Original article

Esophageal Cancer's 100 Most Influential Manuscripts: A Bibliometric Analysis

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ABSTRACT

Background: Bibliometric analysis highlights key topics and publications which have shaped the understanding and management of esophageal cancer (EC). Here the 100 most cited manuscripts in the field of EC are analyzed.

Methods: The Thomson Reuters Web of Science database with the search terms 'esophageal cancer' or 'esophageal carcinoma' or 'oesophageal cancer' or 'oesophageal carcinoma' or 'gastroscopy' was used to identify all English language full manuscripts for the study. The 100 most cited papers were further analysed by topic, journal, author, year and institution.

Results: 121,556 eligible papers were returned and the median (range) citation number was 406.5 (1833 to 293). The most cited paper focused on the role of perioperative chemotherpy in EC (1833 citations). Gastroenterology published the highest number of papers (n=15, 6362 citations) and The New England Journal of Medicine (NEJM) received the most citations (n=12, 12125 citations). The country and year with the greatest number of publications were the USA (n=50), and 1998, 1999 and 2000 (n=7). The most ubiquitous topic was the pathology of EC (n=66) followed by management of EC (n=54), and studies related to EC prognosis (n=44).

Conclusion: The most cited manuscripts highlighted the pathology, management and prognosis of EC and this bibliometirc review provides the most influential references serving as a guide to popular research themes.

INTRODUCTION

Esophageal cancer (EC) is a significant cause of morbidity and mortality worldwide and there is a growing body of evidence encompassing the pathological, clinical, oncological, radiological and basic science features of the disease. Advances in the global knowledge base continue apace and underpin developments that translate into improved treatments and patient survival.

The establishment of a citation rank list identifies published work that has had the greatest intellectual influence [1]. A citation is received when a publication is referenced by another peer-reviewed article and work that has the greatest impact on the scientific community is likely to be cited many times. Citation analysis involves ranking and evaluating an article or journal based on the number of citations it receives. In addition to determining the most frequently cited articles, this analysis is also used to rank journals in terms of impact [1].

Many medical specialties have utilized the citation rank analysis to identify the most influential papers in their field which includes; trauma and orthopaedic surgery [2], plastic surgery [3], general surgery [4] and oncology [5] and gastric cancer [6]. To date, no study has been undertaken to determine the most influential papers in the field of esophageal cancer. Analysis of these data provides insight into how our understanding of esophageal cancer has developed and how this information has changed our management of the disease. The aim of this study was to determine the topics and specifically the studies that have been most influential related to the improved understanding and management of esophageal cancer.

METHODS

A search of the Thomson Reuters Web of Science citation indexing database and research platform was completed using the search terms ‘esophageal cancer’ or ‘esophageal carcinoma’ or ‘oesophageal cancer’ or ‘oesophageal carcinoma’ or ‘gastroscopy’. The returned dataset was filtered to include only English language and full manuscripts and sorted by number of citations; a method initially developed by Paladugu and colleagues [4]. The 100 most cited manuscripts were identified from the large number of manuscripts returned. The dataset was then further evaluated examining title, first and senior author, institution and department of the first author, topic, year of publication and the country of origin. The individual and 5 year impact factors (both for the year 2013) of each journal publishing the manuscripts were recorded.

RESULTS

The Web of Science search returned 121,556 full-length, English language papers. Table 1 lists the 100 most cited of these papers [7-106]. The number of citations ranged from 1833 for Cunningham et al (Perioperative chemotherapy versus surgery alone for resectable gastroesophageal cancer) [7] to 293 for Orringer & Sloan (Esophagectomy without thoractomy) [106]. The oldest manuscript featured in the top 100 was by Wynder et al (A study of etiological factors in cancer of esophagus) and published in 1961 [61]. The most recent manuscript was published by van Hagen et al (Perioperative chemoradiotherapy for Esophageal or junctional cancer) in 2012 [31].

The 100 most influential papers were across 32 journals with the number of manuscripts per journal ranging from 1 to 15 (table 2). Although Gastroenterology published the most papers (n=15 and 6362 citations), The New England Journal of Medicine (NEJM) had the most citations (n=12 and 12125 citations). The NEJM also had the highest impact factor (54.420) and 5-year impact factor (50.810).

The country with the greatest number of publications in the top 100 was the United States of America (USA) with 50 publications followed by Germany with 10 publications. The National Cancer Institute Bethesda had the highest amount of citations with 5081 and was the highest number of publications in the top 100 with 6 manuscripts (table 3). One author had 3 and 12 authors had 2 first author publications in the top 100.

A possible limitation of this type of study is that historical manuscripts may accrue a larger number of citations despite lacking the impact of newer publications. To

control for this, the number of citations were divided by the number of years since publication to give a citation rate (table 4) [7, 8, 9, 10, 11, 12, 16, 27, 31, 76]. The citation rate for the top 10 manuscripts ranged from 227 for Bang et al (Trastuzumab in combination with chemotherapy versus chemotherapy alone for treatment of HER2-positive advanced gastric or gastro-oesophageal junction cancer (ToGA): a phase 3, open-label, randomised controlled trial) [11] to 69 for Hvid-Jensen et al (Incidence of Adenocarcinoma among Patients with Barrett's Esophagus) [76]. USA had the most papers in the top 10 citation rate with 4 followed by UK and Australia with 2.

Pathology of esophageal cancer was the topic most widely studied with 66 of the top 100 papers covering the topic (table 5). Fifty-four manuscripts looked at the management of esophageal cancer of which 40 related to surgery. Forty four papers studied the prognostic basis of clinicopathological factor with 34 papers describing clinical trials of chemotherapy. Twenty-seven manuscripts were science papers with 18 relating to the genetic basis of esophageal pathophysiology or management.

DISCUSSION

Esophageal cancer is the sixth leading cause of cancer death accounting for approximately 400,000 deaths worldwide in 2012 [107]. The identification of etiological factors, how genetic aberrations relate to pathogenesis and optimisation of surgery and chemotherapy regimens have led to improvements in patient prognostication and management. The results of the current study confirm that these topics were highly represented with 87 manuscripts of the top 100 influential papers covering these areas. Recently published manuscripts had a higher citation rate, which suggests a significant

influence within the top 100 within the next 5 to 10 years.

Influential publications are more likely to be cited by the scientific community and these citations form the basis of the impact factor. The impact factor of a journal quantifies the average citations of the manuscripts published within the journal during a specific period. Therefore, journals with a higher impact factor are recognized as being of a higher quality and more likely to contain influential publications. Journals with very high impact factors (54.42 – 29.35); NEJM, Lancet, JAMA and Nature Genetics only represent 17% of all publications in the top 100. Furthermore, the median impact factor was 15.69 and 18% of publications were in journals with an impact factor of 5.07 or less. A possible explanation for this relates to the novelty of the results. Novelty can be classified as relating to science in general or only esophageal cancer. Findings that have already been established in other cancers may then be re-established in esophageal cancer. These manuscripts are unlikely to be published in high impact scientific journals, however, within the context of this study they are likely to be considered influential.

On review of the topics covered in the top 100, pathology and management of EC, specifically the influence of surgery and chemotherapy on prognosis, were well studied accounting for 87 manuscripts. The results of the MAGIC Trial [7] and the ToGA Trial [11] had the highest amount of citations and the highest citation rate respectively. Furthermore, management (54%), prognosis (44%), clinical trials (34%) and chemotherapy (34%) were highly represented in the top 100 manuscripts. The importance of these topics is confirmed by their publication in high impact factor journals; NEJM, Lancet and Journal of Clinical Oncology. This reflects the growing influence of

biomarkers and personalized medicine in managing patients with esophageal cancer. Surgery remains the mainstay of treatment and the only potential cure for esophageal cancer, and it was represented in 40 manuscripts of the top 100. Other topics included aetiology (38%), basic science (27%) and genetics (18%). which support the development of novel treatments through improved understanding of malignant behavior of cancer cells in EC

Even with advances in surgical techniques and perioperative care, esophageal cancer still remains a leading cause of cancer death worldwide [107]. Consequently, there has been a greater effort in developing chemotherapeutic agents and the emergence of these studies in the top 100 confirms their importance to the scientific community. The majority of studies have looked at chemotherapy regimens in the adjuvant setting, however approximately a third of studies looked at neoadjuvant chemotherapy and this reflects recent developments in the care of patients with EC. The recent heightened importance of studies related to chemotherapy is reflected by their publication in higher impact factor journals such as NEJM, Lancet and Journal of Clinical Oncology.

The main limitation of this manuscript is the potential for several types of bias, which may affect results. Disproportionate citation may result from institutional bias, language biases, self citation or powerful person bias. In addition, older journals may receive more citations. Although an attempt to control for this was made by using the citation rate index, it may take a number of years for influential manuscripts to accrue citations due to the publication lead-time for their citing manuscript. Therefore, recently published manuscripts that have reached enough citations for inclusion in the top 100

have added importance. A further limitation is the inclusion of only first and senior authors and the institution of the first author. It is possible that several first authors will have co-authored other papers in the top 100 and are therefore under represented in the current study format. Finally, using a wildcard search term such as esoph* may have identified additional papers and this is also a relative weakness of this study.

CONCLUSION. The most cited manuscripts highlighted in this study describe the pathology, prognosis and management of EC including surgery and regimens that have resulted in the contemporary understanding and treatment of EC. Arguably, given the perceived relative lack of novelty to the science community in general, 40% of manuscripts were published in journals with impact factors of less than 10. In addition to providing a reference of what could be considered as the most influential papers in esophageal cancer, this work serves as a reference for researchers and clinicians alike as to the most popular research themes in esophageal cancer. This study also suggests that newer manuscripts have a higher citation rate, which will have a significant impact on the top 100 within the next 5 to10 years.

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TABLE AND FIGURE LEGENDS

Table 1. The Top 100 Cited Paper in Esophagus Cancer. Manuscripts without a first author are specified with *

Table 2. Journals with the Top 100 Cited Esophagus Cancer Papers

Table 3. Institutions with the Highest Number of Papers in the Top 100

Table 4. The Top 10 Cited Papers in EC

Table 5. Most Frequently Referenced Topics **Numbers may not add up to 100 and numbers within each group may not add up to total in each group due to an overlap of subjects covered in the individual manuscripts*

Table 1. The Top 100 Cited Paper in Esophageal Cancer.

Rank	Citations	First Author		Rank	Citations	First Author
1	1833	Cunningham, D[7]		51	406	Hollstein, M[57]
2	1818	Blot,D[8]		52	405	Earlam, R[58]
3	1765	Lagergren, J[9]		53	399	Chow, W[59]
4	1450	Devesa, S[10]		54	397	Sydenham, E[60]
5	1363	Bang Y[11]		55	388	Wynder, E[61]
6	1310	Enzinger, P[12]		56	385	Jiang, W[62]
7	1251	Walsh, T[13]		57	384	Reid, B[63]
8	1249	Herskovic, A[14]		58	382	Urschel, J[64]
9	854	Bosset, J[15]		59	382	Gammon, M[65]
10	853	Cunningham, D[16]		60	382	Leprise, E[66]
11	807	Cooper, J[17]		61	381	Chow, W[67]
12	806	Earlam, R[18]		62	377	Haggitt, R[68]
13	777	Kelsen, D[19]		63	375	Eads, C[69]
14	761	Hulscher, J[20]		64	372	Orringer, M[70]
15	753	Urba, S[21]		65	371	Nygaard, K[71]
16	748	Pera, M[22]		66	370	Bass, AJ[72]
17	722	Bancewicz, J[23]		67	369	Botterweck, A[73]
18	713	Hameeteman, W[24]		68	360	Franceschi, S[74]
19	711	Muller, J[25]		69	353	Lordick, F[75]
20	684	Mandard, A[26]		70	345	Hvid-Jensen, F[76]
21	656	Gebski, V[27]		71	344	Vaughn, T[77]
22	655	Pohl, H[28]		72	343	Farrow, D[78]
23	635	Webb, A[29]		73	340	Fiorica, F[79]
24	590	Zimmermann, K[30]		74	339	Sjoquist, K[80]
25	585	van Hagen, P[31]		75	338	Blot, W[81]
26	581	Akiyama, H[32]		76	335	Isono, K[82]
27	568	Minsky, B[33]		77	334	Ichihara, F[83]
28	542	Knyrim, K[34]		78	332	Ychou, M[84]
29	531	Shaheen, N[35]		79	332	Hirota, W[85]
30	530	Stahl, M[36]		80	331	Flamen, P[86]
31	529	Mirvish, S[37]		81	329	Gossner, L[87]
32	508	Rheeder, J[38]		82	327	Kato, J[88]
33	498	Luketich, J[39]		83	325	Skinner, D[89]
34	490	Haggitt, R[40]		84	324	Shirvani, V[90]
35	475	Wilson, K[41]		85	323	Cameron, A[91]
36	466	Spechler, S[42]		86	321	Ross, P[92]
37	454	Weber, W[43]		87	321	Ando, N[93]
38	450	Lagergren, J[44]		88	320	Engel, L[94]
39	448	Mori, T[45]		89	317	Reid, B[95]
40	447	Tepper, J[46]		90	311	Zhou, G[96]
41	444	Ell, C[47]		91	307	Brown, L[97]
42	437	Jiang, W[48]		92	306	LI, J[98]
43	435	Reid, B[49]		93	306	Forastiere, A[99]

44	429	Bedenne, L[50]		94	306	Tio, T[100]
45	429	Skinner, D[51]		95	303	Akiyama, H[101]
46	427	Al-Sarraf, M[52]		96	301	Siewert, J[102]
47	420	Burmeister, B[53]		97	300	Hulscher, J[103]
48	415	Levine, D[54]		98	295	Corley, D[104]
49	409	Drewitz, D[55]		99	293	Stahl, M[105]
50	407	Chu, F[56]		100	293	Orringer, M[106]

Table 2. Journals with the Top 100 Cited Gastric Cancer Papers

Journal title	**Impact Factor as of 2015**	**5 Year Impact Factor**	**Number of Manuscripts in the Top 100**	**Number of citations**
Gastroenterology	16.72	13.81	15	6362
Journal of Clinical Oncology	17.88	17.26	13	5826
New England Journal of Medicine	54.42	50.81	12	12125
Annals of Surgery	7.19	8.26	7	2805
Journal of the National Cancer Institute	15.16	14.79	7	2696
Cancer	4.90	5.69	4	2904
Lancet Oncology	24.73	24.23	4	1774
British Journal of Surgery	5.21	4.96	3	1922
Cancer Epidemiology Biomarkers & Prevention	4.13	4.57	2	687
JAMA	30.39	29.27	2	2625
Journal of Thoracic and Cardiovascular Surgery	4.17	4.07	2	618
Lancet	39.21	39.32	2	2085
Proceedings of the National Academy of Sciences of the United States of America	9.81	10.58	2	791
American Journal of Clinical Pathology	2.51	2.98	1	377
American Journal of Gastroenterology	10.76	9.15	1	409
American Journal of Surgery	3.85	4.10	1	382

Annals of Internal Medicine	17.81	17.47	1	450
Annals of Thoracic Surgery	3.85	4.10	1	300
Applied and Environmental Microbiology	3.67	4.36	1	407
Cancer Letters	5.62	4.96	1	529
Clinical Cancer Research	8.19	7.83	1	334
GUT	13.32	9.99	1	340
Human Pathology	2.77	2.99	1	490
International Journal of Epidemiology	9.18	8.62	1	369
Journal of Agricultural and Food Chemistry	2.91	3.27	1	397
Molecular & Cellular Proteomics	6.56	6.89	1	311
Nature Genetics	29.35	32.41	1	370
Oncology	2.42	2.58	1	335
Phytopathology	3.12	3.33	1	508
Seminars in Oncology	3.90	3.68	1	338
World journal of Surgery	2.64	2.84	1	371

Table 3. Institutions with the highest number of papers in the top 100

Institution	**Number of publication in top 100**	**Total number of citations**
National Cancer Institute Bethesda	6	5081
University of Amsterdam	4	2080
Fred Hutchison Cancer Research Center	3	1122
Memorial Sloan-Kettering Cancer Center	3	1733
Royal Marsden Hospital	3	2789
Technische Universität München	3	1108
University of Michigan Medical Center	3	1431
University of Washington	2	1289
Columbia University	2	822
International Epidemiology Institute	2	1701
Karolinska Institute	2	2215
Kliniken Essen-Mitte	2	823
Mayo Clinic	2	1071
The London Hospital, Whitechapel	2	1211
Toranomon Hospital	2	884
University of North Carolina	2	978
University of Texas Southwestern Medical Center	2	777

Table 4. Top 10 papers with the highest citation rate

Rank	Citation rate	First author	Senior author	Title	Institution	Country
1	227	Bang, Y[11]	ToGA Trial Investigators	Trastuzumab in combination with chemotherapy versus chemotherapy alone for treatment of HER2-positive advanced gastric or gastro-oesophageal junction cancer (ToGA)	International Epidemiology Institute	USA
2	183	Cunningham, D[7]	Yu, J	Perioperative chemotherapy versus surgery alone for resectable gastroesophageal cancer	Royal Marsden Hospital	UK
3	146	van Hagen, P[31]	Cross Group	Preoperative Chemoradiotherapy for Esophageal or Junctional Cancer	Erasmus University Medical Center	The Netherlands
4	107	Cunningham, D[16]	Andrew R	Capecitabine and oxaliplatin for advanced esophagogastric cancer	Upper Gastrointestinal Clinical Studies Group of the National Cancer Research Institute	UK / Australia
5	104	Lagergren, J[9]	Nyren O	Symptomatic gastroesophageal reflux as a risk factor for esophageal adenocarcinoma	Karolinska Institute	Sweden
6	101	Enzinger, P[12]	Mayer, R	Medical progress - Esophageal cancer	Harvard Medical School	USA
7	81	Devesa, S[10]	Fraumeni J	Changing patterns in the incidence of esophageal and gastric carcinoma in the United States	National Cancer Institute	USA

8	73	Gebski, V[27]	Australasian Gastro-Intestinal Trials Group.	Survival benefits from neoadjuvant chemoradiotherapy or chemotherapy in oesophageal carcinoma: a meta-analysis	University of Sydney	Australia
9	73	Blot, D[8]	Fraumeni J	Rising incidence of adenocarcinoma of the esophagus and gastric cardia	National Cancer Institute	USA
10	69	Hvid-Jensen, F[76]	Funch-Jensen P	Incidence of Adenocarcinoma among Patients with Barrett's Esophagus	Clinical Institute University of Aarhus	Denmark

Table 5. Most frequently referenced topics

Subject	**Number of papers**
Pathology	66
Management	54
Prognosis	44
Surgery	40
Aetiology / Pathophysiology	38
Chemotherapy	34
Clinical trials	34
Epidemiology	27
Science	27
Genetics	18

* Due to overlap of topics, cell numbers do not add up to 100