cell transfer and chemotherapy in the first-line treatment of metastatic and/or locally recurrent nasopharyngeal carcinoma	Molecular Therapy	2014	Chia WK	National Cancer Centre Singapore	70	4

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Table 2. Continued.

Rank	Title	Journal	Year	First Author	Institute	Citation	Class
6	Significant efficacies of neoadjuvant and adjuvant chemotherapy for nasopharyngeal carcinoma by meta-analysis of published literature-based randomized, controlled trials	Annals of Oncology	2013	OuYang PY	Sun Yat-sen University Cancer Center	69	1
7	Evolution of treatment for nasopharyngeal cancer - success and setback in the intensity-modulated radiotherapy era	Radiotherapy and Oncology	2014	Lee AWM	University of Hong Kong-Shenzhen Hospital	66	4
8	Progress report of a randomized trial comparing long-term survival and late toxicity of concurrent chemoradiotherapy with adjuvant chemotherapy versus radiotherapy alone in patients with stage III to IVB nasopharyngeal carcinoma from endemic regions of China	Cancer	2013	Chen Y	Sun Yat-sen University Cancer Center	65	2

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Table 2. Continued.

Rank	Title	Journal	Year	First Author	Institute	Citation	Class
9	Preliminary results of trial NPC-0501 evaluating the therapeutic gain by changing from concurrent-adjuvant to induction-concurrent chemoradiotherapy, changing from fluorouracil to capecitabine, and changing from conventional to accelerated radiotherapy fractionation in patients with locoregionally advanced nasopharyngeal carcinoma	Cancer	2015	Lee AWM	Pamela Youde Nethersole Eastern Hospital	61	2
10	Phase I trial of recombinant modified vaccinia ankara encoding Epstein-Barr viral tumor antigens in nasopharyngeal carcinoma patients	Cancer research	2013	Hui EP	The Chinese University of Hong Kong	55	4

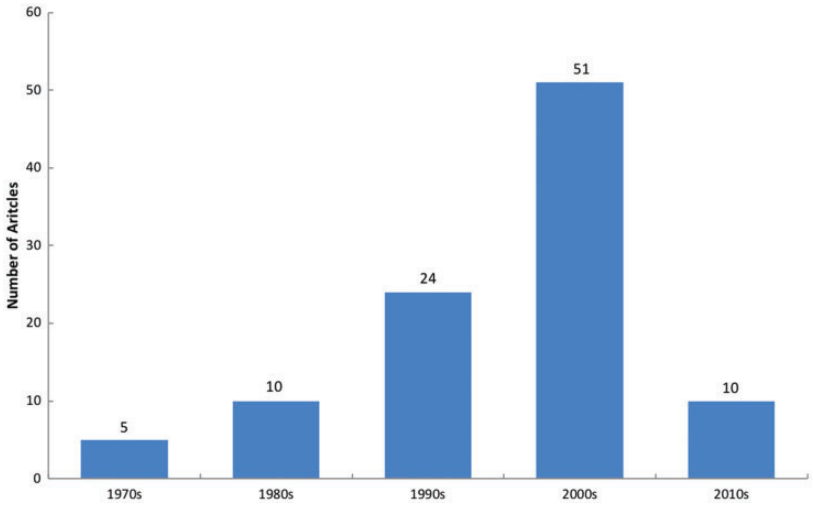

Figure 1. Number of articles published by decade.

Table 3. Journals with more than one published article.

Journal	Number of Articles (n=83)	Impact Factor 2017
International Journal of Radiation Oncology Biology Physics	16	5.6
Journal of Clinical Oncology	14	26.4
Cancer Research	11	9.1
International Journal of Cancer	7	7.4
Proceedings of the National Academy of Sciences of the United States of America	4	9.5
Blood	3	15.1
Cancer	3	6.5
Clinical Cancer Research	3	10.2
Journal of the National Cancer Institute	3	11.2
Lancet	3	53.3
New England Journal of Medicine	3	79.3
Seminars in Cancer Biology	3	10.2
American Journal of Pathology	2	4.1
Journal of General Virology	2	2.5
Lancet Oncology	2	36.4
Nature Genetics	2	27.1
Oncogene	2	6.9

The type of articles

Among the 100 articles, the number of articles on basic research, clinical research, and reviews was 50, 36, and 14, respectively. Most of the basic research articles focused on the pathogenesis, detection, and diagnosis of NPC (Figure 3).

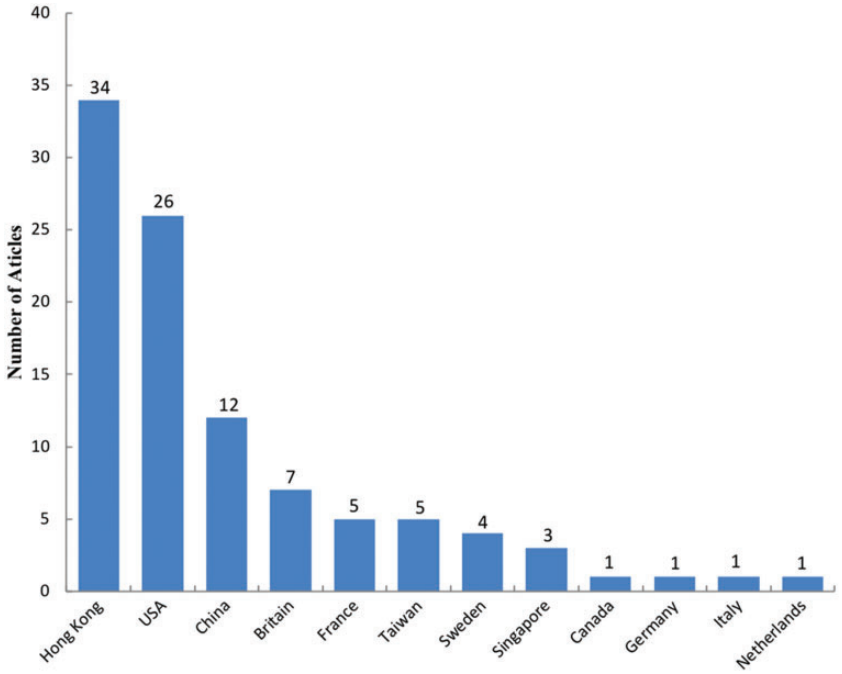

Figure 2. Origins of the top 100 most impactful articles on NPC.

Table 4. Institutions contributing to more than one published article.

Institutions	Number of Articles (n=58)
Prince of Wales Hospital	17
Sun Yat-Sen University Cancer Center	8
Queen Elizabeth Hospital	5
Institute Gustave Roussy	4
Queen Mary Hospital	4
The Chinese University of Hong Kong	4
Lineberger Comprehensive Cancer Center	3
Pamela Youde Nethersole Eastern Hospital	3
Memorial Sloan-Kettering Cancer Center	2
National Cancer Institute	2
Taichung Veterans General Hospital	2
The Ohio State University Medical Center	2
University of Binningham	2

Study types of clinical articles

The types of studies were 36 clinical articles, of which most were randomized trials (n=18), followed by case-series (n=15), systematic reviews (n=2), and non-randomized controlled cohort study (n=1).

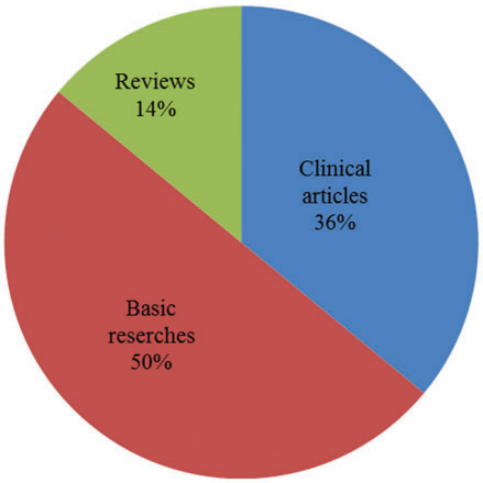

Figure 3. The type of articles.

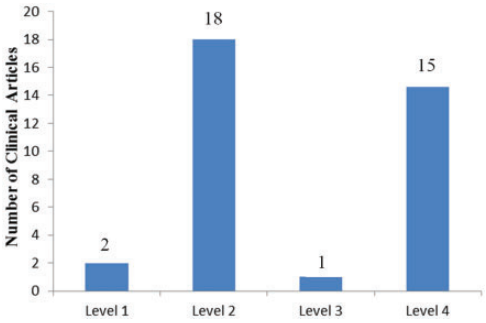

Figure 4. Level of 36 clinical articles based on "The Oxford 2011 Levels of Evidence".

The level of evidence

Among the 36 clinical articles, two, 18, one, and 15 articles were graded as having Level 1, 2, 3, and 4 evidence, respectively, based on "The Oxford 2011 Levels of Evidence" (Figure 4).

Classification of treatment methods

The 36 clinical articles were mainly divided into nine treatment categories (Table 5). The top three were concurrent chemotherapy (n=11), intensity-modulated radiation therapy (IMRT, n=10), concurrent chemoradiotherapy plus adjuvant chemotherapy (n=4), and radiotherapy (n=4).

Comparation between 1970–2018 and 2013–2018 in the top 10 most-cited clinical articles

Based on the level of clinical evidence, the ratios (1970–2018 vs. 2013–2018) of Level 1, Level 2, and Level 4 evidence were 1:2, 5:4, and 4:4, respectively. None of the top 10 most-cited articles described Level 3 evidence (non-randomize controlled cohorts).

Comparing the clinical treatment patterns, the ratios (1970–2018 vs. 2013–2018) of concurrent chemotherapy, IMRT, radiotherapy, neoadjuvant chemotherapy, T lymphocytes, and recombinant vaccinia virus were 4:5, 4:2, 2:0, 0:1, 0:1, and 0:1, respectively.

Discussion

In our study, bibliometric analysis was used to identify the top 100 most impactful articles in NPC. These articles are representative of the many landmarks that have taken place in NPC over the past decades.

Our study showed that the highest ranking article was published by the *Journal of Clinical Oncology* in 1998.[10] It suggested that concurrent chemoradiotherapy was superior to radiotherapy alone and that patients benefited from progression-free survival and overall survival. Because it had a large enough sample size and was a randomized controlled trial, it provided reliable evidence for clinicians to use for treating patients with NPC in the future.

The second highest ranking article was a review of NPC that was published by *The Lancet* in 2005.[11] It provided researchers with a notable and useful summary of the

Table 5. Treatment reported by 36 clinical articles on the top 100 list.

Treatment	Number of Articles (n=36)
Concurrent chemotherapy	11
IMRT	10
Concurrent chemoradiotherapy plus adjuvant chemotherapy	4
Radiotherapy	4
Neoadjuvant chemotherapy	3
Surgery	1
T lymphocytes	1
Chemotherapy after recurrent tumor	1
Radiotherapy after recurrent tumor	1

IMRT, intensity-modulated radiation therapy.

pathology, clinical symptoms, diagnosis, tumor grading system, and treatment methods for NPC, and thus, it was well accepted and cited by other researchers.

The third highest ranking article was the application of IMRT in NPC, which was published by the *International Journal of Radiation Oncology Biology Physics* in 2002.[12] It showed that IMRT can better control the recurrence of primary tumors and can protect salivary glands and adjacent important tissues to the greatest extent. Thus, this result had a significant impact on the future application of IMRT in NPC.

With the exception of the 2010s, the number of articles increased by decades. Thus, over half of the articles in our study were published in the 2000s. The finding is consistent with those of other bibliometric studies.[6,13,14] The result demonstrates that new articles with novel discoveries and advanced technologies continue to be published.

Based on the average citation count for a single article over the past decades, the highest citation count was the 1970s, whereas the lowest count was the 2010s. This finding shows that because of the time-dependent citation analysis,[9] previous articles have more citations compared with current articles.

Some bibliometric studies reported that journals with high impact factors, such as *NEJM* and *The Lancet*, were the leading journals.[15,16] However, we found that the *International Journal of Radiation Oncology Biology Physics* was the most productive journal, despite having an impact factor of 5.6. This result shows that highly impactful articles are published in a specialized journal and are not limited to well-known general medical journals.

It has been shown that the most productive authors and institutions were always from the USA.[13,16,17] In our study, Hong Kong was the most prolific region and Chan ATC, who contributed six articles, was from the Prince of Wales Hospital in Hong Kong. NPC has regional characteristics such as being common in the eastern and southeastern parts of Asia and eastern Africa. Thus, there are enough clinical research cases in Hong Kong. The findings indicate that Hong Kong has advanced technology and management concepts, and this region is good for researchers to learn and collaborate.

For the type of article, basic research articles on NPC accounted for half of the articles. They were mostly concerned with the epidemiology, pathogenesis, detection, and diagnostic techniques, such as

Epstein–Barr virus (EBV)-associated DNA, microRNA, and its associated genomes. Among them, a noteworthy article was published in 1976 by Henle and Henle[18] in the *International Journal of Cancer*, which was a study on NPC and EBV. It revealed the close relationship between EBV-related immunoglobulin A and NPC in serum, which was a milestone and laid the foundation for the determining the diagnosis and prognosis of NPC.

Some bibliometric articles on surgical tumors reported that more than half of the articles were of low-quality (Level 4).[19] In our study, most clinical articles were scored as Levels 1 or 2 on the level-of-evidence grading scale. These results indicate that a high-quality NPC study was relatively easy to conduct and receive more citations compared with a low-quality study.

One of the Level 1 articles[20] showed that concurrent chemoradiotherapy can confer survival benefits to patients with NPC, which was consistent with another highly cited article.[21] This article also pointed out that the efficacy of induction chemotherapy and intensive chemotherapy before concurrent chemoradiotherapy would need to be further confirmed.

Based on the only article regarding surgery in the top 100 articles, the NPC tumor in patients with stage T1 or T2 did not disappear after radiotherapy, and radical resection of the tumor can prolong their survival time. For patients with stage T4 NPC, palliative cytoreductive surgery failed to confer benefits because of extensive tumor invasion of the skull base and cranial nerves.[22] However, surgery is mostly used for some patients who needed a biopsy to confirm the diagnosis or who had tumor recurrence after radiotherapy based on a recent guideline (NCCN Clinical Practice Guidelines for Head and Neck Cancer, Version 3, 2019).[23]

Among the top 10 clinical articles from 1970 to 2018, one article on retrospective analysis written by Lee AWM in 1992 suggested that radiotherapy can increase the local tumor control rate and prolong overall survival and progression-free survival.[24] His subsequent and highly cited article published in 2005 described a retrospective analysis of 2687 patients in Hong Kong, and confirmed the therapeutic effect of radiotherapy.[25] Therefore, his articles provided a basis for future randomized clinical trials of IMRT.

For the top 10 clinical articles from 2013 to 2018, half were focused on concurrent chemoradiotherapy, while IMRT was described in only 20% of these articles. The findings show that the effect of IMRT was confirmed[26,27] and related research was reduced accordingly. Additionally, neoadjuvant chemotherapy,[28] T-lymphocyte immunotherapy,[29] and recombinant vaccinia virus gene therapy[30] had emerged. The results show that these new therapies are the current research priorities and the trends for future treatments.

There are some limitations in this paper. First, the citation count used for the citation analysis did not include self-citation. Second, because of the influence of certain time factors, it would be unfavorable for the most recently published articles in the citation analysis. Third, the database used in this article was the WoS. Although it is the most commonly used database with citation analysis capabilities, a small number of articles may have been missed.

Conclusions

To the best of our knowledge, this study is the first bibliometric study to identify the most impactful articles in the area of NPC. The findings indicate that articles with novel discoveries, advanced technologies, and a high quality level of evidence will receive more citations. Recognition of

important historical contributions to this field may guide future investigations into NPC.

Author contributions

All authors were involved in the study. Q.-T. Yang and M.-Y. Chen conceived and designed the study. Q.-W. Wu, T. Yuan, and Z.-P. Zhang analyzed the data and wrote the paper. Q. Wang, H.-Y. Deng, and H.-J. Qiu performed the search strategy. X.-Y. Wang, and X.-K. Huang collected the data.

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Declaration of conflicting interest

The authors declare that there is no conflict of interest.

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