

# An Analysis of Global Research Trends and Top-Cited Research Articles in Cardio-Oncology

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## Abstract

**Background:** As novel cancer therapies continue to improve patient outcomes, there is an increased need for prevention and management of the cardiovascular side effects of these therapies. For this reason, the field of cardio-oncology has experienced significant scientific growth, particularly during the last decade. This study aims to assess the global publication trends and highlight the top-cited scientific articles related to cardio-oncology.

**Methods:** A comprehensive bibliometric analysis of multiple scientific databases was performed to characterize global publication trends in cardio-oncology from 1864 to 2020 and to determine the top-cited papers addressing cardio-oncology as a field of study.

**Results:** We identified 1,294 publications with 14,494 citations that describe cardio-oncology as a field. Cardio-oncology was the most prevalent term in the literature and was first mentioned in an article from Italy in 1996. There was no further mention of the term “cardio-oncology” until 2003, and later again in 2008. After 2010, there was a consistent increase in the number of publications and citations in cardio-oncology. Among the top 50 most cited papers, there was a noticeable trend of higher number of review articles (n = 28, 56%, with 3,208 citations), followed by guidelines and position papers (n = 9, 18%, with 2,299 citations) and original research articles (n = 9, 18%, with 1,451 citations). The most common specialty for the senior corresponding authors of the top 50 most cited papers was cardiology (n = 36; 72%), followed by oncology (n = 5; 10%); and the most prevalent countries of origin were the USA (n = 26; 52%), Italy (n = 8; 16%), and Canada (n = 6; 12%).

**Conclusion:** Our quantitative analysis of publication trends in the field of cardio-oncology objectively showed the growing scientific interest in the field. To our knowledge, this is the first bibliometric

analysis that determined the top 50 most cited articles in the field of cardio-oncology.

**Keywords:** Bibliometric analysis; Cardio-oncology; Onco-cardiology; Cardio-hemato-oncology; Research trends; Top articles

## Introduction

Cardio-oncology is an emergent discipline that focuses on preventing and reducing cardiotoxicity related to cancer therapies [1]. Bibliometrics implements statistical methods to analyze publications and explore the growth or impact of a field. It can also provide an objective measure of landmark articles and peer recognition of scientific work by identifying the most cited publications in a given field [2]. As the cardio-oncology field continues to advance, it is important to recognize the significant evolution of this body of academic work and highlight the publications that have introduced and defined the field. In this study, we assessed the global research trends and growth of the field of cardio-oncology and analyzed the top 50 most cited articles.

## Materials and Methods

A bibliometric analysis of the literature in the field of cardio-oncology was performed using the multidisciplinary databases Scopus, Pubmed, and Web of Science Core Collection (WOSCC). The terms “cardio-oncology”, “onco-cardiology”, “cardio-onco-hematology”, and “cardio-immuno-oncology” were searched (both hyphenated and non-hyphenated) for all languages for the years 1864 to 2020. The final search was conducted on March 31, 2021, and the terms were queried as “abstract title, abstract, and keywords” for Scopus and Pubmed, and as “topic” for WOSCC. All articles from the search results were independently verified by two reviewers and were included in the analysis if they addressed cardio-oncology as a field of study in the keywords, title, or abstract. Articles that did not focus on cardio-oncology were excluded. Each article was reviewed for its number of citations, year of publication, and journal of publication. When duplicates were found, the entry with fewer citations was eliminated. For those articles that were co-published in two or more journals, the entry with the highest citations was kept and the citations from the other

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entries were added to this entry. Publication output for each year was analyzed and a list of the 50 most cited articles in the field was generated, as well as a list of journals publishing cardio-oncology articles.

The top 50 most cited articles were reviewed for their citations, year of publication, type of article (i.e., original article, position paper/society guideline, review, systematic review, conference paper, letter to the editor, and case report), journal, and characteristics of the corresponding author (i.e., field of study and country of origin). Due to the public nature of the data used in the study, informed consent for this study was not obtained and it was exempt from Institutional Review Board approval. This study was conducted in compliance with all applicable institutional ethical standards for human study.

## Results

As of March 31, 2021, a total of 1,294 publications related to cardio-oncology as a field with a total of 14,494 citations were found. There was a consistent increase in the number of articles referring to cardio-oncology and the number of citations over the past two decades (Fig. 1). The articles per year were 1 in 1996, 1 in 2003, 2 in 2008, 7 in 2010, 14 in 2011, 12 in 2012, 28 in 2013, 47 in 2014, 75 in 2015, 115 in 2016, 176 in 2017, 184 in 2018, 261 in 2019, and 371 in 2020.

Cardio-oncology was the first term used to describe the field and has remained the most used in the literature compared to the other names associated with the field. In this regard, we identified additional terms referring to the field which arose later in the literature such as: onco-cardiology (in 2008), cardio-onco-hematology (in 2017), and cardio-immuno-oncology (in 2018). The term cardio-oncology was coined in 1996 by Dr. Daniela Cardinale, a cardiologist from Italy, in an article entitled “Una nuova frontiera: la cardioncologia” in the Italian journal *Cardiologia* (27 citations; first citation in 2010) [3]. There was no further mention of the term “cardio-oncology” until 2003 (one article, one citation), and then later in 2008 (two articles, one and 25 citations). After 2010 and particularly between 2015 and 2020, there has been a significant growth in the number of publications referring to cardio-oncology as a field, likely triggered by the increased recognition of cardiac-related side effects of novel cancer treatments, such as targeted and immunomodulating therapies.

The top 50 most cited articles in the field of cardio-oncology had a combined total of 7,192 citations as of March 2021 (Table 1). The number of citations per publication ranged from 49 to 986 (mean  $143 \pm 157$ ). The most cited articles to date were published between 2010 and 2020, with the majority between 2015 and 2020 ( $n = 31$ , 62%). All articles were in English and most article types were reviews ( $n = 28$ , 56%, with 3,208 citations), followed by guidelines and position papers ( $n = 9$ , 18%, with 2,299 citations) and original articles ( $n = 9$ , 18%, with 1,451 citations). The rest of the articles were one letter to the editor, one systematic review, one case report, and one conference paper.

Among the top 50 most cited papers, the subject matter was varied, with the most common topics being based on clinical

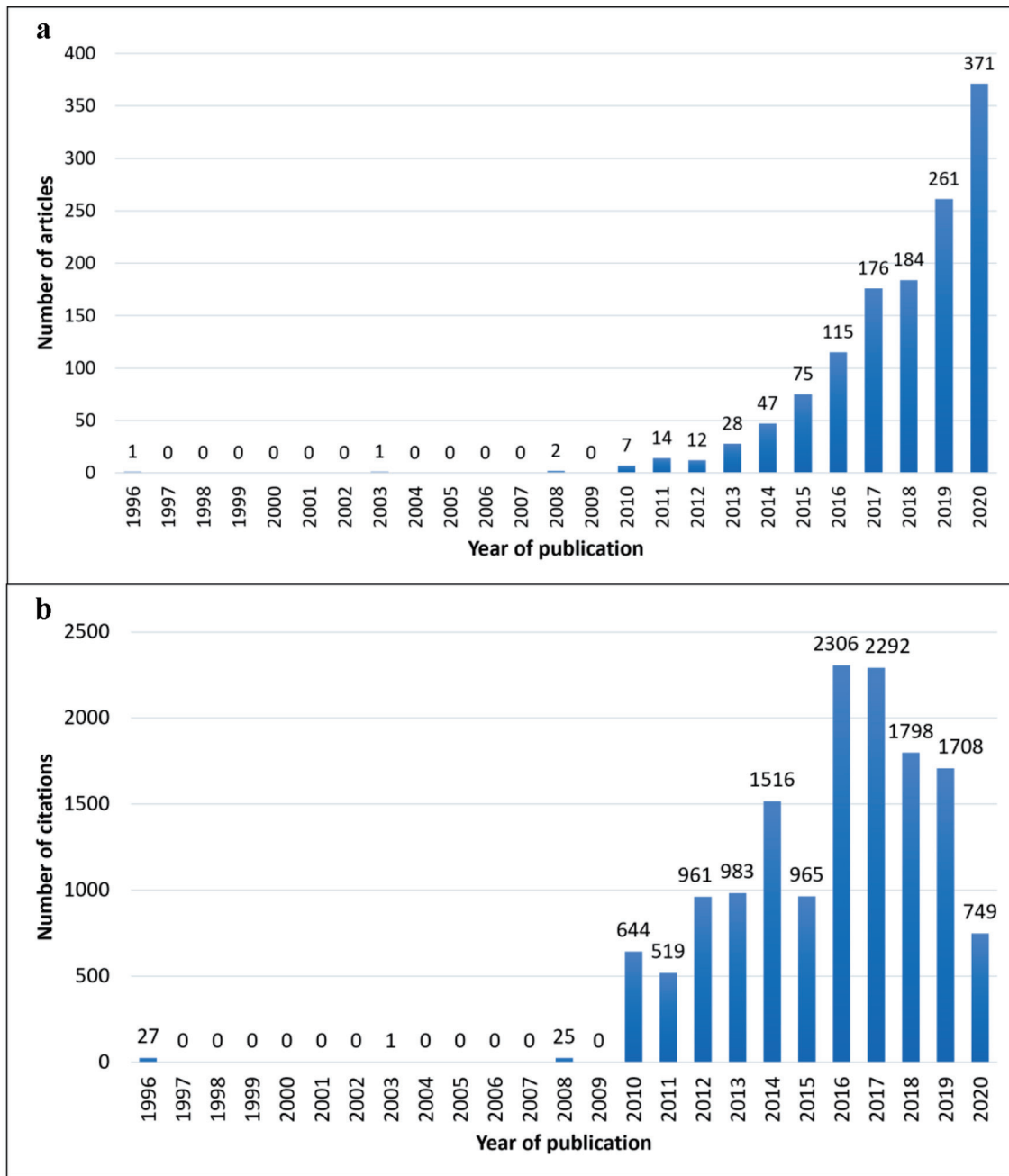
research or practice. The most cited article was titled “2016 ESC position paper on cancer treatments and cardiovascular toxicity developed under the auspices of the ESC Committee for Practice Guidelines”, authored by Zamorano et al and published in 2016 [4]. Interestingly, there were nine guidelines/position papers among the top 50 most cited articles and three (two by professional societies from cardiology and one from oncology) were among the top five most cited articles [4-6]. The review article “Cardiotoxicity of anticancer drugs: The need for cardio-oncology and cardio-oncological prevention” by Albini et al, published in 2010, was the second most cited paper with 499 citations [1]. The most cited original research article was “Myocarditis in patients treated with immune checkpoint inhibitors” (ICIs) by Mahmood et al (321 citations since its publication in 2018), which highlighted the presentation and clinical course of the potentially fatal myocarditis associated with ICIs [7]. Notably, the most common specialty for the senior corresponding authors of the top 50 most cited papers was cardiology ( $n = 36$ ; 72%), followed by oncology ( $n = 5$ ; 10%). The most prevalent countries of origin were the USA ( $n = 26$ ), Italy ( $n = 8$ ), and Canada ( $n = 6$ ).

Table 2 shows the top 10 journals with the highest number of cardio-oncology publications over time. The list includes two dedicated cardio-oncology journals, *JACC Cardio-Oncology* and *Cardio-Oncology*, which launched in 2019 and 2015, respectively. The main focus for the rest of the journals in the list was cardiology. The three journals with the most articles on the 50 most cited list were *Journal of the American College of Cardiology* (eight publications with 1,347 citations), *European Heart Journal* (four publications with 1,372 citations), and *Circulation* (four publications with 241 citations).

## Discussion

This bibliometric analysis of the publication trends in the field of cardio-oncology, from the coining of the term in the first published article in 1996 to date, shows the significant growth of the field in the last years. We quantitatively demonstrated its increasing relevance and attention, based on the number of publications and citations specifically related to the field. In addition, this is the first bibliometric analysis identifying the most cited articles specifically related to cardio-oncology to provide an overview of some of its fundamental developments.

Bibliometric studies of emerging fields and the identification of most cited articles may provide insight on which studies have had the most impact and can help guide further research efforts. However, these assessments may not entirely reflect all the publications that enabled the field's advancement. In this regard, there are many publications of basic, translational, and clinical studies that have contributed significantly to the field of cardio-oncology but have not used the keywords specifically related to the field which were queried in this study. For instance, a paper by Johnson et al published in the *New England Journal of Medicine* in 2016 highlighted fulminant myocarditis as a serious cardiotoxicity with immune checkpoint blockade, and has more than one thousand citations to date [8]. Nevertheless, this article is not present in the list of



**Figure 1.** Trends of global cardio-oncology research. Results from bibliometric analysis from 1864 to 2020 illustrate number of publications (a) and number of citations of articles (b) in cardio-oncology.

the top 50 most cited articles because the terms related to the cardio-oncology field *per se* were not used in the publication title, abstract, or keywords. This highlights the importance of adopting and using standard terms when conducting cardio-oncology research to allow for appropriate dissemination of research in the field.

In all the publications analyzed in our study, there was a noticeable trend of higher number of review articles, guidelines/position papers, and letters to the editors compared to original research articles. The main article type among the top

50 articles were reviews which is consistent with the fact that review articles tend to become highly cited in scientific literature [2]. Similarly, nine articles in the top 50 most cited were guidelines/position papers by professional societies and three were among the top five most cited articles. This also reflects the fact that professional society guidelines and position statements usually become widely cited documents within a field, given their reach to a broader audience and direct impact on clinical practice [9]. In general, the main agents associated with cardiotoxicities discussed in the publications included:

**Table 1.** Fifty Top Cited Articles in Cardio-Oncology<sup>a</sup>

Citations	Year	Journal	Authors	Corresponding author (Country)	Title	Document type	Corresponding author field
1	986	2016 European Heart Journal	Zamorano JL et al	Zamorano JL (Spain)	2016 ESC Position Paper on cancer treatments and cardiovascular toxicity developed under the auspices of the ESC Committee for Practice Guidelines	PP or Guide <sup>b</sup>	Cardiology
2	499	2010 Journal of the National Cancer Institute	Albini A et al	Albini A (Italy)	Cardiotoxicity of anticancer drugs: The need for cardio-oncology and cardio-oncological prevention	Review	Molecular oncology
3	463	2012 Annals of Oncology	Curigliano G et al	Curigliano G (Italy)	Cardiovascular toxicity induced by chemotherapy, targeted agents and radiotherapy: ESMO clinical practice guidelines	PP or Guide	Oncology
4	321	2018 Journal of the American College of Cardiology	Mahmood SS et al	Neilan TG (USA)	Myocarditis in Patients Treated with Immune Checkpoint Inhibitors	Original article	Cardiology
5	288	2011 European Journal of Heart Failure	Eschenhagen T et al	Eschenhagen T (Germany)	Cardiovascular side effects of cancer therapies: A position statement from the Heart Failure Association of the European Society of Cardiology	PP or Guide	Cardiology
6	270	2014 Journal of the American College of Cardiology	Ky B et al	Ky B (USA)	Early increases in multiple biomarkers predict subsequent cardiotoxicity in patients with breast cancer treated with doxorubicin, taxanes, and trastuzumab	Original article	Cardiology
7	256	2013 European Heart Journal	Suter TM et al	Suter TM (Switzerland)	Cancer drugs and the heart: Importance and management	Review	Cardiology
8	218	2017 Canadian Journal of Cardiology	Ezekowitz JA et al	Ezekowitz JA (Canada)	2017 Comprehensive Update of the Canadian Cardiovascular Society Guidelines for the Management of Heart Failure	PP or Guide	Cardiology
9	203	2012 Journal of the American College of Cardiology	Chen J et al	Chen J (USA)	Incidence of Heart Failure or Cardiomyopathy After Adjuvant Trastuzumab Therapy for Breast Cancer	Original article	Cardiology
10	199	2013 JACC: Cardiovascular Imaging	Drafts BC et al	Hundley WG (USA)	Low to moderate dose anthracycline-based chemotherapy is associated with early noninvasive imaging evidence of subclinical cardiovascular disease	Original article	Cardiology
11	184	2016 CA: A Cancer Journal for Clinicians	Curigliano G et al	Curigliano G (Italy)	Cardiotoxicity of Anticancer Treatments: Epidemiology, Detection, and Management	Review	Oncology
12	172	2014 Mayo Clinic Proceedings	Herrmann J et al	Herrmann J (USA)	Evaluation and management of patients with heart disease and cancer: Cardio-oncology	Review	Cardiology
13	164	2017 Journal of the American College of Cardiology	Collier P et al	Collier P (USA)	A Test in Context: Myocardial Strain Measured by Speckle-Tracking Echocardiography	Review	Cardiology

**Table 1.** Fifty Top Cited Articles in Cardio-Oncology<sup>a</sup> - (continued)

Citations	Year	Journal	Authors	Corresponding author (Country)	Title	Document type	Corresponding author field	
14	146	2014	Journal of the American Heart Association	Hahn VS et al	Lemihan DJ (USA)	Cancer therapy-induced cardiotoxicity: Basic mechanisms and potential cardioprotective therapies	Review	Cardiology
15	143	2017	Journal of Clinical Oncology	Pituskin E et al	Paterson DI (Canada)	Multidisciplinary approach to novel therapies in cardio-oncology research (MANTICORE 101-Breast): A randomized trial for the prevention of trastuzumab-associated cardiotoxicity	Original article	Cardiology
16	140	2014	Journal of the American College of Cardiology	Farmakis D et al	Filippatos G (Greece)	Insights Into Onco-Cardiology Atrial Fibrillation in Cancer	Review	Cardiology
17	126	2016	Circulation Research	Lenneman CG et al	Lenneman CG (USA)	Cardio-Oncology An Update on Cardiotoxicity of Cancer-Related Treatment	Review	Cardiology
18	118	2015	Plos One	Focaccetti C et al	Albini A (Italy)	Effects of 5-Fluorouracil on Morphology, Cell Cycle, Proliferation, Apoptosis, Autophagy and ROS Production in Endothelial Cells and Cardiomyocytes	Original article	Molecular oncology
19	111	2015	Journal of the American College of Cardiology	Barac A et al	Barac A (USA)	Cardiovascular health of patients with cancer and cancer survivors: A roadmap to the next level	Review	Cardiology
20	110	2012	Experimental and Molecular Pathology	Weerasinghe P et al	Weerasinghe P (USA)	Oncosis: An important non-apoptotic mode of cell death	Review	Pathology
21	108	2013	Drug Safety	Shah RR et al	Shah RR (UK)	Cardiovascular safety of tyrosine kinase inhibitors: With a special focus on cardiac repolarisation (QT Interval)	Review	Cardiology
22	104	2013	Circulation Research	Ky B et al	Moslehi J (USA)	Emerging paradigms in cardiomyopathies associated with cancer therapies	Review	Cardiology
23	92	2017	Oncotarget	Koleini N et al	Kardami E (Canada)	Autophagy and mitophagy in the context of doxorubicin-induced cardiotoxicity	Review	Molecular biology
24	91	2016	Canadian Journal of Cardiology	Virani SA et al	Virani SA (Canada)	Canadian Cardiovascular Society Guidelines for Evaluation and Management of Cardiovascular Complications of Cancer Therapy	PP or Guide	Cardiology
25	89	2015	Journal of the American College of Cardiology	Li W et al	Moslehi J (USA)	Vascular and Metabolic Implications of Novel Targeted Cancer Therapies: Focus on Kinase Inhibitors	Review	Cardiology
26	82	2014	Journal of Pineal Research	Govender J et al	Engelbrecht, A (South Africa)	Mitochondrial catastrophe during doxorubicin-induced cardiotoxicity: A review of the protective role of melatonin	Review	Physiology

**Table 1.** Fifty Top Cited Articles in Cardio-Oncology<sup>a</sup> - (continued)

Citations	Year	Journal	Authors	Corresponding author (Country)	Title	Document type	Corresponding author field	
27	79	2019	Cardiovascular Research	Hu JR et al	Mosheli J (USA)	Cardiovascular toxicities associated with immune checkpoint inhibitors	Review	Cardiology
28	73	2017	Lancet Oncology	Levis BE et al	Shapiro CL (USA)	Cardiotoxic effects of anthracycline-based therapy: what is the evidence and what are the potential harms?	Review	Oncology
29	73	2020	Annals of Oncology	Curigliano G et al	ESMO Guidelines Committee	Management of cardiac disease in cancer patients throughout oncological treatment: ESMO consensus recommendations	PP or Guide	Oncology
30	69	2019	European Heart Journal	Lancellotti P et al	Lancellotti P (Belgium)	Cardio-oncology services: Rationale, organization, and implementation: A report from the ESC Cardio-Oncology council	Review	Cardiology
31	69	2018	European Journal of Cancer	Cardinale D et al	Latini R (Italy)	Anthracycline-induced cardiotoxicity: A multicenter randomised trial comparing two strategies for guiding prevention with enalapril: The International CardioOncology Society-one trial	Original article	Cardiology
32	68	2017	Journal for Immunotherapy of Cancer	Norwood TG et al	Conry RM (USA)	Smoldering myocarditis following immune checkpoint blockade	Case Report	Oncology
33	68	2016	Catheterization and Cardiovascular Interventions	Iliescu CA et al	Marmagkiolis K (USA)	SCAI Expert consensus statement: Evaluation, management, and special considerations of cardio-oncology patients in the cardiac catheterization laboratory (endorsed by the cardiological society of india, and sociedad Latino Americana de Cardiologia intervencionista)	PP or Guide	Cardiology
34	68	2015	Circulation	Bellinger AM et al	Moslehi J (USA)	Cardio-oncology: How new targeted cancer therapies and precision medicine can inform cardiovascular discovery	Review	Cardiology
35	67	2016	Mayo Clinic Proceedings	Al-Kindi SG et al	Oliveira GH (USA)	Prevalence of Preexisting Cardiovascular Disease in Patients with Different Types of Cancer the Unmet Need for Onco-Cardiology	Original article	Cardiology
36	66	2010	Journal of Pharmacology and Experimental Therapeutics	Minotti G et al	Minotti G (Italy)	Pharmacological foundations of cardio-oncology	Review	Pharmacology
37	65	2013	Journal of Nuclear Cardiology	Schwartz RG et al	Storozynsky E (USA)	Traditional and novel methods to assess and prevent chemotherapy-related cardiac dysfunction noninvasively	Review	Cardiology

Table 1. Fifty Top Cited Articles in Cardio-Oncology<sup>a</sup> - (continued)

Citations	Year	Journal	Authors	Corresponding author (Country)	Title	Document type	Corresponding author field
38	64	2018	Pharmacological Research	Cappetta D et al	De Angelis A (Italy)	Review	Cardiology
39	63	2019	Circulation	Bonaca MP et al	Bonaca MP (USA) Moslehi J (USA)	Review	Cardiology
40	61	2019	European Heart Journal	Sturgeson KM et al	Zaorsky NG (USA)	Original article	Radiation oncology
41	60	2017	Revista Espanola de Cardiologia	Lopez-Fernandez T et al	Lopez-Fernandez T (Spain)	PP or Guide	Cardiology
42	59	2010	Clinical Cardiology	Hong RA et al	Limura T (USA)	Review	Internal medicine
43	59	2016	World Journal of Cardiology	Cuomo JR et al	Weintraub NL (USA)	Review	Cardiology
44	58	2018	Circulation	Scott, JM et al	Scott JM (USA)	Review	Exercise oncology
45	58	2014	International Journal of Cardiology	Patane S	Patane S (Italy)	Letter to Editor	Cardiology
46	58	2018	Basic Research in Cardiology	Davidson SM et al	Yellon DM (UK)	Meeting Report	Molecular and cellular cardiology
47	53	2016	Canadian Journal of Cardiology	Johnson CB et al	Johnson CB (Canada)	Review	Cardiology
48	52	2019	Circulation	Gilchrist SC et al	American Heart Association (USA)	PP or Guide	Cardiology
49	50	2017	Journal of the American Heart Association	Porta-Sanchez A et al	Thavendiranathan P (Canada)	Systematic review	Cardiology
50	49	2013	Journal of the American College of Cardiology	Lal H et al	Force T (USA)	Review	Cardiology

<sup>a</sup>Data as of final search date March 31, 2021. <sup>b</sup>PP or Guide: position paper or guideline.

**Table 2.** Top 10 Journals for Cardio-Oncology Publications<sup>a</sup>

Journal title	Number of published articles
JACC: Cardiooncology	51
Circulation	47
International Journal of Cardiology	40
Journal of the American College of Cardiology	40
European Journal of Heart Failure	36
Current Treatment Options in Cardiovascular Medicine	30
European Heart Journal	23
Cardiooncology	22
Journal of the American Heart Association	19
Current Cardiology Reports	18

<sup>a</sup>Data as of final search date March 31, 2021.

1) traditional chemotherapy agents such as: anthracyclines (i.e., doxorubicin), alkylating agents (i.e., cyclophosphamide), antimetabolites (i.e., 5-fluorouracil, methotrexate, and gemcitabine), and antimicrotubule agents (i.e., paclitaxel, docetaxel, and vincristine); 2) trastuzumab; 3) ICI covering programmed cell death 1 (PD-1) inhibitors (i.e., pembrolizumab and nivolumab) and CTLA-4 inhibitors (i.e., ipilimumab); and 4) tyrosine-kinase inhibitors (i.e., ibrutinib and imatinib).

This bibliometric study used multiple databases and publications in order to capture the growing research trend in cardio-oncology in a comprehensive manner, in contrast with the study of Wei et al where a single database (WOSCC) was queried [10]. Although WOSCC is one of the largest databases for peer-reviewed scientific literature and provides a comprehensive source for bibliometric studies, there are several limitations that need to be considered when querying a single database. Despite a good correlation on the number of indexed articles and citations between several databases, there are known differences among them, leading to articles and citations being missed through the use of a single indexing database [2, 11-14]. In our study, Scopus, WOSCC, and Pubmed were searched in all languages using multiple terms that have been used to refer to the field over the years to avoid missing cardio-oncology publications and citations. This comprehensive approach captured the dynamic nature of this emerging field and resulted in a higher number of articles found in our study when compared to prior publications on the bibliometrics of cardio-oncology. This is illustrated by comparing the 343 publications found by 2018 in studies using a single database [10] with our approach, which found 662 publications by that date.

Although several databases were queried using a comprehensive approach, limitations of this study must be noted. For example, our search strategy was limited to keywords related to cardio-oncology as a field and excluded generic keywords such as “cardiotoxicity” in order to reflect publications that specifically adopted terms that referred to cardio-oncology as a field. As described, this approach did not include some scientific papers related to long-standing research on the cardiotoxic effects of cancer therapies that have created the foundation of

knowledge in current cardio-oncology. This can account to the fact that few articles among the top 50 most cited are original research articles. Despite this, our results show that the scientific output specifically classified as cardio-oncology research, including original basic and translational studies, has increased significantly over the past two decades, greatly influenced by cardiology and oncology leaders in the field and supported by dedicated cardio-oncology journals, cardio-oncology societies, and scientific events globally.

**Conclusion**

Cardio-oncology has blossomed as a field and its impact is expected to continue to expand. In this study, we showed the growing scientific interest in the field of cardio-oncology and analyzed its top 50 most cited articles. Despite the growth of the field, there is a need to expand our research efforts towards more original basic and translational research studies and to adopt standard terms for the indexing of research related to the field.

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None to declare.

**Financial Disclosure**

None to declare.

**Conflict of Interest**

The authors have no conflict of interest to disclose.

**Informed Consent**

Not applicable.



## Author Contributions

G. A. Suero-Abreu designed the study, engaged in data collection, reviewed the literature, analyzed and interpreted the data, and drafted and reviewed the manuscript. A. Barajas-Ochoa designed the study and search strategy, engaged in data collection, reviewed the literature, analyzed and interpreted the data, and reviewed the manuscript. R. Berkowitz oversaw the design of the study, engaged in data interpretation, and provided critical reviews of the manuscript.

## Data Availability

The authors declare that data supporting the findings of this study are available within the article.

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