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A bibliometric study of the top 100 most cited articles on melanoma: insights into research trends and characteristics

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Abstract

Improving insights into the current research and literature on melanoma is useful for healthcare providers to apply the latest advancements for offering better care to patients. Herein, this bibliometric study analyzed the characteristics and trends in melanoma research through the top-cited articles. The top 100 most cited articles on melanoma were published between 1969 and 2020, and the average number of citations was 36.8-893.9 (mean 176.8). Notably, the frequencies of the main key words, including antineoplastic agents, genetics, randomized controlled trials, metastatic melanoma, BRAF, and monoclonal antibodies, during 2010-2020 were significantly higher than those during 1969-2009. Specifically, the main study topics after 2010 were drug research aspects, such as drug safety, drug efficacy, drug resistance, drug withdrawal, cytotoxic T lymphocyte-associated protein 4 (CTLA-4), programmed cell death 1/programmed death-ligand 1 (PD-1/PD-L1), ipilimumab, nivolumab, trametinib, dabrafenib, vemurafenib, and various drug adverse effects. The emergence of immunotherapy caused a burst of citations and substantially changed the distribution of the top-cited articles.

Introduction

Melanoma ranks as the fifth most common solid malignancy in adults worldwide, and its incidence rate is increasing, particularly in White populations.[1] Cutaneous melanoma accounts for >90% of all melanoma cases diagnosed in the majority of populations, and most of these cases occur due to exposure to ultraviolet radiation.[1] Currently, surgery remains the preferred treatment for early-stage melanoma, with up to 80% of patients surviving for 5 years.[2,3] For advanced or metastatic melanoma, the 5-year overall survival (OS) rate of patients with metastatic melanoma may be less than 20%.[1] The pathogenesis, risk factors, and immunogenicity of melanoma remain to be fully elucidated, and there is a lack of effective treatment options.[4] Consequently, the past few decades have witnessed the publication of numerous scientific research articles in the field of melanoma. Improving insights into the most influential research and literature on melanoma is therefore valuable for clinicians, who can then apply the latest advancements to provide more effective care to patients.

Bibliometric analysis of a disease is frequently conducted to recognize study hotspots and investigate the latest diagnostic and treatment trends based on the citation data.[5,6] The study topics and design and levels of evidence-based medicine of highly cited articles may influence the trends in clinical practice and subsequent research. In addition, the citation rating of articles significantly recognizes authors, institutions, countries of origin, and journals within a particular scientific community.[7] Top-cited articles are often seminal publications in a research field and their academic

value can represent the authority within a field. A bibliometric analysis of top-cited articles can capture the current important scientific output in the field and grasp cutting-edge scientific dynamics.[8-10] Therefore, the present bibliometric study aimed to identify the 100 most cited publications in the field of melanoma research to highlight the most significant advancements in this field over the past decades. This knowledge can be used to better understand the classical studies that have significantly contributed to the field of melanoma.

Materials and Methods

The top 100 most cited articles on melanoma were retrieved from the Web of Science database maintained by the Institute for Scientific Information, in accordance with the methodology described previously.[8-10] The literature search was conducted on January 2, 2025, by using the medical subject term "melanoma" in the title, without any restriction on the year of publication. Paper types were restricted to original articles and reviews, and language was restricted to English as the global language for information exchange. According to the number of citations in descending order, a list of the top 100 most cited articles was created by sorting all the retrieved articles. For articles with the same count of total citations, the article with the highest citation density (citations per year) was positioned higher in the ranking. The titles and abstracts of these 100 articles were then reevaluated to confirm their relevance to melanoma research. Data search and extraction were performed independently by two investigators, and any discrepancy in the results was resolved through consensus. The articles were classified as primary research studies (basic or clinical research) or secondary research (review and guidelines). According to the method used in previous studies,[11] the evidence level of clinical articles was determined using the classification proposed by the Oxford Centre for Evidence-Based Medicine. In this descriptive study, variables are presented as numbers and percentages. Microsoft Office Excel 365 and the Bibliometrix Biblioshiny package in R software were used for statistical analysis of the bibliometric data.

Results

Bibliometric characteristics

Detailed information on title, abstract, key words, citation count and density, year of publication, journal, authorship, affiliation, country/region of origin, and document types of the top 100 most cited articles on melanoma are presented in *Supplementary Table 1*. The top 100 articles published from 1969 to 2020 were identified, and their various characteristics were analyzed (Figure 1A). The total and mean number of citations were 211,437 and 2,114, respectively, with a range of 1,074 (rank no. 100) to 12,515 (rank no. 1). The average number of citations per year (Figure 1B), adjusted for year

of publication, was 36.8-893.9 (mean 176.8). The most cited article was a randomized controlled trial conducted by Hodi *et al.* and published in the *New England Journal of Medicine* in 2010; this study reported that ipilimumab, which blocks cytotoxic T lymphocyte-associated protein 4 (CTLA-4), improved the overall survival of patients with previously treated metastatic melanoma. Figure 1C shows the citation trajectory over time for the top 10 key articles with the highest citation density.

The top 100 articles on melanoma research were published across 21 different scientific journals (Table 1). Among these, the journal with the largest number of articles published was the *New England Journal of Medicine* (29), followed by the *Journal of Clinical Oncology* (14), *Science* (12), and *Nature* (11). Figure 2A shows cloud graphs of contributing authors, institutions, and countries/regions of origin. A total of 232 authors contributed to the top 100 articles. The contributing author with the largest number of articles was Schadendorf Dirk (19), followed by Ribas Antoni (16), Robert Caroline (15), and Wolchok Jedd D. (15). The authors were affiliated with 226 different institutions. The contributing institution with the highest number of articles was Harvard University (37), followed by the University of California System (31), the Memorial Sloan Kettering Cancer Center (28), and the University of Sydney (22). The authors were from 30 different countries. The country of origin with the largest number of articles was the United States (93), followed by Australia (31), Germany (29), and France (25).

Research characteristics

Among the top 100 articles, there were 48 clinical studies, 46 experimental research studies, 3 articles on guidelines (the American Joint Committee on Cancer [AJCC] melanoma staging guidelines), and 3 review articles. Of the 48 clinical studies, 41, 3, and 4 studies were on therapeutic, diagnostic, and prognostic topics, respectively. Among the 41 therapeutic studies, 23 studies were randomized, double-blind, controlled, phase 3 trials. The types of clinical studies and level of evidence are shown in Table 2.

Based on the frequency of key words in the included articles (Figure 2B), we analyzed the research trends and characteristics of melanoma research. The article entitled "*Improved survival with ipilimumab in patients with metastatic melanoma*", published in the *New England Journal of Medicine* in 2010, was a significant milestone in melanoma research, as it marked the beginning of a new era of immunotherapy. Hence, the years of publication were divided into two categories: before 2010 (42 articles) and after 2010 (2010-2020; 58 articles), so that the included articles could reflect the research trends to some extent. Moreover, the same common key words were used throughout this period, including skin neoplasms, clinical trial, human tissue, gene mutation, mitogen-activated

protein kinase, pathology, and cancer survival.

Before 2010, interleukin-2 (12), membrane glycoproteins (6), HLA-A antigen (4), interferon-alpha (4), peptide fragments (3), and PTEN phosphohydrolase (2) were the main distinctive key words in the top 100 articles on melanoma research. Importantly, the main key words changed from 1969-2009 to 2010-2020, including antineoplastic agents (from 5 to 36), genetics (from 6 to 20), randomized controlled trials (from 2 to 17), and metastatic melanoma (from 1 to 14). Specifically, drug-related key words changed from 1969-2009 to 2010-2020, comprising drug safety (from 2 to 15), drug efficacy (from 3 to 17), drug resistance (from 5 to 12), drug withdrawal (from 0 to 10), monoclonal antibody (from 3 to 37), CTLA-4 (from 3 to 11), programmed cell death 1/programmed death-ligand 1 (PD-1/PD-L1) (from 2 to 24), ipilimumab (from 1 to 18), nivolumab (from 0 to 10), BRAF (from 11 to 22), trametinib (from 0 to 4), dabrafenib (from 0 to 4), vemurafenib (from 1 to 4), treatment outcome (from 6 to 12), and drug-related adverse effects (fever, rash, pruritus, fatigue, asthenia, hypothyroidism, hyperthyroidism, abdominal pain, headache, dyspnea, colitis, pneumonia, decreased appetite, diarrhea, nausea, vomiting, vitiligo, arthralgia, myalgia, alopecia, drug eruption, and chill).

Discussion

This is the first bibliometric analysis to provide more comprehensive knowledge of the top 100 cited articles on melanoma, with emphasis on key words and trends in the field. We found that 58 of the top 100 articles were published after 2010 (2010-2020), and the year of publication with the most articles (14 papers) was 2015. The total citation count (141,715) of 58 articles was more than twice the count (69,722) of 42 articles published before 2010 (1969-2009). Most of the newer articles included were focused on immunotherapy involving PD-1/PD-L1 and CTLA-4, which confirmed the emerging importance of targeted immunotherapy in melanoma literature and the research field. The development of immunotherapy has resulted in a surge of citations, which significantly changed the distribution of the top-cited articles. The top 10 articles with the highest citation density (citations per year), with a range of 358.6 (rank no. 10) to 893.9 (rank no. 1), may have had disproportionate influence, as these articles were cited at least once a day on average. Nine of the top 10 articles involved PD-1/PD-L1 and CTLA-4, and most were paradigm-shifting trials.

This bibliometric analysis updated the information on the journals of publication, leading authors, institutions, and countries/regions that contributed to the top 100 cited articles in melanoma literature. Regarding the journals of publication, most of the top 100 articles were published in prestigious international journals, such as the *New England Journal of Medicine*, the *Journal of Clinical Oncology*, *Science*, and *Nature*. Renowned journals are often selected by authors for publishing their

high-quality research papers and tend to be cited frequently in their research articles. A change was noted in the contributing authors and institutions of the top 100 cited articles in melanoma literature. It highlights the impact of the United States on the field of melanoma research, which could be attributed to the large, well-funded grant support provided to research and high-ranking researchers who produce high-quality research.

The strength of this bibliometric study lies in the key word analysis of the top 100 articles on melanoma research. For early-stage primary melanoma, surgical excision with a safety margin is the typical management approach. Before 2010, the prognosis for melanoma associated with unresectable locoregional or distant sites was poor, and less than 10% of patients with advanced melanoma survived beyond a few years.[1] In recent years, targeted drug therapies, particularly immune checkpoint inhibitors, such as CTLA-4 inhibitors (ipilimumab) and PD-1 inhibitors (nivolumab and pembrolizumab), have dramatically improved the survival of melanoma patients because of a series of landmark approvals from 2011 onward.[1] The relatively recent discovery of immunologic targets has created renewed interest in melanoma research. The development of newer immunotherapeutic approaches has significantly changed the treatment landscape of metastatic melanoma patients, although immunotherapy has adverse effects and varying rates of effectiveness due to immune evasion. As mentioned earlier, the key words listed in Figure 2B reflect the directions and concerned topics in melanoma research, which can guide the trends in research characteristics and clinical practice.

We also provided insights into the study topics and the level of evidence. In the current bibliometric analysis, 54 and 46 articles were based on clinical and experimental studies, respectively. More than 50% of the experimental articles were published in *Science*, *Nature*, and *Cell*, and most of them were experimental studies on potential targeted immunotherapy after 2010. In a previous bibliometric analysis,[11] 81 and 19 of the top 100 articles on melanoma were on clinical and experimental studies, respectively; moreover, these articles were published in 64 relevant journals, which did not include *Science*, *Nature*, and *Cell*.[12] Therapeutics was the main topic in the clinical articles, and clinical trials for melanoma therapy were often of a higher level of evidence. After 2010, most of the therapeutic studies focused on targeted drug therapies, particularly immune checkpoint inhibitors. With advancements in melanoma research, a better understanding of the interrelated molecular, clinical, and pathological features of melanoma emerged, which resulted in three revisions of the AJCC melanoma staging system published in 2001, 2009, and 2017. Additionally, there were 2 articles on sentinel node biopsy (*Supplementary Table 1*), which is routinely used to assess the risk of harboring occult regional nodal metastasis; these articles provided prognostic information and

guidance related to treatment selection after the initial surgery.

Our study has some limitations. The high-quality articles in recent years were not included because their impact and citation frequency could not be appropriately determined due to the limited time from their publication. Although there is a definite time effect in bibliometric analysis, we have calculated the citation density of all articles, which explains their scientific impact annually. Moreover, the citation analysis did not correct for self-citation. As reported by Joyce *et al.*,[11] American authors tend to cite local articles instead of international articles. Moreover, some journals favor authors located in the same country; for example, some journals appear to have a strong preference for citations of articles published in the United States.[11] The authors tend to cite previous highly cited articles regardless of their content and quality through the snowball effect. It is important to acknowledge that there are limitations to using citation counts as a proxy for scientific quality, as some highly cited papers may be flawed or controversial.

Conclusions

The present bibliometric analysis of the top 100 most cited articles on melanoma not only provides a historical perspective on scientific development but also reveals trends in key topics and clinical practice for further investigations in melanoma research. The top 100 cited articles in melanoma research reflect the trends in this field over the past decades and demonstrate significant advancements in research, particularly in immune checkpoint therapy. We believe that the list of the most cited articles presented in this study could serve as an important source of information for researchers and clinicians, who can use these bibliometric data to guide their research and identify pivotal articles and authors who have impacted clinical practice.

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Figure 1. Number (A) and citation density (B) of the top 100 cited articles on melanoma, organized by year of publication. (C) The citation trajectory over time for the top 10 most-cited articles with the highest citation density.

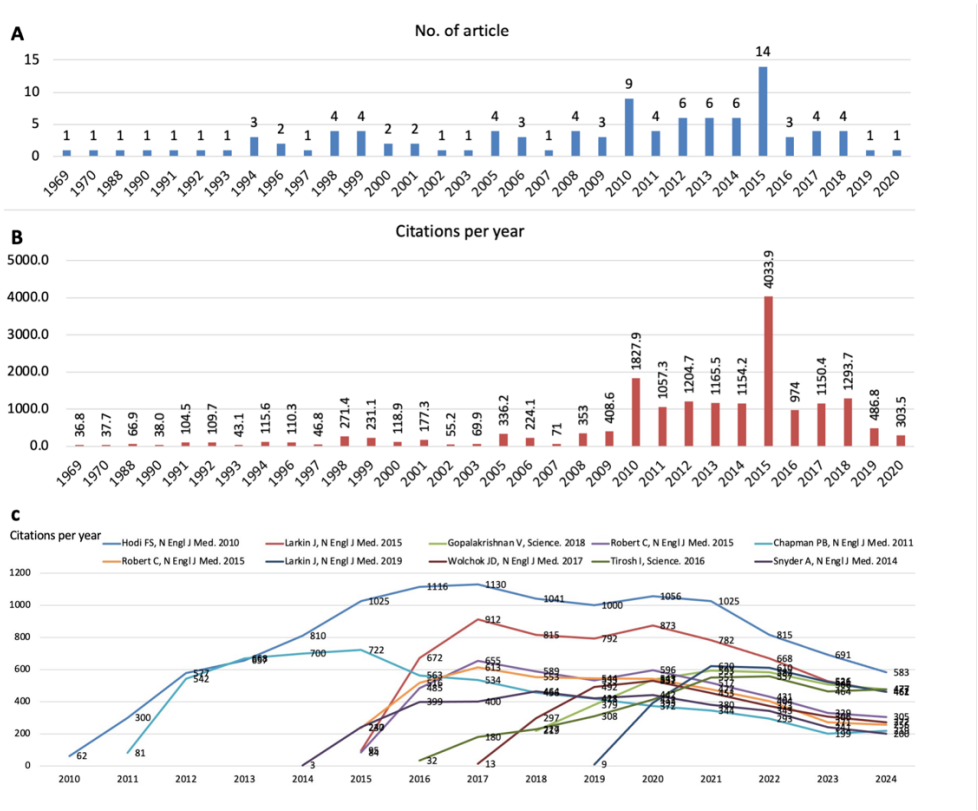

Figure 2. Cloud graphs of (A) contributing authors, institutions, countries/ regions of origin, and (B) key words in the top 100 most cited articles on melanoma. The font size indicates the number of papers; a larger size means more papers in the cloud graphs.

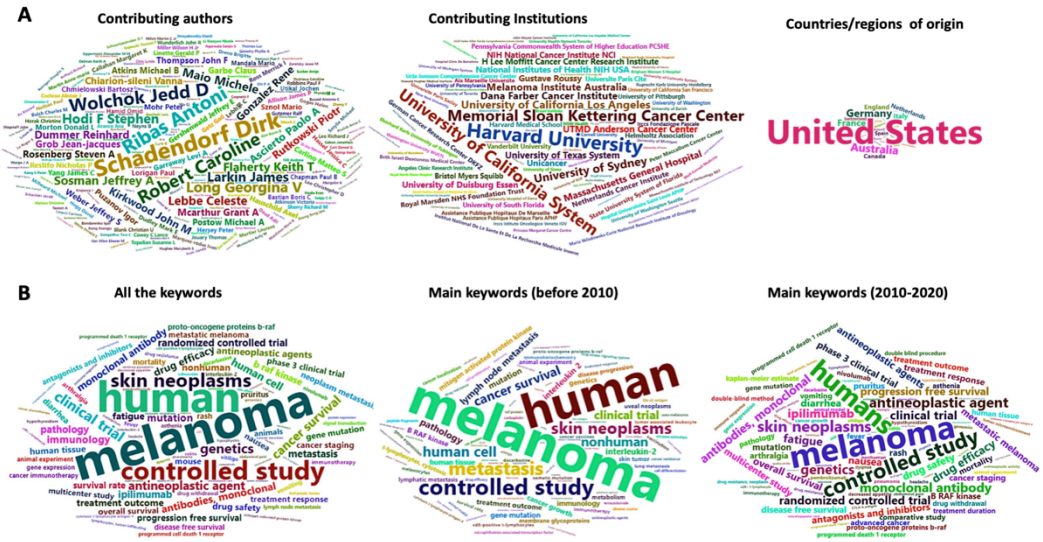

Table 1. Journals in which the 100 most cited articles on melanoma were published.

Journal name	Record count
New England Journal of Medicine	29
Journal of Clinical Oncology	14
Science	12
Nature	11
Proceedings of the National Academy of Sciences of USA	5
Cell	4
Journal of Experimental Medicine	4
Nature Medicine	4
Lancet	3
Cancer Research	2
Nature Genetics	2
American Journal of Pathology	1
Annals of Surgery	1
Archives of Surgery	1
CA: A Cancer Journal for Clinicians	1
Cancer	1
Cancer Cell	1
Clinical Cancer Research	1
JAMA: Journal of the American Medical Association	1
Lancet Oncology	1
Science Translational Medicine	1

Table 2. Types of clinical studies and level of evidence.

Topic	No. of articles
Therapeutic	41
Level 1	23
Level 2	4
Level 3	9
Level 4	5
Diagnostic	3
Level 1	0
Level 2	0
Level 3	3
Level 4	0
Prognostic	4
Level 1	1
Level 2	0
Level 3	3
Level 4	0

Online Supplementary Material

Supplementary Table 1. Detailed information on the top 100 most cited articles on melanoma.