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Characteristics and trends of oral leukoplakia research

A bibliometric study of the 100 most cited articles

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Abstract

Background: Bibliometric analysis highlights the key topics and studies which have shaped the understanding and management of a disease of interest. Here the top-cited articles on oral leukoplakia (OL) were characterized, and research patterns and trends were analyzed.

Methods: A comprehensive search was performed and identified in the Scopus database up to 22 February 2019 for the 100 most-cited articles on OL.

Results: The number of citations of the 100 selected articles varied from 116 to 1418, with a mean of 226.7 citations per article. Both Journal of Oral Pathology and Medicine and Oral Surgery Oral Medicine Oral Pathology Oral Radiology were journals with the most articles published (n = 10). Both Hong W.K. and Lippman S. were the most frequently contributing authors (n = 9). United States (n = 43) and M.D. Anderson Cancer Center (n = 12) was most contributing country and institution, respectively. Systematic reviews/meta-analysis (n = 3) and randomized controlled trial (n = 7) were study designs with high evidence level. It is noteworthy that the majority of high-quality articles were the research of chemopreventive drugs (n = 21) and molecular markers/targets (n = 10), which may indicate a trend of key topics.

Conclusions: The results of this first citation analysis of the most-cited articles on OL provide a historical perspective on scientific evolution, and suggest further research trends and clinical practice in the field of OL.

Abbreviations: EBM = evidence-based medicine, IF = impact factor, JCR = Journal of Citation Reports, OL = oral leukoplakia.

Keywords: bibliometrics, citation analysis, most cited, oral leukoplakia

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1. Introduction

Oral leukoplakia (OL) is the best-known potentially malignant disorder of oral cancer, which is a leading cause of cancer death worldwide.[1,2] The mean rate of malignant transformation of OL is 3.5%, with a wide range between 0.13% and 34.0% in literature.[3] Currently, no evidence of a treatment is effective for preventing the malignant development of OL.[4] Given this, the research significance of OL is highly regarded in the field.[5] Increasingly large number of articles related OL have been published. It might be possible that clinicians and researchers do not always tend to evaluate the quality of articles, and might encounter some difficulties to recognize the major research areas of the concerned field.[6]

Citation analysis is the area of bibliometrics that utilizes citation data to evaluate the academic influence of an article in its particular field.[7] It is a definitely useful tool that the frequency and pattern of citations are objective parameters for evaluating the scientific performance within the designated area.[8] The topics, study design, and levels of evidence-based medicine (EBM) of highly cited articles may influence the trends in clinical practice and further research.[9–11] The number of citations of an article usually indicates the interest of the researchers on using the data to perform their own studies. A bibliometric analysis enables researchers to identify study key topics and to explore the updated insights into a particular field.[12] In addition, citation rating of articles significantly recognizes authors, institutions and countries of origin, and journals within a particular scientific community.[7,8]

Top-cited articles and citation analyses have been reported in some diseases such as oral cancer,[13] oral submucous fibrosis,[14] and rheumatoid arthritis.[15] However, no citation analysis of this type have yet been published on OL, as the most important and best-known potentially malignant disorder. In the present study, we, therefore, identified the top-100 most cited articles on OL and analyzed the characteristics, including the number of citations, topic, study design, evidence level, authorship, year of publication, contributing institution as well as country of origin. It is noteworthy that we would highlight the analysis of historical patterns and research trends of OL.

2. Materials and methods

2.1. Data source

As per the Gondivkar et al[13] method, we used the Scopus citation index to obtain citation information about published articles on OL. Of note, the advantage of Scopus database offers more coverage and provides results of more consistent accuracy for citation analysis compared to other databases.[16–18] And Scopus has the advantage of providing advance export functionality of structured data, for instance, which can automatically exclude self-citing. Using medical subject heading term "OL" in the title, abstract and keywords, we searched in the Scopus database up to 22 February 2019. There was no restriction in the search regarding publication year, language, or study design and type of the articles.

With the mentioned search strategy, 6129 articles on OL were published since its inception in 1939. The articles were categorized in descending order based on their number of citations. Titles and abstracts of these articles were screened, the articles on "oral hairy leukoplakia" were excluded, and the articles on "proliferative verrucous leukoplakia" were included. The titles and abstracts were then reevaluated to assure their relevance to OL. In cases of articles with the same number of total citations, the articles with highest citation density (citations per year) were positioned higher in the ranking. This study did not require any human/animal subjects to acquire ethics committee approval.

2.2. Data extraction

A list of top-100 articles was created by sorting among all the retrieved articles according to the number of citations in descending order. All the articles were reviewed and recorded the following information: authorship, publication title, publication year, number of citations, citation density, journal and its impact factor (IF, 2017 Journal of Citation Reports (JCR): Science Edition), institution and country of origin of the first author, study type, study design, and level of evidence. Articles were classified as primary research studies (epidemiological, basic, or clinical) or secondary research (narrative review, systematic review or meta-analysis). Study design was classified as clinical trial, cohort study, case–control study, cross-sectional study, case series, animal studies, and in vitro studies. As per the method used in previous studies on oral cancer[13] and oral submucous fibrosis[14], the evidence level of the article was analyzed using the classification proposed by the Oxford Centre for Evidence-Based Medicine (http://www.cebm.net/index.aspx?o=5653). Two independent authors (LW and ZY) carried out the

screening and subsequent analysis of the articles. In case of discrepancy, the opinion of a third author (WL) was requested to achieve consensus.

3. Results

3.1. Characteristics of articles included

With the search strategy algorithm, 6129 articles on OL were searched in the Scopus database for the period 1939 to the time of the search. From the collection, the top 100 most cited articles published from 1963 to 2015 were identified and their various characteristics analyzed. The total number of citations and that after removal of self-citations was 22,673 and 21,349, respectively. The overall h index and h index after removal of self-citations was 100 and 98, respectively. The mean number of citations was 226.7, with a range of 116 (article rank No. 100) to 1418 (article rank No. 1). The top-3 articles were each cited more than 700 times, and represented 3 different study topics and designs.

The most cited article was a prospective cohort study by Chen et al published in 2001 in the journal Anticancer Research; this study reported a phase I clinical trial of curcumin, a chemopreventive agent, in patients with high-risk or premalignant lesions including OL. The second most cited article was a narrative review by Kramer et al published in 1978 in the journal Oral Surgery Oral Medicine Oral Pathology; this review clarified the definition of OL and related lesions. The third most cited article was a retrospective cohort study by Silverman et al published in 1984 in the journal Cancer; this follow-up study investigated malignant transformation of 257 patients with OL. The whole information on ranking, author, title, year and journal of publication, number of citations, citation density, and journal IF of the each included article on OL is shown in supplementary Table S1, http://links.lww.com/MD/D81. The number of articles on the top 100 list by decade of publication is shown in Figure 1.

3.2. Topic and type of study, study design, and evidence level of the articles included

The topic, type of study, study design, and level of EBM of the 100 most cited articles on OL is shown in Table 1. The top-5 study topics were chemopreventive drugs (21 articles), etiology and risk factors of oral cancer and premalignant lesions including OL (16 articles), epidemiology of oral mucosal diseases including OL (13 articles), follow-up outcome studies (11 articles), and molecular markers/targets of oral carcinogenesis (10 articles). There were 53 primary research articles, 44 narrative review articles, and 3 systematic review or meta-analysis articles. The study design of chemopreventive drugs was principally randomized controlled trial (RCT, 7 articles) and prospective cohort (3 articles). The study design of epidemiology and follow-up outcome studies was principally cross-sectional and retrospective/prospective cohort, respectively. The top-3 risk factors, betel quid chewing, tobacco and alcohol use, were mainly concluded by narrative review (9 articles). With regard to the evidence level, only 3 systematic review or meta-analysis articles were considered evidence level 1 and 7 RCT articles were considered evidence level 2. The 20 cohort studies were considered evidence level 3, and the other 70 articles were considered lower level.
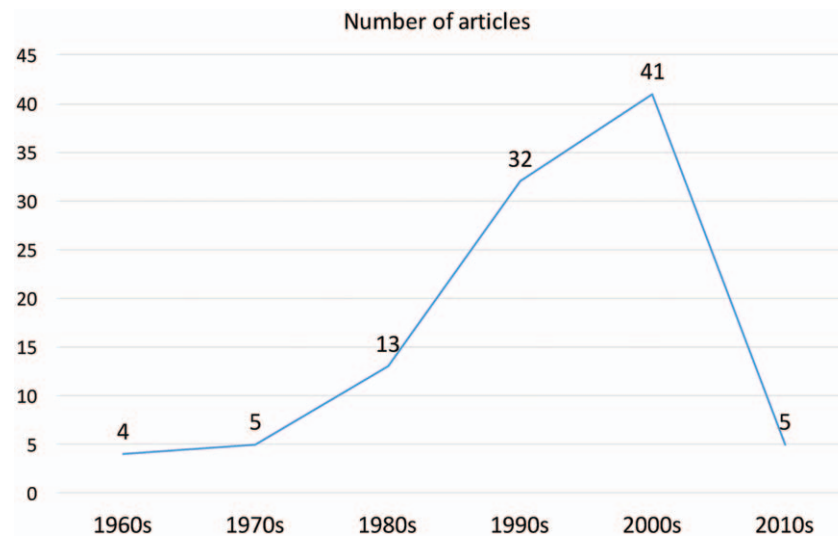
Figure 1. The number of articles on the top 100 list by decade of publication.

Table 1

The topic, type of study, study design, and level of evidence-based medicine of the 100 most cited articles on oral leukoplakia.

Article topic and the type of study/study design	No. of articles	Evidence level (EL)
Treatment	24	
Chemopreventive drug		
Narrative review	7	EL5
Vitamin A, retinoid and beta-carotene		
Randomized controlled trial (RCT)	5	EL2
Prospective cohort	2	EL3
Basic reach (In vitro and case control)	2	EL5
Natural products, e.g., curcumin and tea		
Randomized controlled trial (RCT)	2	EL2
Prospective cohort	1	EL3
Basic reach (In vitro and animal study)	2	EL5
Surgery: Retrospective cohort	1	EL3
Photodynamic: Narrative review	1	EL5
An oral mucosa equivalent for surgical defects repaired: Case control	1	EL4
Etiology and risk factors	16	
Betel quid chewing, tobacco and alcohol use, etc		
Case control	3	EL4
Narrative review	9	EL5
Human papillomavirus		
Systematic review with meta-analysis	2	EL1
Narrative review	2	EL5
Epidemiology of oral mucosal diseases including leukoplakia	13	
Cross-sectional	10	EL4
Narrative review	3	EL5
Follow-up outcome studies of OPL	11	
Retrospective/prospective cohort	9	EL3
Systematic review	1	EL1
Narrative review	1	EL5
Molecular markers/targets of oral carcinogenesis	10	
Retrospective/prospective cohort	4	EL3
Case series	2	EL4
In vitro and animal study	1	EL5
Narrative review	3	EL5
Oral cancer with emphasis on the importance of early diagnosis	8	
Narrative review	7	EL5
Prospective cohort: oral brush biopsy	1	EL3
Definition and classification of OPL		
Narrative review	5	EL5
Utility and subjectivity of oral dysplasia		
Case control	3	EL4
Proliferative verrucous leukoplakia: Retrospective cohort	2	EL3
Verrucous hyperplasia: Case series	1	EL4
Animal model of oral carcinogenesis: Narrative review	2	EL5
Head and neck cell lines including leukoplakia: In vitro study	1	EL5
Field cancerization: Narrative review	1	EL5
A genetic progression model of oral cancer: Narrative review	1	EL5
Comprehensive: narrative review	2	EL5

3.3. Authors, institution and country of origin, and journal of publication

The most influential authors, institutions and countries of origin within a particular scientific community are often recognized in the most cited articles. The top-5 contributing authors were Hong W.K. (9 articles), Lippman S. (9 articles), Pindborg J.J. (8 articles), van der Waal I. (6 articles), and Reibel J. (6 articles). The detailed information on authors (first Author, coauthor, and last author) with at least 4 articles included in the 100 most cited articles was showed in Table 2. The top-4 contributing countries were United States (43 articles), United Kingdom (9 articles), Denmark (7 articles), and China including Taiwan and Beijing (7 articles). The top-4 contributing institutions were M.D. Anderson Cancer Center, University of Texas, Houston (12 articles), National Cancer Institute, Bethesda, Maryland (5 articles), King's College Dental Institute, Denmark Hill Campus, London (5 articles), and Academic Centre for Dentistry Amsterdam (ACTA), Amsterdam (5 articles). The detailed information on countries and their institutions of origin with at least 2 articles of the 100 most cited articles showed in Table 3.

The top 100 articles were published in different scientific 47 journals. The journal of publication with largest number were

Table 2

Authors with at least 4 articles included in the 100 most cited articles on oral leukoplakia.

Rank	Name	First Author	Coauthor	Last Author	Total
1	Hong W.K.	1	2	6	9
2	Lippman S.	4	4	1	9
3	Pindborg J.J.	2	4	2	8
4	van der Waal I.	2	0	4	6
5	Reibel J.	2	4	0	6
6	Silverman S.	3	0	1	4
7	Warnakulasuriya S.	3	0	1	4
8	Mao L.	1	1	2	4
9	Sankaranarayanan R.	1	3	0	4
10	Lee J.J.	1	3	0	4
11	Lotan R.	1	3	0	4

Table 3

Countries and their institutions of origin with at least 2 articles of the 100 most cited articles on oral leukoplakia.

Rank	Country with at least 2 articles	No. of articles total n=92	Institution with at least 2 articles	No. of articles total n=56
1	United States	43	M.D. Anderson Cancer Center, University of Texas, Houston	12
			National Cancer Institute, Bethesda, Maryland	5
			School of Dentistry, University of California, San Francisco	3
			Johns Hopkins Medical Center, Baltimore	2
			College of Dental Medicine, Medical University of South Carolina, Charleston	2
			Department of Oral Health Practice, University of Kentucky, Lexington	2
2	United Kingdom	9	King's College Dental Institute, Denmark Hill Campus, London	5
3	Denmark	7	School of Dentistry, University of Copenhagen, Copenhagen	4
			Royal Dental College, Copenhagen	3
4	China (Taiwan and Beijing)	7		
5	Netherlands	6	Academic Centre for Dentistry Amsterdam (ACTA), Amsterdam	5
6	India	6	Tata Memorial Centre, Mumbai	4
			Regional Cancer Centre, Medical College Campus, Kerala	2
7	Canada	4	British Columbia Cancer Agency, Vancouver	3
8	Hungary	2	Faculty of Dentistry, Semmelweis Medical University, Budapest	2
	Finland		Institute of Dentistry, University of Turku, Turku	2
	Sweden			
	Japan			
	Italy			

Journal of Oral Pathology and Medicine (10 articles) and Oral Surgery, Oral Medicine, Oral Pathology, Oral Radiology (10 articles), followed by Oral Oncology (8 articles) and Cancer Research (6 articles). There were 56 articles published in the 10 journals with at least 2 articles in top 100 list. The detailed information on period of publication, the name and IF of these journals with at least 3 articles in the most cited articles showed in Table 4. It is particularly noteworthy that 3 narrative review articles on oral cancer with emphasis on the importance of early diagnosis were published on journal CA: A Cancer Journal for Clinicians (IF = 244.585, 2017 JCR). Moreover, 2 RCT article on chemopreventive drug published on New England Journal of Medicine (IF = 79.258, 2017 JCR).

4. Discussion

Bibliometric analysis helps in evaluating the historical perspective and research trends in the targeted field which has undergone changes over the decades.[9–11] It is well known that both IF of publication journal and citation rating of an article are the major determinants for evaluating the influence of an article.[19] It has been suggested that classic papers are these that labeled articles

achieving more than 100 citations[20,21]; The knowledge and understanding of these classic papers can provide extra insights into better understanding of the concerned field and help guide the education.[9–11] To the best of our knowledge, there is not available report concerning citation of articles on OL in literature. This is the first study that evaluated the characteristics of the 100 most cited articles on OL, as the most important and best-known potentially malignant disorder.

All the articles included in this bibliometric analysis on OL can be considered classic, since the number of citations with at least 116. Although the citation count does not indicate the scientific value of an article, it does represent its impact in the advancement of the respective research or clinical area and the number of researchers associated with their concerning field.[9–11] Journals with high IF are attracted by authors in selecting for their high-quality papers, whereas speciality journals are also selected to publish their high-quality articles over general medical journals.[19] In the present study, we noted that 21 of 100 most cited articles were published in 7 journals with high IF > 9, namely CA: A Cancer Journal for Clinicians, New England Journal of Medicine, Nature Medicine, Journal of Clinical Oncology, Journal of the National Cancer Institute, Clinical Cancer

Table 4

Journals with at least 3 articles in which the 100 most cited articles on oral leukoplakia were published.

Rank	Journal (abbreviated name)	No. of articles total n=56	Impact factor (2017 JCR)	Period of publication (No. of articles)
1	J. Oral Pathol. Med.	10	2.237	1980s (1), 1990s (2), 2000s (7)
2	Oral Surg. Oral Med. Oral Pathol. Oral Radiol.	10	1.718	1970s (2), 1980s (2), 1990s (5), 2000s (1)
3	Oral Oncol.	8	4.636	1990s (2), 2000s (5), 2010s (1)
4	Cancer Res.	6	9.13	1990s (6)
5	New Engl. J. Med.	5	79.258	1980s (2), 1990s (2), 2000s (1)
6	Cancer	5	6.537	1960s (2), 1970s (1), 1980s (2)
7	Ca Cancer J. Clin.	3	244.585	1990s (1), 2000s (1), 2010s (1)
	J. Clin. Oncol.	3	26.36	1990s (1), 2000s (2)
	Community Dent. Oral Epidemiol.	3	1.992	1980s (2), 2000s (1)
	J. Am. Dent. Assoc.	3	2.486	1960s (1), 1990s (1), 2000s (1)

Research, Cancer Research. Besides, 79 articles were published in 40 journals with IF < 8; the journals of publication with largest number (rank 1–3) were the speciality journals, namely Journal of Oral Pathology and Medicine (n = 10), Oral Surgery Oral Medicine Oral Pathology Oral Radiology (n = 10), and Oral Oncology (n = 8). This demonstrates that the researchers follow these 3 journals most frequently for achieving information on OL.

All the articles included in this analysis were published in English language. Hong W.K. and Lippman S. (both 9 articles) from the most contributing institution, M.D. Anderson Cancer Center, University of Texas, Houston (12 articles), stood out top in the rank on the list. The majority of articles included were published by authors and institutions in the United States (n = 43), in agreement with the results of a relevant study on oral cancer.[12] United States has a strong influence on research in the health sciences; this can be attributed to the high level of financial grant support given to research in that country and a large number of American researchers.[12] Indeedly, the United States is the leading country for medical research publications.

In our bibliometric analysis, we highlighted the analysis of the topic, type of study, study design, and level of EBM of the 100 most cited articles on OL, so as to guide the trends in future research and clinical practice. In recent era, great importance has been given to EBM, and efforts are being made to improve the quality of research.[22] However, the large majority of the most cited articles in the field of OL had a low evidence level, and minority of these articles, 3 systematic reviews/meta-analyses and 7 RCTs, had a high evidence level. It is noteworthy that the aims of all the RCTs were the research of chemopreventive drugs. Besides, the topics of 17 (81%) of the mentioned 21 articles published in journals with high IF > 9 were chemopreventive drugs, molecular markers/targets of oral carcinogenesis, and early diagnosis of oral cancer. These emphasize the impact of the topic of the article, their quality and their relevance to further research and clinical practice.

The largest number of the top cited articles classified by topic was the research of chemopreventive drug (n = 21), which may reflect the most importance of chemoprevention of OL malignant transformation. The majority of articles were research of vitamin A, retinoid and beta-carotene, but these agents were demonstrated to be ineffective in reducing the long-term risk of oral cancer in a large chemoprevention trial.[23] Increasing evidence indicates that natural products, for example curcumin and tea, have preliminary chemopreventive effectiveness, as mentioned by the relevant articles included in this study. It is noteworthy that another important topic was molecular markers/targets (n = 10), which could provide for development of molecular-targeted drugs of oral cancer prevention. These suggested the research of natural products and molecular-targeted drugs may be the new direction. It is evident that there is not only a strong need for more research on oral cancer chemoprevention, but also need to identify and develop biomarkers that correlate with the disease progression or regression for therapeutic targets.

We are aware of certain limitations in the bibliometric analysis on OL, although we attempted to minimize the potential defects. First, we used only Scopus database not do other different databases for analysis, because the advantage of Scopus database can automatically exclude self-citing. Scopus also provides about 20% more coverage than Web of Science, whereas Google Scholar provides results of inconsistent accuracy.[16–18] Secondly, citation count does not directly reflect quality of an article but enable a quantitative evaluation of the scientific impact of an article in a designed field. Authors tend to cite previous highly cited articles independently of content and quality through snowball effect. Thirdly, there is definite time effect in bibliometric analysis, but we have calculated citation density of each article which explains their scientific impact annually.

5. Conclusion

The current study for the first time reported the characteristics of the top-100 most cited articles on OL. The results of this study not only provide a historical perspective on scientific evolution but also reveal trends of key topics and clinical practice in further research in the field of OL. We believe that the list of top-cited articles presented herein will definitely be the important source information for researchers and clinicians. We hope that the recent era of EBM will influence the quality of articles in OL research.

Author contributions

Conceptualization: Yu Zhang.
Data curation: Wei Liu, Yu Zhang.
Formal analysis: Wei Liu.
Funding acquisition: Xi Yang, Linjun Shi.
Investigation: Yu Zhang.
Methodology: Lan Wu.
Resources: Lan Wu, Xi Yang, Linjun Shi.
Supervision: Xi Yang.
Validation: Lan Wu, Linjun Shi.
Visualization: Xi Yang.
Writing – original draft: Wei Liu.
Writing – review & editing: Linjun Shi.

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