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The most influential articles on kidney transplantation

A PRISMA-compliant bibliometric and visualized analysis

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Abstract

Background: Kidney transplantation (KT) has become common in the treatment of end-stage renal disease. However, to date, there have been no bibliometric analyses of KT research to identify the most influential articles. The purpose of this research is to identify and characterize the 100 most cited articles that focus on KT and to clarify the trends in the accomplishments in this field.

Methods: We searched the Thomson Reuters Web of Science citation indexing database and used keyword mapping of VOSviewer. The top 100 most cited manuscripts were analyzed based on their titles, authors, institutions, countries of origin, years of publication, and topics.

Results: The *New England Journal of Medicine* has published the most manuscripts on kidney transplantation (n = 26) and is the most cited journal (n = 15,642). The United States has the highest number of publications (n = 61). Kashika is the corresponding author with the most published papers (n = 5; 2892 citations). The most common topics of publication are immunosuppressant (n = 34), clinical outcome (n = 26), and pathology (n = 22). Keywords related to immunosuppressant are the most common in keyword mapping with VOSviewer.

Conclusions: This bibliometric analysis of KT research provides the research characteristics and publication trends of this topic. In KT research, immunosuppressants and post-transplant clinical outcomes have been important topics.

Abbreviations: KT = kidney transplantation, LT = liver transplantation, T100 = 100 most cited articles, WoS = Web of Science.

Keywords: bibliometrics, immunosuppressive agents, kidney transplantation

1. Introduction

Kidney transplantation (KT) has become common as an alternative treatment in patients with end-stage renal disease.[1] KT, which was implemented approximately 50 years ago, has improved long-term results with the development of immunosuppressants.[2] Donors, including living and deceased, are needed for KT. Immunosuppressants have been developed for graft survival, and pathology has been further developed for the diagnosis of kidney grafts sensitive to immune conditions. In particular, research on KT is focused on rejection, pathology, and immunosuppressants.

Bibliometric analysis is used to identify publication trends, including authorships, years of publication, countries, and topics in a particular field.[3] It aims to determine research themes that have been most influential in developing the understanding and management of a field. The degree of intellectual impact of a publication can be identified through the list of citation rankings.[4] Using citation ranking, many medical researchers have identified and analyzed the most influential articles in various medical fields, such as orthopedic surgery,[5] plastic surgery,[6] and oncology.[7] However, to date, there have been no bibliometric analyses of KT research to identify the most influential articles. The purpose of this research is to identify and characterize the 100 most cited articles (T100) that focus on KT and clarify the trends in the accomplishments in this field.

2. Methods

The Institutional Review Board approved the review of medical articles using a publicly available database (Ilsan Paik Hospital Institutional Review Board No. 2021-04-030). A search of the Thomson Reuters Web of Science (WoS) citation indexing database was completed (1983–2019) using the following search terms: "kidney transplant*," "renal transplant*," "kidney allograft*," "renal allograft*," "kidney graft*," and "renal graft*." The search was conducted on a single day, April 20,

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The datasets generated during and/or analyzed during the current study are not publicly available, but are available from the corresponding author on reasonable request.

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Table 1

Journals with 5 or more articles in the top 100.

Journal title	Impact factor 2019	Five year impact factor	Number of manuscripts in the top 100	Number of total citations
New England Journal of Medicine	74.699	72.098	26	15,642
Transplantation	4.546	4.043	24	12,883
American Journal of Transplantation	7.338	6.613	15	10,047
Journal of the American Society of Nephrology	9.274	9.024	9	3851
Kidney International	8.945	8.967	8	6598
Lancet	60.390	59.345	5	3014

2020, to prevent changes in the number of citations as much as possible. Articles other than original or review articles were excluded, and only articles written in English were included. All articles were sorted by the number of citations, based on a method initially developed by Paladugu et al[8]; the title and abstract of each article were thoroughly read and evaluated for inclusion by 2 independent reviewers (JWH and HJ) to ensure their relevance to KT. Because only the characteristics of KT needed to be analyzed, studies involving other transplantations, such as liver and pancreas transplantation, were excluded, even though KT was included. Animal studies were also included if the study was performed for renal allografts.

The selected T100 were then evaluated further according to the following parameters: year of publication, country of origin, institution, authorship, journal, number of citations, and article topic. Since a potential bias in this type of study is that older manuscripts have had more time to be cited, the citation rate was analyzed by dividing the number of citations by the number of years since publication. If the number of publications was the same, the ranking was determined based on the total number of citations.

All articles were analyzed according to their topic: immunosuppressant, clinical outcome, pathology, graft outcome, and donor. The "clinical outcome" group included post-transplant diabetes, infection, cancer, quality of life, medication adherence, and practice guideline. The "pathology" group included pathologic, immunologic, and molecular studies about post-transplant allograft nephropathy and included the diagnostic classification such as Banff. The "graft outcome" group included graft survival, graft rejection, and graft function. The "donor" group included management of living and deceased donors and operative graft perfusion in KT.

VOSviewer version 1.6.15 software (Leiden University, Leiden, Netherlands) was used to analyze the relationship between the keywords to generate a map and cluster visualization.[9] In the network visualization, each circle represented a keyword, and the size of circles represented the frequency of occurrence. Larger circles indicate that the keywords appear more frequently. The circle color on the map indicates the cluster to which the keyword belongs. The line between each circle indicates that the keywords are connected, and the length of the line represents the degree of the relationship. Overlay visualization reveals a changing trend of keywords as time progresses by representing the color of each circle.[10] The blue color represents that the timing of keyword appearance is earlier, and the red color represents that the timing is later. Before performing the analysis, keywords were manually standardized by the authors because different expressions of the same keywords may lead to errors in the results.[11]

3. Results

The WoS database search returned 93,167 full manuscript publications. Table S1, Supplemental Digital Content, http://links.lww.com/MD2/A843 lists the T100. The number of citations ranged from 2418 for Racusen et al ("The Banff 97 working classification of renal allograft pathology")[12] to 363 for Colvin et al ("Antibody-mediated renal allograft rejection: Diagnosis and pathogenesis").[13] The mean number of citations for all articles was 586.4 ± 284.9. The citation rate was the highest for the article "Banff 07 classification of renal allograft pathology: Updates and future directions" by Solez et al.[14] Although the citation rate was applied to prevent time bias, the citation rate of each article was not quite different from its citation numbers, as shown in Table S1, Supplemental Digital Content, http://links.lww.com/MD2/A843.

The T100 are published between 1983 and 2013. The years with the highest number of publications are 1999 and 2000, with a total of 10 papers. The oldest article on the T100, which discusses the Epstein–Barr virus-induced B-cell lymphoproliferative disease after KT, was published in 1983.[15] The most recent article, "Complement-binding anti-HLA antibodies and kidney-allograft survival" was published in 2013.[16]

The T100 are published in 15 journals (Table 1). The *New England Journal of Medicine* has published the highest number of articles (n = 26; 15,642 citations), followed by *Transplantation* (n = 24; 12,883 citations). Half of the T100 are published in the 2 aforementioned journals.

The highest number of contributions comes from the United States (n = 61), followed by Canada (n = 11) and France (n = 5) (Fig. 1). Although the United States has published more than half of the T100, the institution that has published the highest number of articles is University Alberta in Canada (Table 2). Seven corresponding authors have more than 3 papers on the T100. Kasiske and Meier–Kriesche have the highest number of articles on the T100 (n = 5) (Table 3).

The primary subject matter of the articles is categorized as follows: immunosuppressant, clinical outcome, pathology, graft outcome, and donor (Fig. 2). The most studied topic in publications on KT is "Immunosuppressant" (n = 31), followed by "Clinical outcome" (n = 25) and "Pathology" (n = 20). Throughout the period, the topic of "Clinical outcome" has been continuously studied. Studies on "Pathology" have increased since 1991, and the studies of "Immunosuppressant" have increased significantly since 1996. Figure 2 shows the topical trend of the T100 over a 5-year period from 1981 to 2015.

Author-selected keywords of the T100 were analyzed through a co-occurrence network analysis tool using VOSviewer. A total of 106 keywords were extracted from the T100, with a total frequency of 137 (Table S2, Supplemental Digital Content, http://

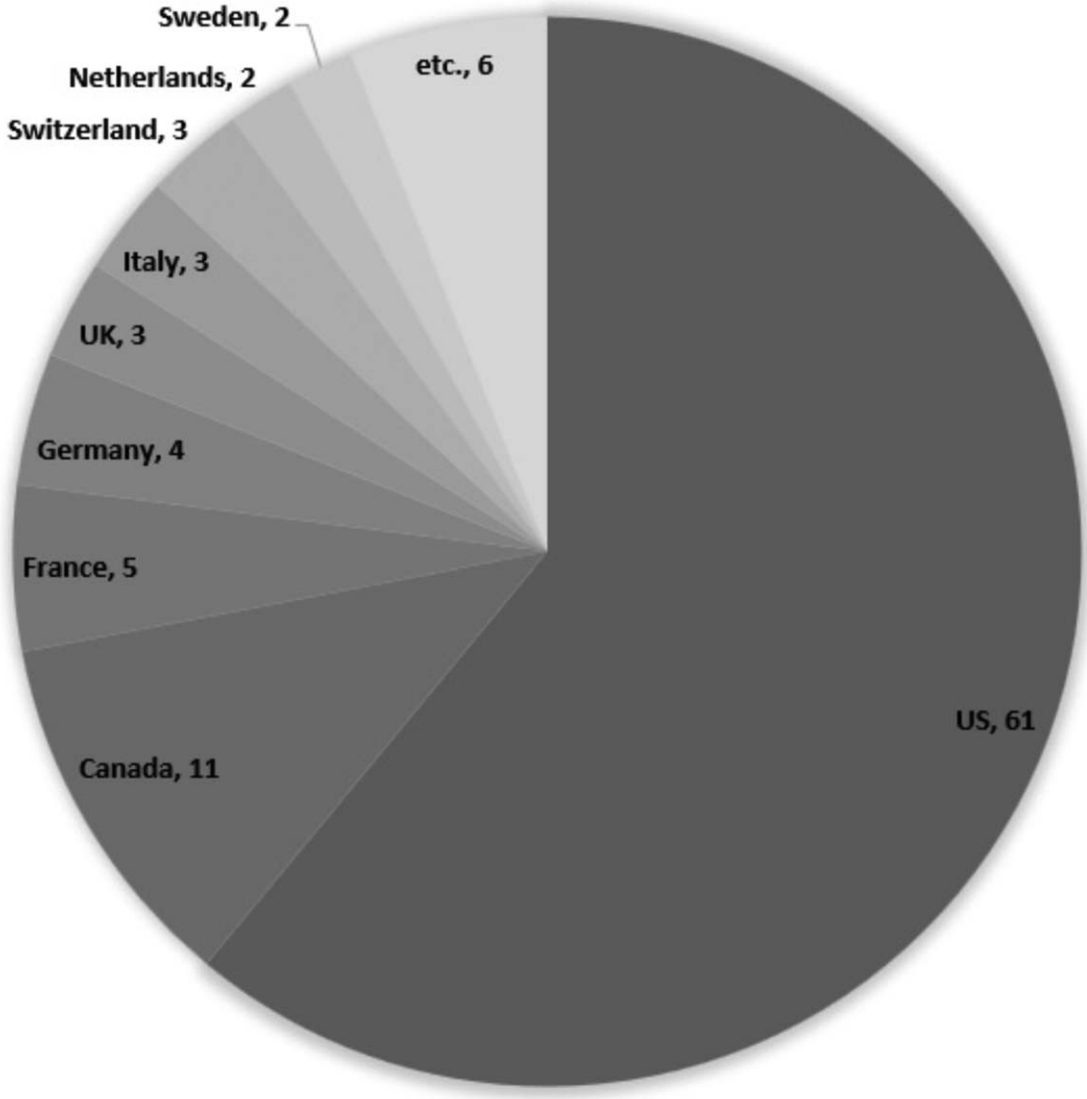

Figure 1. Countries that have contributed to the 100 most cited articles on kidney transplantation.

links.lww.com/MD2/A844). In the network visualization, the highest frequency of occurrence is kidney transplantation (n=8), followed by graft survival (n=6) and antibody-mediated rejection (n=4). Figure 3A is a network formed by 106 keywords and 898 links; it is divided into 5 clusters: red, green, blue, yellow, and purple. The red cluster is the largest, consisting of 32 keywords, including kidney, transplantation, mycophenolate-mofetil, tacrolimus, sirolimus, and cyclosporine. The green

Table 2

Institutions with 3 or more articles in the top 100.

Institution	Country	Number of publications in top 100	Total number of citations
University of Alberta	Canada	7	5420
Massachusetts General Hospital	US	7	3261
University of Michigan	US	6	3033
University of Florida	US	5	2623
University of Minnesota	US	5	2447
Johns Hopkins University	US	3	3649
University Hospital of Basel	Switzerland	3	1810
University of Texas	US	3	1544

Table 3

Corresponding authors with 3 or more articles in the top 100.

Rank	Author	Number of publications in top 100	Total number of citations
1	Kasiske, BL	5	2892
2	Meier-Kriesche, HU	5	2623
3	Halloran, PF	4	2480
4	Hirsch, HH	3	1810
4	Kahan, BD	3	1544
4	Port, FK	3	1403
4	Colvin, RB	3	1131

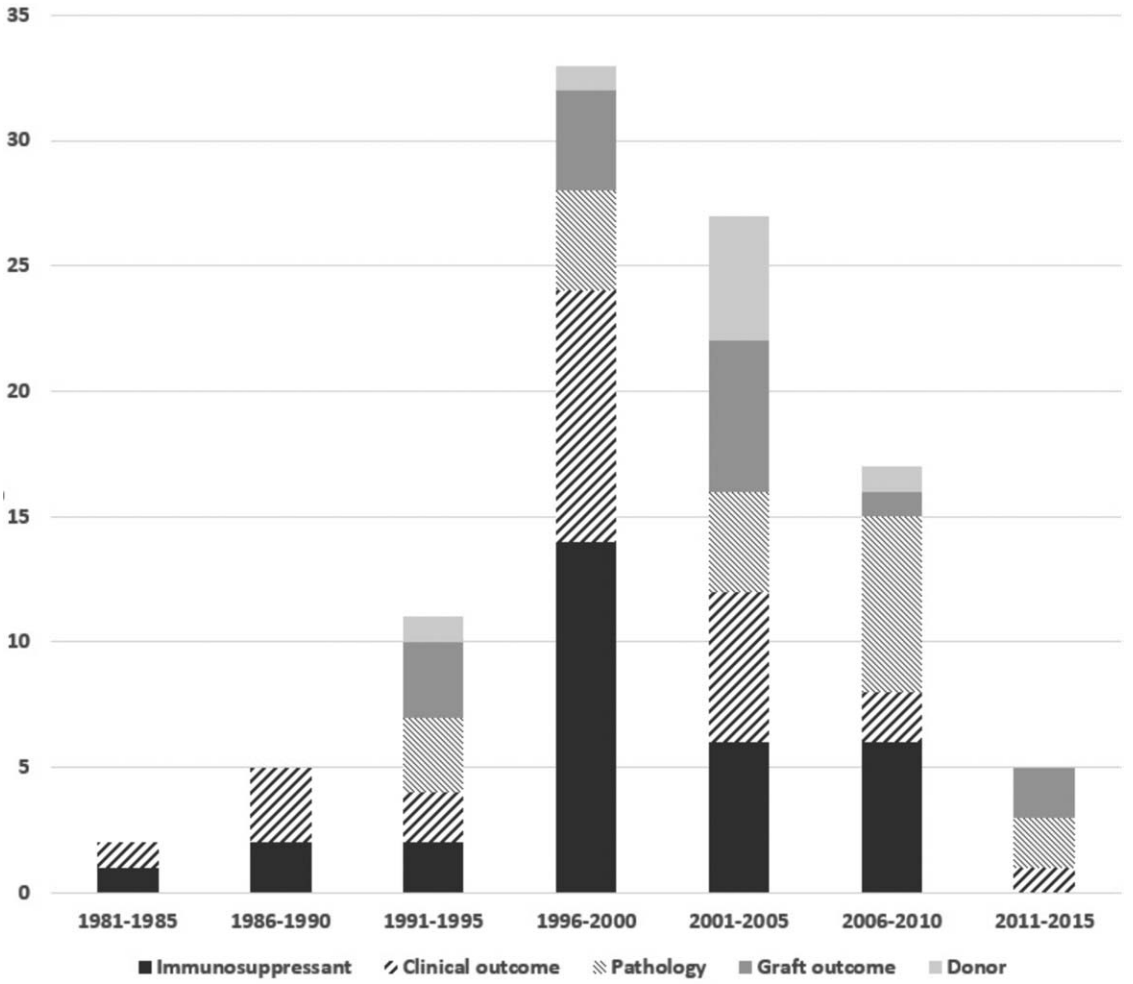

Figure 2. The topical trend of the 100 most cited articles on kidney transplantation by 5-year periods.

cluster includes 20 keywords, mainly related to kidney transplantation, graft survival, waiting list, and era effect. The blue cluster consists of 18 keywords, mainly antibody-mediated rejection, kidney transplants, dialysis, end-stage renal disease, nonadherence, and donor-specific antibody. The yellow cluster includes 16 keywords, mainly malignancies, immunosuppression, and cardiovascular disease. The purple cluster is the smallest cluster with 15 keywords, mainly about acute rejection, Banff, acute allograft rejection, and acute cellular rejection.

In the overlay visualization, keywords related to transplantation (average published year, 2000) or graft survival (average published year; 2004) in the T100 appear in the early phase (Fig. 3B). However, recently, keywords related to immunosuppression (average published year, 2009) or antibody-mediated rejection (average published year, 2010) have appeared. Notably, keywords of transplantation-related diseases, such as malignancies or cardiovascular disease have appeared in recent years.

4. Discussion

Bibliometric analysis is used to identify publication trends and has been used in various fields.[3] Only in the field of solid organ transplantation, the bibliometric analyses of overall transplantation,[17] liver transplantation (LT),[18] and heart transplantation[19] have been sequentially published since 2014. Unfortunately, there have been no previous bibliometric studies on KT fields. To the best of our knowledge, this is the first bibliometric study to evaluate the subspecialty of KT. In the research topics, there are differences between LT and KT. In the T100 on LT, there are many studies on donors, including allocation, and surgery, including preservation and size mismatching.[18] The T100 on KT are mainly focused on immunology and clinical aspects rather than surgery. Robotic KT has become more common in KT surgery, and research on robotic KT is also being active.[20]

An important theme in the history of KT is the introduction of innovative surgery and the development of immunosuppressants. The first human KT was performed with a deceased donor in 1933 by Voronoy. Although the result of the graft was not good, it is a pioneer surgery in the history of clinical KT. This historical event is first reported in a Spanish journal in 1936.[21] A successful KT was reported in identical twins in 1955 by Murray, which won him the Nobel Prize in 1990.[22] In 1962, the first useful immunosuppressants including azathioprine and 6-mercaptopurine were used in a KT from a deceased donor.[23] Since then, the combination of azathioprine and corticosteroid has become the standard immunosuppressant treatment.[24] Antilymphocyte globulin, consisting of polyclonal antibodies

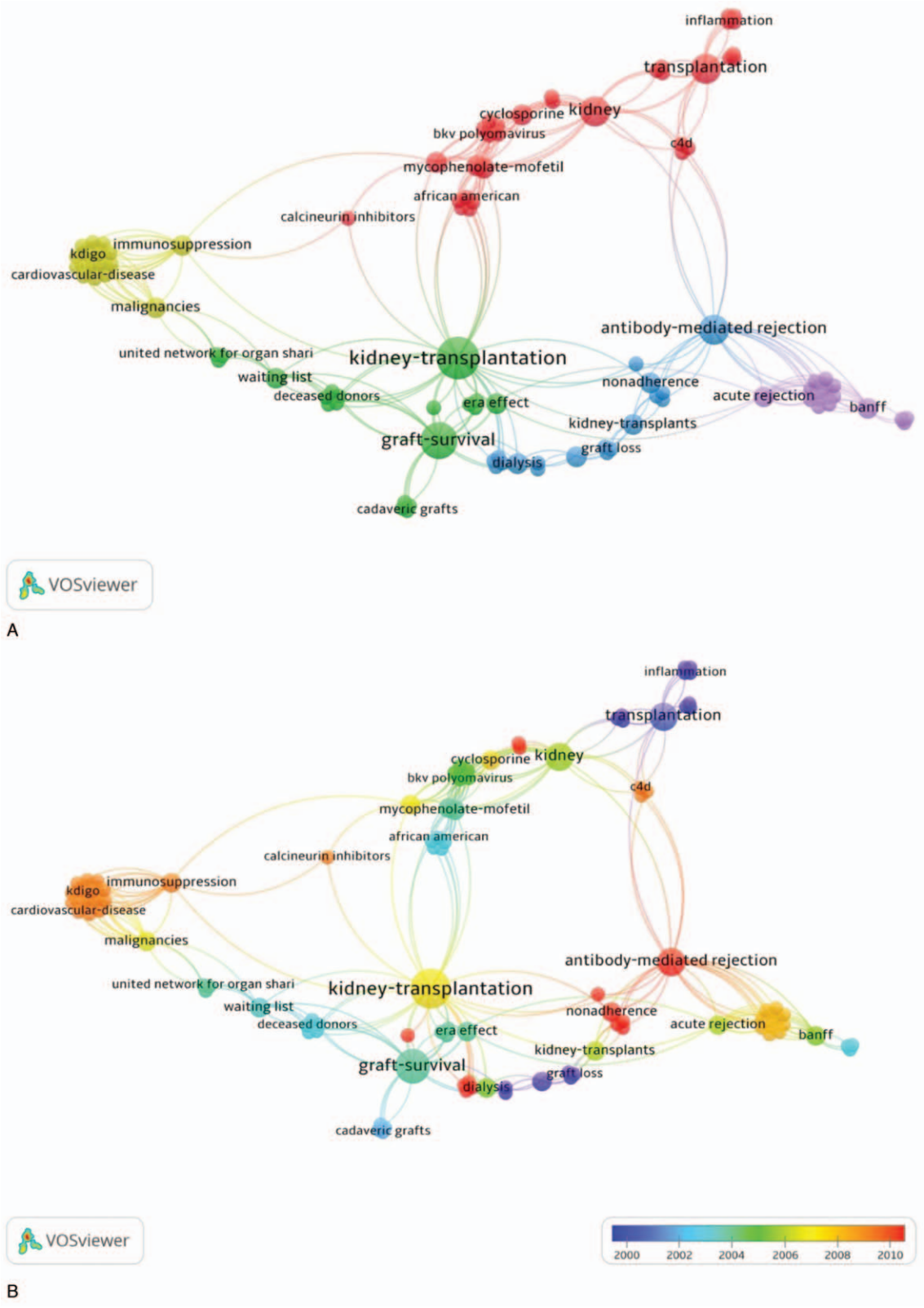

Figure 3. Keyword co-occurrence analysis of the 100 most cited articles on kidney transplantation. (A) Keyword co-occurrence network visualization of the 100 most cited articles. Each circle represents a keyword, and the size of the circles represents the frequency of occurrence. Larger circles indicate that the keyword appears more frequently. Keywords included in the same cluster are displayed in the same color. The distance between the 2 circles shows the degree of the relationship. (B) Keyword co-occurrence overlay visualization. The color of the circle represents the average year of publication, from blue (distant year) to red (last year).

obtained from various animals, is used as an adjuvant.[25] In the 1980s, the combinations of cyclosporine improved the results of KTs.[26] FK 506, discovered in 1984, is now widely used as a standard immunosuppressant in KT.[27] Since then, various immunosuppressants have been introduced more rapidly, thus improving KT results. Recently, due to the shortage of kidney allografts, interest in and research on expanded criteria donors, including elderly deceased and high Kidney Donor Risk Index donors, has increased.[28] For the best preservation of kidney allografts, many studies such as hypothermic machine perfusion and donor pretreatment are being conducted.[29]

VOSviewer analyzes large-scale bibliographic data and the relationships between keywords selected by authors in their own publications and cluster publications based on direct citation relations.[30] It also shows the time trend of keyword changes to inform the progress of the research field. In a recent bibliometric analysis, trend analysis was diversified through the keyword mapping methods of VOSviewer.[31] The keywords presented in the T100 on KT are mainly distributed in 5 clusters: transplantation, graft survival, immunosuppressant, rejection, and post-transplant clinical outcome. Interestingly, keyword analysis through VOSviewer shows that keywords such as "malignancy" or "cardiovascular diseases," which are complications that can occur after KT, have emerged relatively recently, along with the long history of KT. Expanded criteria donor, graft preservation, and immune tolerance, which have recently been increasing interest in transplantation, were not included as keywords. Although there are many topics related to transplantation, it is difficult to clearly classify them as studies on KT. The authors thought that the artificial classification by the authors could induce another bias.

As in many previous bibliometric analyses, our study has some limitations. First, only 1 database was used in our study as a reference source. This can result in the omission of articles not recognized by WoS, although it is the largest bibliometric database currently available. Second, influential recent articles were rarely included in our study because they might need the time to accumulate citations.[32] Lastly, although a significant portion of the literature was not written in English, articles in languages other than English were not included in our database.

5. Conclusions

This bibliometric analysis of KT research provides the research characteristics and publication trends of this topic. In KT research, immunosuppressants and posttransplant clinical outcomes have been important topics.

Author contributions

Conceptualization: Ji Woong Hwang.
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Formal analysis: Heungman Jun.
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Writing – original draft: Heungman Jun, Ji Woong Hwang.
Writing – review & editing: Heungman Jun, Ji Woong Hwang.

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