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Publication Trends of Research on Immune Tolerance After Kidney Transplantation: A Bibliometric Analysis from 1976 to 2024

Yanji Yang[1,2], Hehua Song[1,2], Hao Li[1,2], Qiang Zhong[1,2], Zhouke Tan[1,2]

[1]Department of Renal Transplant, Affiliated Hospital of Zunyi Medical University, Zunyi, Guizhou, 563000, People's Republic of China; [2]Organ Transplant Center, Affiliated Hospital of Zunyi Medical University, Zunyi, Guizhou, 563000, People's Republic of China

Correspondence: Zhouke Tan, Email tanzhouke@zmu.edu.cn

Purpose: The field of immune tolerance after kidney transplantation has witnessed substantial growth in research over the decades. To systematically evaluate the trends and hotspots in this area, a bibliometric analysis was conducted spanning from 1976 to 2024.
Methods: A bibliometric analysis was conducted using the Web of Science Core Collection database. VOSviewers, CiteSpace and the R package "bibliometrix" were used for visualization.
Results: The analysis examined 1033 English articles, highlighting the involvement of 6608 authors from 3461 institutions across 53 countries/regions. The research showed a 4.14% annual growth in publications, peaking in 2016 and declining recently. The most cited article was "Marked prolongation of porcine renal xenograft survival in baboons through the use of alpha1,3-galactosyltransferase gene-knockout donors and the cotransplantation of vascularized thymic tissue (488 citations)" published in the *Nature medicine* (IF = 58.7) in 2005. The USA led in both publication volume and citations, with significant contributions from Harvard University and Massachusetts General Hospital. High-impact journals like *Transplantation* dominated. The keywords "tolerance", "induction", and "T-cells" exhibited the highest co-occurrence frequency. Meanwhile, "breast cancer", "magnetic resonance imaging", "deep learning", "machine learning", "neoadjuvant chemotherapy", and "radiomics" were identified as keywords with the strongest recent citation bursts.
Conclusion: This bibliometric analysis highlights the evolving trends and hotspots in research on immune tolerance after kidney transplantation. Future studies should continue to explore the integration of machine learning in understanding and predicting immune tolerance.
Keywords: bibliometrics, publication, kidney transplantation, immune tolerance, survival

Introduction

Kidney transplantation is the definitive treatment for end-stage renal disease (ESRD), offering significant improvements in survival and quality of life over dialysis.[1,2] Although modern immunosuppressive regimens have markedly reduced acute rejection rates, they remain ineffective against chronic rejection—a major cause of late graft loss—while simultaneously increasing long-term risks of infection, nephrotoxicity, and malignancy.[3,4] Consequently, achieving operational tolerance, defined as stable graft function without ongoing immunosuppression, represents the paramount goal in transplantation. The rare but documented success of complete immunosuppression withdrawal in some patients confirms that clinical tolerance is attainable.[5] Analyzing research trends in immune tolerance is therefore essential to guide future therapeutic innovations toward this objective.

Immune tolerance in transplantation involves complex mechanisms, such as mixed chimerism induction, T-cell depletion, and costimulatory blockade.[4] Promising clinical strategies are emerging; for instance, a recent Phase 3 trial showed that donor-derived cell therapy (MDR-101) induced durable chimerism and operational tolerance in kidney recipients.[6] Similarly, donor-modified immune cell (MIC) infusion has demonstrated sustained potential in early-phase

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studies.[7] In the clinical setting, transplant tolerance is considered “operational”, defined by stable graft function without immunosuppression. However, its study is significantly hampered by the absence of validated biomarkers. Currently, no assays exist to reliably confirm the presence, robustness, or durability of donor-specific unresponsiveness. This critical gap impedes clinical research, complicates the management of patients on minimal or no immunosuppression, and hinders the safe weaning of immunosuppressive drugs.[8] This gap impedes the safe withdrawal of immunosuppression—a step fraught with the risk of graft loss[9]—and hinders the broader application of tolerance protocols. Furthermore, the development of standardized, reproducible protocols is essential. Such protocols must be broadly applicable across transplant centers to reliably induce tolerance.[8] A comprehensive analysis of research trends is therefore crucial to navigate these challenges and advance the field.

Bibliometric analysis is a quantitative approach used to examine publication trends, patterns, and research impact within a scientific discipline.[10] By evaluating metrics such as publication volume, citation frequency, and collaboration networks, it offers valuable insights into the evolution of research topics, highlights influential contributors and institutions, and helps identify emerging fronts.[11] While previous bibliometric studies have explored broader aspects of kidney transplantation, such as research prospects,[12] the transplant microenvironment and graft survival,[13] and antibody-mediated rejection,[14] none have specifically addressed the domain of immune tolerance. Our study fills this gap by mapping the intellectual structure and temporal development of the field, providing a systematic foundation for guiding future investigations and resource allocation in tolerance-focused research.

Materials and Methods

Search Strategies and Data Collection

A comprehensive literature search on immune tolerance after kidney transplantation from 1976 to 2024 was conducted on the Social Sciences Citation Index (SSCI) and the Science Citation Index Expanded (SCIE) from Web of Science Core Collection (WoSCC) due to its focus on high-quality, globally peer-reviewed academic publications, primarily traditional academic literature, including journal articles, conference proceedings, and books.[15] Additionally, the WoSCC database is multidisciplinary and comprehensive, offering a complete citation network and key bibliometric indices (eg, JCR, IF, and H-index).[16] Therefore, we selected it to obtain global academic information for bibliometric analysis according to previous studies. The search formula is (TS = (kidney transplantation OR renal transplantation OR kidney grafting)) AND TS = (immune tolerance).[13] Synonyms were fully considered to ensure a comprehensive search. This study focused on English-language articles, excluding reviews, meeting abstracts, editorial materials, proceeding papers, letters, early access publications, notes, book chapters, corrections, retracted publications, news items, and non-English studies. To ensure consistency with database updates, literature retrieval was conducted on 9 July 2024. All collected information was in text format, including publication and citation counts, titles, countries/regions, institutions, journals, authors, and keywords, for subsequent bibliometric analysis. Several data-cleaning techniques were employed, such as the supplementation of missing values, analysis for duplicate literature, and the merging of synonyms.[17]

Statistical Analysis

Microsoft Excel was utilized to identify and compute bibliometric indicators. For a thorough visualization analysis of the academic data, tools such as VOSviewer (V 1.6.20), CiteSpace (V 6.3.R1), and Bibliometrix (R 4.3.3) (https://bibliometric.com/) were employed.

VOSviewer mapped and visualized the co-occurrence of countries, institutions, authors, and keywords within the selected literature, revealing key research themes and collaborations in the field.[18] The network map depicted nodes representing these entities, with node size proportional to their frequency of occurrence and color indicating distinct research clusters (or average publication year for keywords). Thicker lines between nodes indicated stronger co-occurrence relationships.[11] CiteSpace analyzed the temporal evolution of research trends on immune tolerance after kidney transplantation, generating time-zone maps from January 1976 to July 2024.[19] By slicing each year and specifying keywords as node types, a visual timeline of relevant keywords was created. The top 5 keywords per slice were selected using a combined pruning method. The resulting maps displayed clusters of research topics, with cluster size reflecting significance and color gradient indicating the research time span.[20] R-bibliometrix was utilized for advanced statistical analysis and the calculation of bibliometric indices, including the H-index, G-index, and M-index for top authors and institutions.[10] The H-index (Hirsch index) evaluates both productivity and citation impact, while the G-index focuses on broader citation counts, and the M-index balances paper production and received citations.[21,22] In this study, authors' H-index were sourced directly from the WoSCC database. Keyword analysis of the selected articles was conducted using "Author Keywords" from Biblioshiny and "Keywords Plus" from VOSviewer. "Keywords Plus" provided more precise results and was thus selected as the primary data source for the analysis. Journal Citation Reports (JCR) metrics, such as Impact Factor (IF) 2023 and quartile ranking (Q1-Q4) 2023, were used to evaluate journal influence.

Results

An Overview of Publications

By July 2024, a total of 1686 studies concerning the research theme of immune tolerance after kidney transplantation were identified. After excluding 504 reviews, 9 meeting abstracts, 26 editorial materials, 75 proceeding papers, 3 letters, 1 early access publication, 1 note, 5 book chapters, 1 correction, 3 retracted publications, 1 news item, and 23 non-English studies, 1033 English articles were included for subsequent bibliometric analysis. The earliest-identified article was published in 1976 (Figure 1). The investigation revealed that 6608 authors from 3461 institutions spanning 53 countries/regions participated in creating these manuscripts for this study. These manuscripts were published across 273 journals and referenced 27,797 sources. On average, each publication had 8.23 co-authors, with an international co-authorship rate of 17.91%. Additionally, these publications included 1463 author keywords, and each received an average of 30.57 citations (Figure 2A).

From 1976 to 2024, the annual growth rate of publications related to immune tolerance after kidney transplantation was 4.14%. The fitted curve for the annual number is shown in Figure 2B, with the fitting equation being y = 1.0715x-5.7066 (R^2 = 0.7624), with extra Segmented Regression Analysis (Figure S1 and Appendix 1) and Corresponding trend data (Appendix 2). Initially, there were fewer publications, with the first peak appearing in 1991 (11 articles), followed by a fluctuating increase. The number of publications reached its peak in 2016 (49 articles). In recent years, there has been a declining trend.

The most cited article was "Marked prolongation of porcine renal xenograft survival in baboons through the use of alpha1,3-galactosyltransferase gene-knockout donors and the cotransplantation of vascularized thymic tissue" published in the *Nature Medicine* (IF = 58.7) in 2005, with a total of 488 citations.[23] The article, titled "$CD4^+CD25^+$ immune regulatory cells are required for induction of tolerance to alloantigen via costimulatory blockade" published in the *Journal of Experimental Medicine* (IF = 12.6) in 2001 accumulated a total of 470 citations.[24] The article, titled "Tolerance and Chimerism after Renal and Hematopoietic-Cell Transplantation" published in the *New England Journal of Medicine* (IF = 96.2) in 2008 accumulated a total of 392 citations[25] (Table S1).

Distribution and Collaborative Networks of Countries

These publications were from 53 countries/regions. The USA was far ahead in terms of the number of articles (n = 395), accounting for 38.24% of the total, and ranked first in total citations (TC = 15,526). China (n = 101, 9.78%) and France (n = 70, 6.78%) follow closely in second and third place in terms of article volume, respectively. Together, these three countries contributed more than half of the total publications (54.80%) (Figure 3A and Table S2).

Subsequently, the international collaboration between countries was examined, with 53 countries involved. The USA exhibited the highest intensity of collaboration (total link strength = 179), engaging in close partnerships with numerous countries such as Germany, China, Japan, France, and the UK. Germany (total link strength = 87) and France (total link strength = 80) followed closely in terms of collaboration intensity, while China ranked only sixth (Figure 3B).

Distribution and Collaborative Networks of Institutions

A total of 3461 institutions participated in the publication. Harvard University published the highest number of articles (n = 224), followed by Massachusetts General Hospital (n = 141) and Harvard Medical School (n = 126), all located in the

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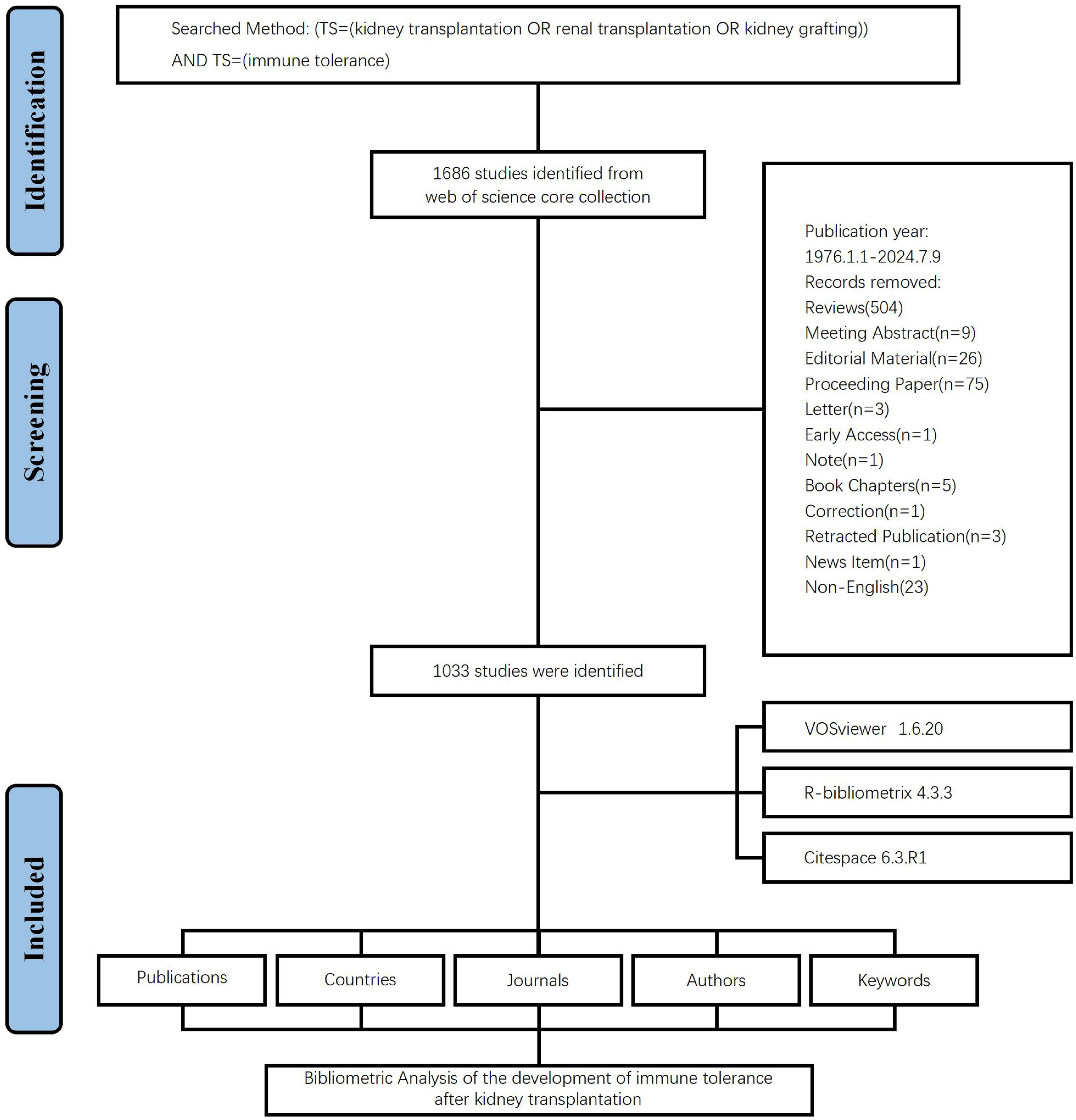

Figure 1 Flow diagram of the bibliographic retrieval process.

USA (Figure 4A). In terms of international collaboration, 95 institutions participated with a minimum of 5 articles each. The University of Nantes had the highest volume of collaborations (total link strength = 52), primarily with the Inserm (total link strength = 42), both located in France. Massachusetts General Hospital (total link strength = 42) in the USA ranked third in international collaboration (Figure 4B).

Authors and Co-Authors

There were 6608 authors participating in the publications of relevant articles. Sachs DH topped the list with the highest H-index of 19. The author also topped the total publications (TP = 28). The most highly cited paper by the author is the aforementioned "Marked prolongation of porcine renal xenograft survival in baboons through the use of

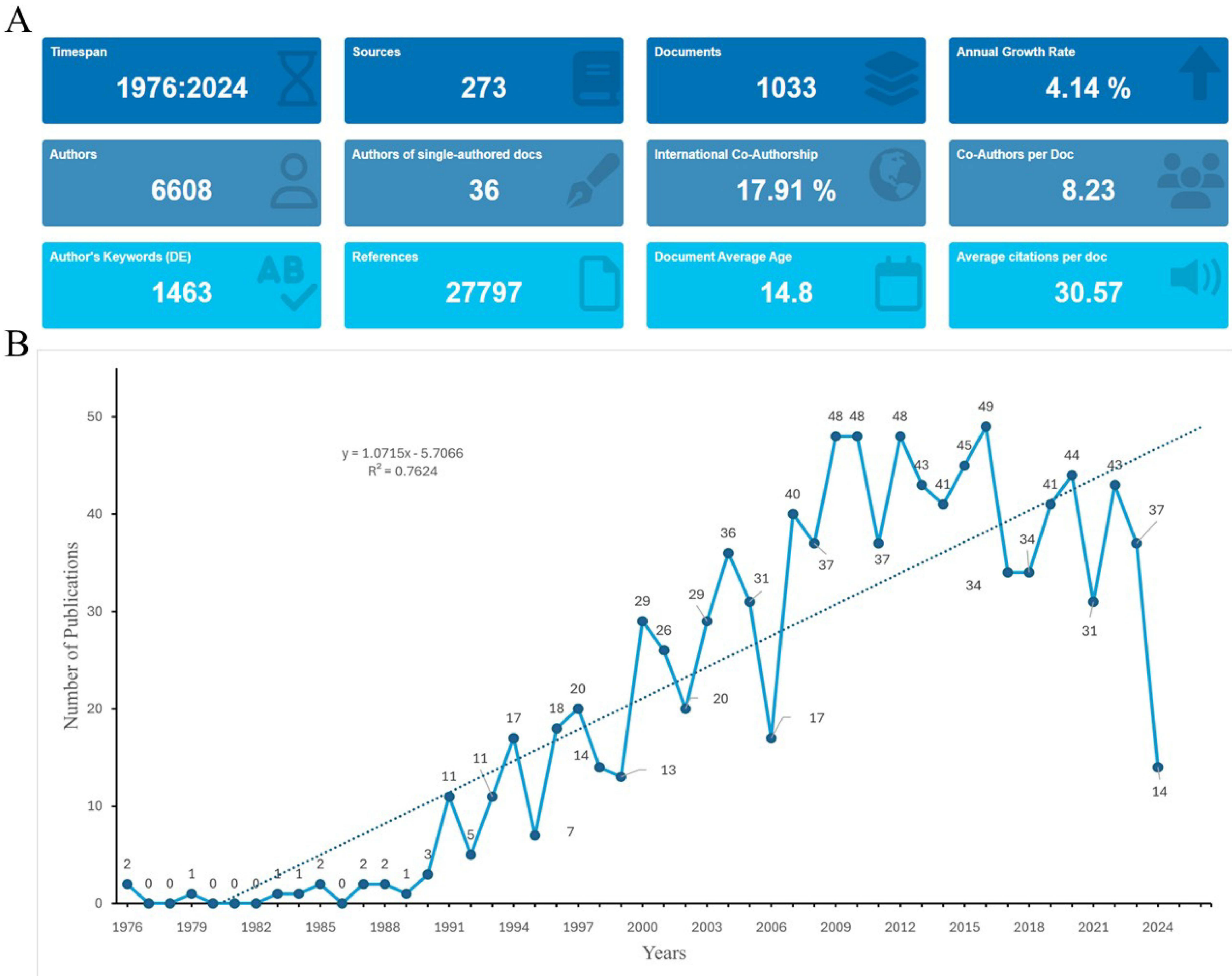

Figure 2 Analysis of the general information. (**A**) A summary of quantitative analysis of the publications. (**B**) Annual output of research from 1976 to 2024.

alpha1,3-galactosyltransferase gene-knockout donors and the cotransplantation of vascularized thymic tissue" with a total of 488 citations.[23] Brouard Sophie (H-index = 13) and Yamada K (H-index = 13) are tied for second place among the high-impact authors (Table S3). Regarding international collaboration, Brouard Sophie (total link strength = 83) topped the list, followed by Soulillou Jean-Paul (total link strength = 73) and Giral Magali (total link strength = 71) (Figure 5).

Contributions and Collaborative Networks of Journals

The articles were published across 273 journals. The journal *Transplantation* (IF 2023 = 5.3, Q1) topped the high-impact journals with the highest H-index of 43, the most total publications (TP = 177) and the most total citations (TC = 5739). *American journal of transplantation* (IF 2023 = 8.9, Q1) and *Journal of immunology* (IF 2023 = 3.6, Q2) ranked 2nd and 3rd with an H-index of 34 and 28, respectively. *Kidney international* achieved the highest IF in 2023 (14.8) among the top 20 high-impact journals (Table S4).

In terms of international collaboration, *Transplantation* (total link strength = 422) exhibited the strongest link strength in the co-occurrence network, indicating that it was most frequently cited in conjunction with other journals, suggesting thematic or partial connections among the research published in them. *American journal of transplantation* (total link strength = 361), and *Journal of immunology* (total link strength = 143) ranked second and third, respectively (Figure 6A).

In the coupling network, *Transplantation* (total link strength = 19,769) exhibited the strongest link strength, signifying that it shared a substantial number of references with the highest number of other journals, highlighting

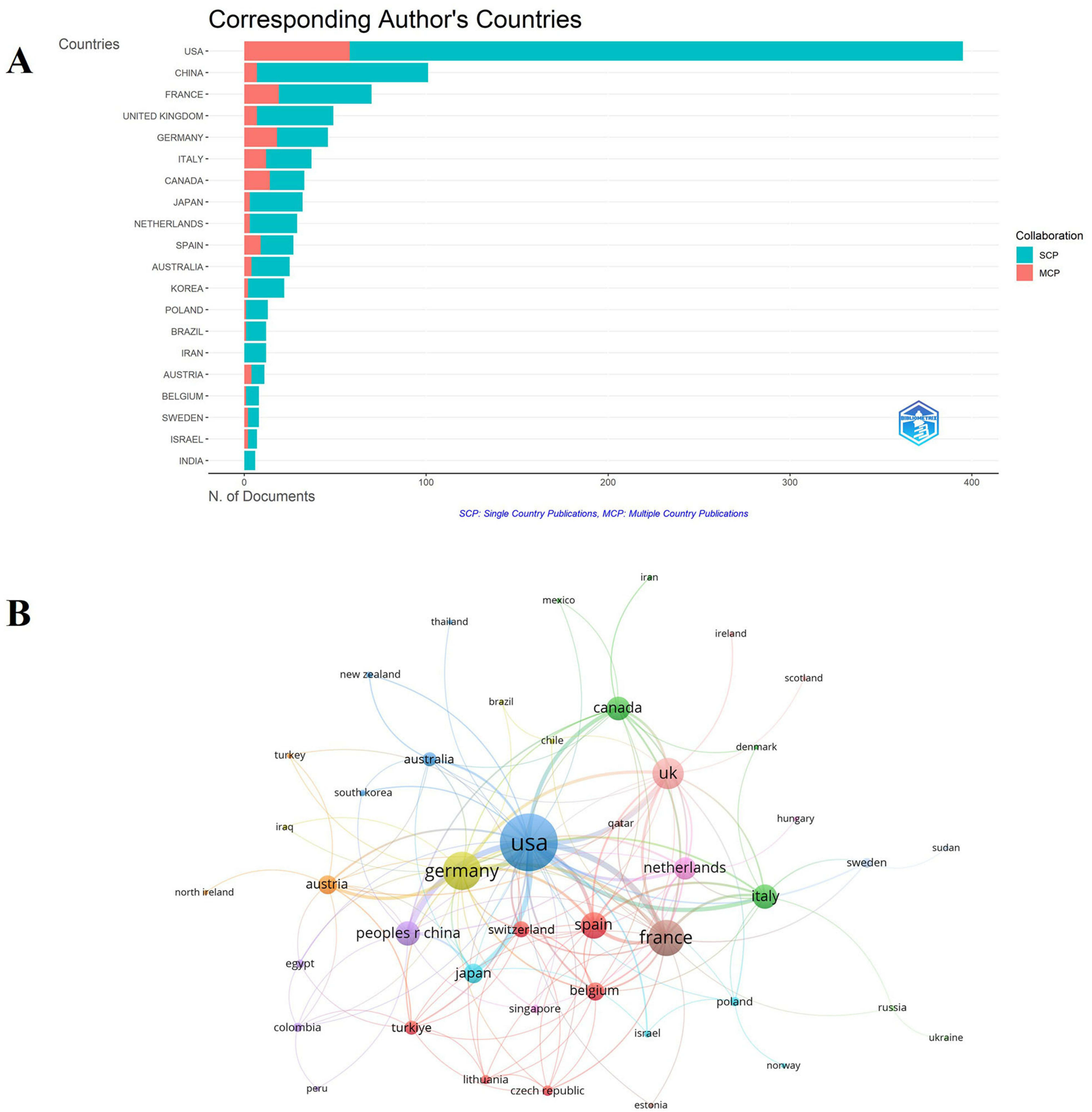

Figure 3 Analysis of countries. (**A**) Distribution of responding author's publications by country. (**B**) Visualization map depicting collaboration among different countries.

a shared knowledge base or research focus. *American journal of transplantation* (total link strength = 15,068), and *Transplant immunology* (total link strength = 6914) ranked second and third, respectively (Figure 6B).

Keyword Co-Existence Network and Burst Keywords

In total, 103 keywords with a minimum of 16 occurrences were identified and illustrated in Figure 7A, with thicker lines indicating stronger associations. The keyword "tolerance" (total link strength = 1168) exhibited the strongest total link strength, followed by "induction" (total link strength = 808) and "T-cells" (total link strength = 629). Other noteworthy keywords demonstrating substantial intensity include "rejection" (total link strength = 613), "recipients" (total link strength = 494), "survival" (total link strength = 403), "dendritic cells" (total link strength = 358), "immunosuppression"

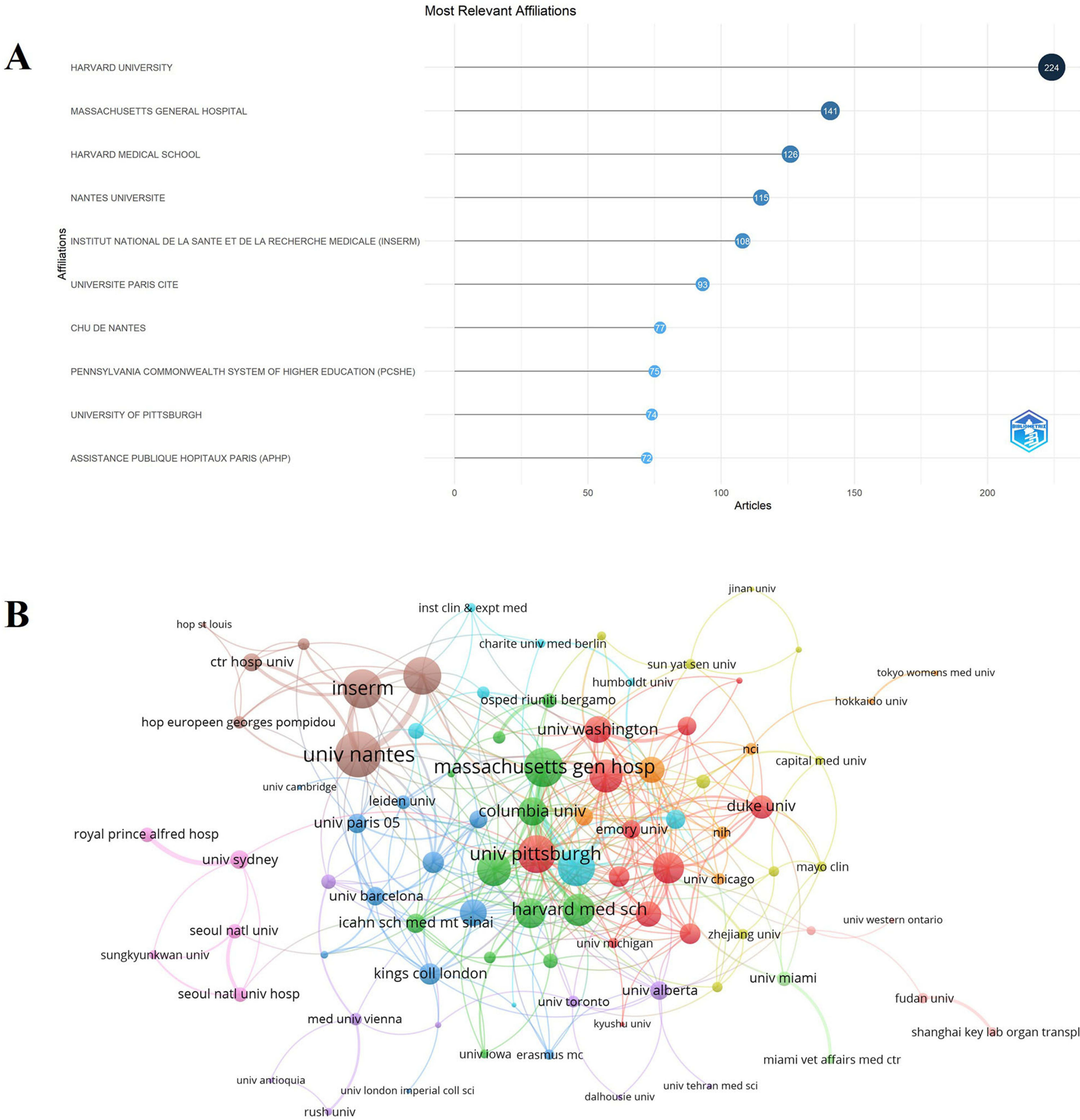

Figure 4 Analysis of institutions. (**A**) Top 10 institutions ranked by article count. (**B**) Visualization map depicting collaboration among different institutions.

(total link strength = 324), "activation" (total link strength = 267), "renal allografts" (total link strength = 253), and "chimerism" (total link strength = 223).

The top 20 keywords with the strongest citation burst between 1994 and 2024 showcase the hotspots and trends in the field (Figure 7B). The years between 1994 and 2016 have seen the bursts of several keywords such as "T cells" (strength 43.69, 1994–2014), "induction" (strength 38.89, 1994–2012), "rejection" (strength 31.04, 1994–2013), "monoclonal antibody" (strength 21.76, 1994–2005), "bone marrow transplantation" (strength 14.52, 1996–2015), "dendritic cells", (strength 26.39, 2000–2016), and "expression" (strength, 15.05, 2000–2010). These keywords, with the longest burst spanning 20 years, have dominated the research hotspots for over two decades since 1994. It was until 2019 that a shift in

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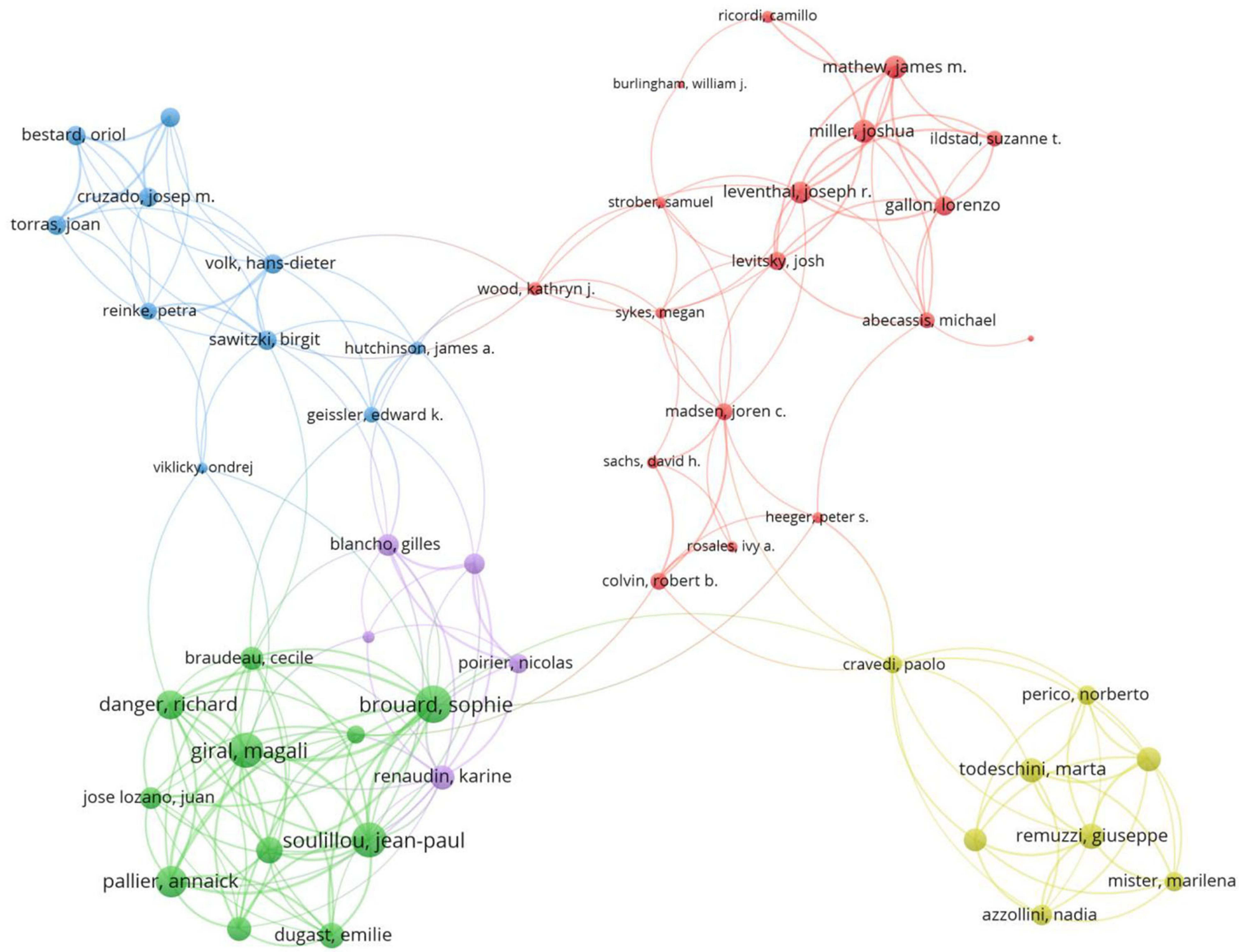

Figure 5 The visualization map depicting collaboration among authors.

the bursting keywords occurred, with "images" (strength 14.44, 2019–2024), "features" (strength 14.35, 2019–2022) and "magnetic resonance imaging" (strength 19.21, 2020–2024) taking the lead.

The keyword "breast cancer" (strength 56.06, 2021–2024) began to experience burst in 2021, demonstrating the highest intensity. In the same year, other keywords such as "machine learning" (strength 24.8, 2021–2024), "neoadjuvant chemotherapy" (strength 16.66, 2021–2024), and "radiomics" (strength 15.16, 2021–2024) also saw a surge. "Deep learning" (strength 18.05, 2022–2024) emerged as the latest keyword to experience a significant burst.

Discussion

This bibliometric analysis presents an overview of research trends on immune tolerance after kidney transplantation from 1976 to 2024. A total of 1033 English articles were identified and analyzed. The annual growth rate of publications was 4.14%, peaking in 2016. The most highly cited article focused on xenotransplantation survival in baboons. The USA led in both publication volume and total citations. Harvard University, Massachusetts General Hospital, and Harvard Medical School were the top institutions. Sachs DH topped the list of authors with the highest h-index and total publications. The journal *Transplantation* emerged as the most influential. The recent trends highlight the emergence of keywords related to imaging and machine learning. This analysis underscores the evolving research landscape and identifies key contributions, trends, and emerging hot spots in the field.

The most highly cited article "Marked prolongation of porcine renal xenograft survival in baboons through the use of α1,3-galactosyltransferase gene-knockout donors and the cotransplantation of vascularized thymic tissue" reported by the

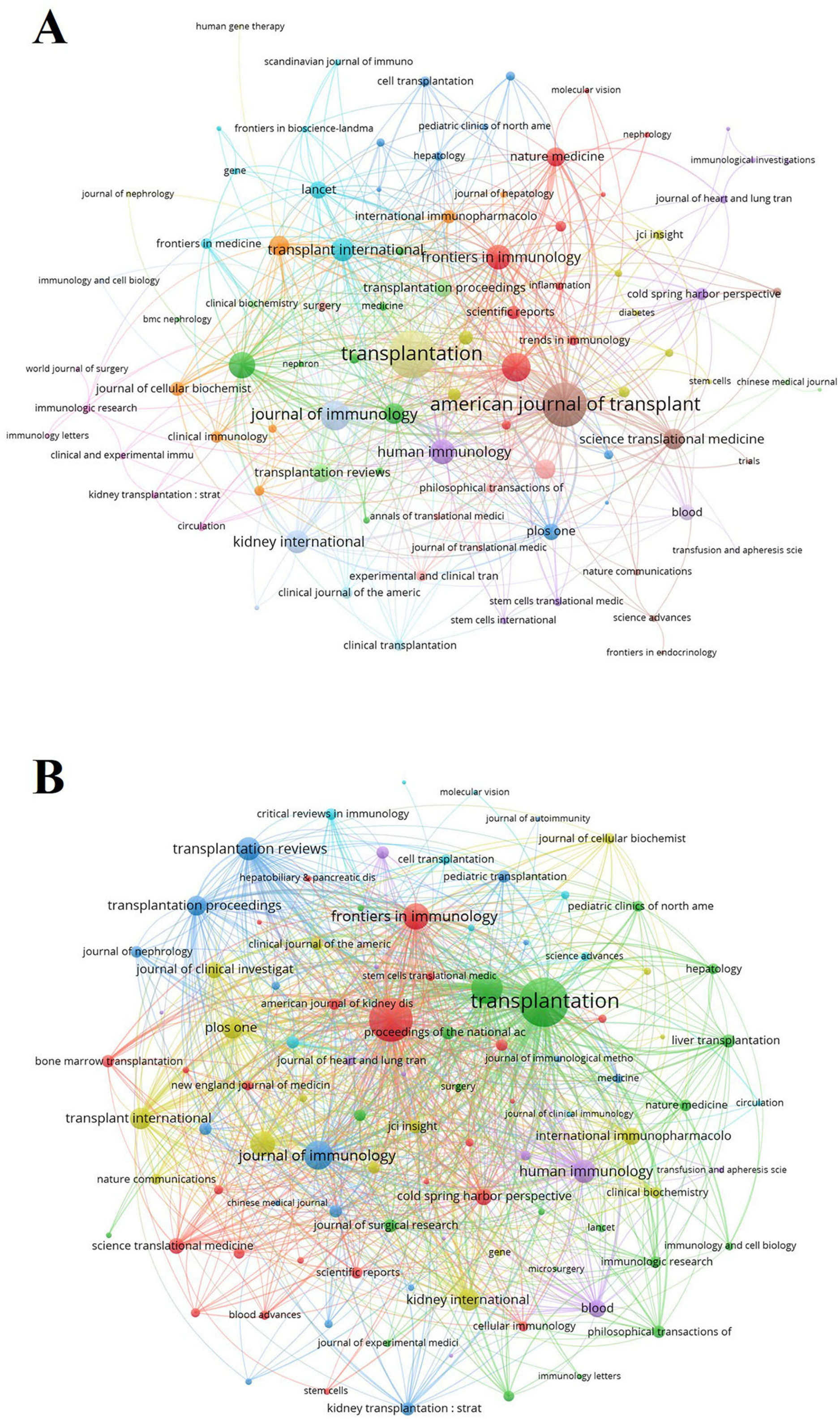

Figure 6 Analysis of journals. (**A**) The co-occurrence networks of journals. (**B**) The coupling networks of journals.

most influential author, Sachs DH, addressed a critical challenge in xenotransplantation, demonstrating the potential of gene-knockout technology to overcome immune rejection.[23] Two other highly cited articles addressed distinct but related topics: one focused on CD4+CD25+ immunoregulatory cells and their role in inducing tolerance to allogeneic antigens,

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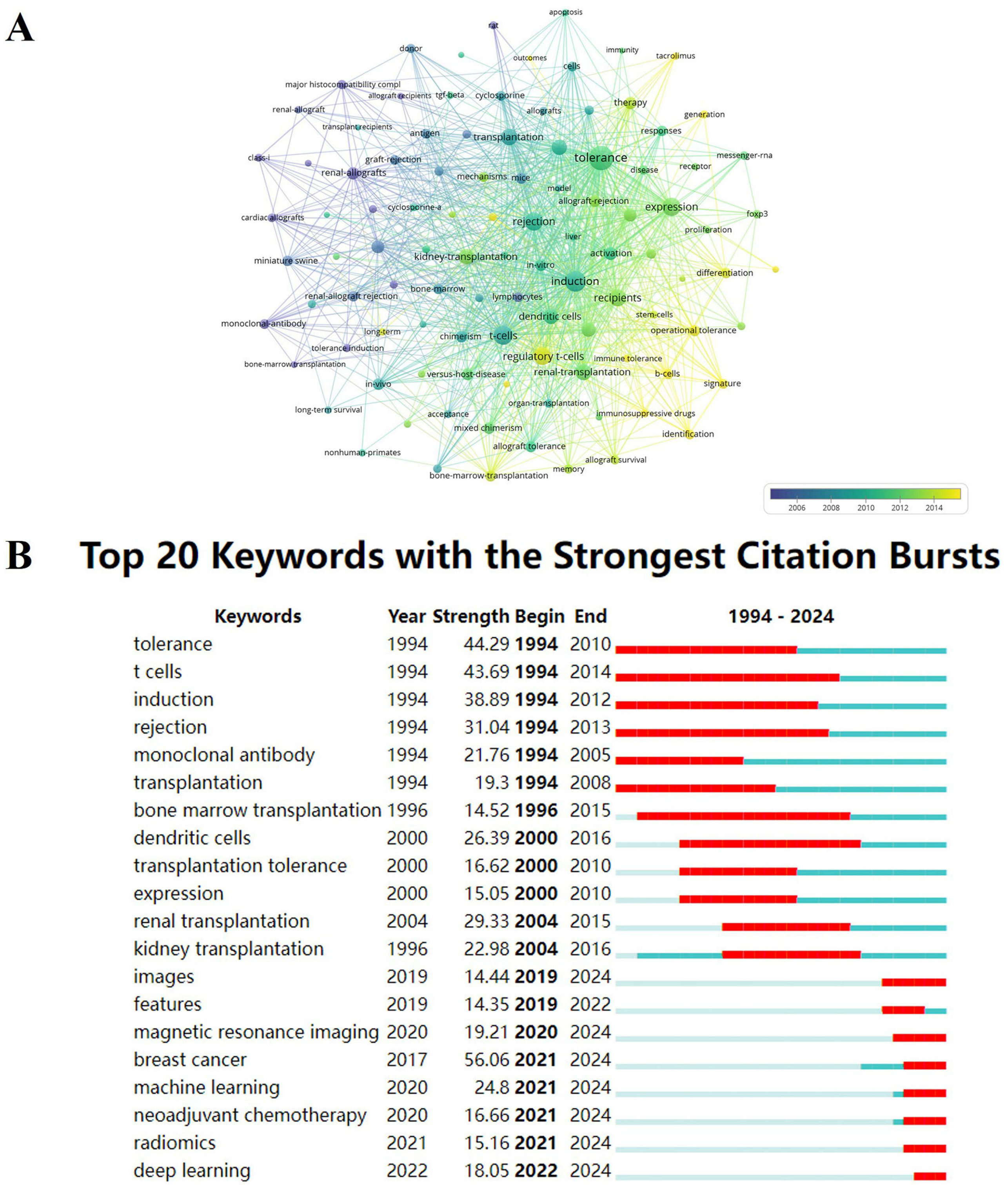

Figure 7 Analysis of keywords. (**A**) Visual analysis of keyword co-occurrence network. (**B**) Top 20 keywords with the strongest citation bursts.

while the other examined tolerance and chimerism following combined renal and hematopoietic-cell transplantation.[24,25] These articles have contributed to advancing our understanding of immune tolerance mechanisms and their clinical applications.

The number of publications reached its zenith in 2016 but has declined slightly in recent years. This decline may suggest a maturing of the field, with researchers focusing on refining existing knowledge rather than exploring new areas. The USA led in both the number of publications and total citations, reflecting its significant investment in research, drug development, and active collaboration. Institutions like Harvard University, Massachusetts General Hospital, and Harvard Medical School contributed significantly to this output. In contrast, while China ranked second in terms of publications, its impact is relatively limited, suggesting a need for enhanced collaboration and research quality. Furthermore, the preference for the journal *Transplantation* can be attributed to its specialized focus on transplantation research, which aligns well with the complex themes explored in immune tolerance studies.

Hotspots and Frontiers

The keywords identified in our bibliometric analysis provide valuable insights into the evolving landscape of research on immune tolerance after kidney transplantation. Following closely behind "tolerance" was the keyword "induction", highlighting the significant research focus on methods and strategies to induce immune tolerance.[26] The frequent mention of "T-cells" underscores the importance of understanding their behavior and regulation in the context of kidney transplantation, as they are often the primary effectors of allograft rejection.[27]

The frequent occurrence of "rejection" indicates the persistent challenge of preventing immune-mediated allograft damage,[28] while "recipients" and "survival" emphasize the ultimate goals of transplantation to improve patient outcomes and graft longevity.[29] The inclusion of "dendritic cells" and "activation" highlights the intricate immune mechanisms involved in tolerance and rejection. Dendritic cells, as professional antigen-presenting cells, play a crucial role in shaping the immune response, while the activation status of immune cells is a critical determinant of allograft acceptance or rejection.[30] Similarly, "immunosuppression" is a cornerstone of current transplantation therapy, aimed at suppressing the recipient's immune system to prevent rejection.[31] However, the ongoing research into alternative strategies, such as tolerance induction, suggests a shift towards more targeted and less toxic therapies.[26]

On the other hand, the top 20 keywords with the strongest citation bursts from 1994 to 2024 provide a longitudinal perspective on evolving research hotspots in the field of kidney transplantation immune tolerance.

Between 1994 and 2016, burst analysis revealed a focus on fundamental immunological mechanisms, as reflected by high-impact keywords such as "T cells", "induction" and "rejection". The prominence of "T cells" and "dendritic cells" underscores the central role of immune cell regulation in tolerance induction, as evidenced by extensive studies in this period.[32] Research related to "induction" strategies—aimed at modulating immune pathways to promote tolerance—was particularly active, consistent with its high burst strength.[33] Similarly, the persistent attention to "rejection" reflects the ongoing effort to understand and mitigate graft loss.[34] During this phase, basic and translational studies delved deeply into key signaling pathways. For example, the PD-1 pathway was identified as a critical regulator of T-cell response and peripheral tolerance, with evidence showing its role in inhibiting alloreactive T cells and fostering regulatory T-cell development.[35,36] Subsequent work demonstrated that combining programmed cell death 1 (PD-1) overexpression with cytotoxic T lymphocyte-associated antigen-4 (CTLA-4) blockade could enhance graft survival in experimental models.[37] Beyond these well-characterized checkpoints, recent investigations have begun exploring novel targets such as lymphocyte activation gene 3 (LAG-3), T cell immunoglobulin mucin domain-containing protein 3 (TIM-3), and T cell immunoglobulin and ITIM domain (TIGIT), often in combination therapies, to amplify tolerance induction while limiting systemic immunosuppression.[38,39]

The burst analysis also captures a thematic shift in research emphasis. The appearance of "monoclonal antibody" and "bone marrow transplantation" signals a move toward more targeted therapeutic strategies. Monoclonal antibodies enable precise immunomodulation, becoming essential in rejection prophylaxis and autoimmune management,[40] whereas bone marrow transplantation represents a tolerance-induction strategy via donor-cell chimerism.[41] The sustained burst strength of these keywords over two decades highlights their foundational role in shaping the immunotherapeutic landscape in transplantation.

A notable transition occurred around 2019, when imaging-related terms such as "images", "features" and "magnetic resonance imaging" emerged as new burst keywords. This suggests a growing incorporation of non-invasive imaging techniques into transplant research, likely aimed at improving graft assessment, rejection diagnosis, and immune

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monitoring.[42] The rise of these terms marks a perceptible pivot from a predominantly immunology-driven agenda toward one increasingly engaged with translational imaging and quantitative phenotyping.

The recent surge in keywords such as "breast cancer" may initially seem unrelated to kidney transplantation. However, it is likely that this burst reflects the broader application of immune tolerance research to other organ transplant settings, including breast reconstruction surgery using allografts.[43] Furthermore, triple-negative breast cancer (TNBC) in particular can foster an immune-tolerant microenvironment that promotes disease progression. Targeting specific molecules, such as CD84, may therefore represent a promising therapeutic approach against TNBC.[44] This trend underscores the interdisciplinary nature of immune tolerance research and its potential to impact a wide range of medical specialties.

More significantly, the emergence of keywords in recent years signals a transformative shift in research focus, representing the cutting-edge technologies and therapeutic strategies that are shaping the future of kidney transplantation research. "Machine learning" and "deep learning" are particularly noteworthy, as they offer powerful tools for analyzing complex datasets and identifying patterns that may not be apparent through traditional methods. In the aspect of immune tolerance after kidney transplantation, the application of artificial intelligence (AI) mainly focuses on predicting transplantation rejection, optimizing personalized immunosuppressive therapy, and improving long-term graft survival rates.[45–47] For example, Raynaud et al developed a dynamic AI model to predict the graft survival rate in kidney transplant recipients. The results indicated that the immunological characteristics of the recipients, graft interstitial fibrosis and tubular atrophy, graft inflammation, and repeated measurements of estimated glomerular filtration rate (eGFR) and proteinuria were independent risk factors for graft survival. The final model demonstrated accurate calibration and high discriminative ability in the development cohort.[48] Basuli and Roy indicated that AI-driven algorithms can optimize immunosuppressive regimens and enhance patient care. These algorithms are capable of processing and analyzing complex clinical data, including patients' genomic information, drug metabolism profiles, and immune status, thereby formulating the best immunosuppressive strategy for each individual patient.[49] In addition, Thongprayoon et al suggested that the application of Electronic Health Records (EHRs) in conjunction with AI is anticipated to revolutionize research in the field of kidney transplantation. By analyzing extensive long-term follow-up data, AI algorithms can identify key factors affecting the long-term survival of grafts and provide clinicians with personalized long-term management strategies.[50] These technologies are poised to revolutionize the way we approach kidney transplantation, from predicting transplant outcomes to personalizing therapeutic interventions.

"Neoadjuvant chemotherapy" and "radiomics", on the other hand, represent novel therapeutic and diagnostic strategies, respectively. Neoadjuvant chemotherapy, typically used in the treatment of cancer, may have potential applications in kidney transplantation by reducing the risk of rejection or improving allograft survival.[51,52] Radiomics, which involves extracting quantitative features from medical images, offers a promising means of assessing allograft function and predicting outcomes non-invasively.[53]

However, these bursts also highlight key research bottlenecks. For instance, while imaging technologies offer promising tools for assessing allograft functions, their integration into routine clinical practice remains a challenge.[42] Similarly, the application of machine learning and deep learning in kidney transplantation is in its infancy, with many questions still unanswered regarding their efficacy, safety, and ethical implications.[45] As research continues to evolve, addressing these bottlenecks will be crucial for advancing the field and improving patient outcomes.

Above all, the citation bursts of keywords over the past few decades provide a valuable insight into the evolving trends and hotspots in research on immune tolerance after kidney transplantation. The shift from traditional immune mechanisms and therapeutic strategies to innovative technologies and interdisciplinary approaches reflects the dynamic nature of this field. The current focus on imaging, machine learning, radiomics, and deep learning indicates a promising direction towards personalized and precision medicine. Looking ahead, AI is poised to revolutionize immune tolerance research in kidney transplantation through several key advancements. Emerging tools like generative AI and federated learning could address data scarcity while protecting privacy. Integrating multi-omics data with AI platforms may reveal novel tolerance biomarkers, enabling early interventions. Real-time AI monitoring systems using wearables could dynamically adjust immunosuppression based on patient status. Explainable AI (XAI) will bridge algorithmic insights and clinical decisions, while standardized global registries improve model generalizability. Ethical frameworks must evolve to address data ownership and algorithmic bias, ensuring equitable advancements in graft survival and patient outcomes.[49,54]

Strengths and Limitations

This study boasts several notable strengths. Firstly, it presents a comprehensive overview of research on immune tolerance after kidney transplantation, spanning from 1976 to 2024, encompassing a total of 1686 studies and ultimately analyzing 1033 English articles. This extensive dataset allows for a deep dive into the evolution and trends of the field. Secondly, the study highlights key turning points and emerging trends, such as the shift in research focus towards imaging techniques and artificial intelligence in recent years, providing valuable insights for future research directions. However, the study also has its limitations. Firstly, the analysis is limited to the WoSCC database, potentially excluding relevant studies published in other databases. This could lead to an incomplete picture of the research landscape. Secondly, by focusing only on English articles, the study may have overlooked important contributions from non-English speaking countries, thereby introducing a language bias. Furthermore, while the study provides a detailed analysis of keywords and their citation bursts, it does not delve into the specific content or methodologies of the studies, which could offer deeper insights into the research trends and advancements.

Conclusions

This bibliometric analysis outlines the evolving research landscape of immune tolerance in kidney transplantation and provides informative insights for future studies. The USA has demonstrated a leading role in the field, as evidenced by its highest publication output and citation impact. Keyword evolution analysis indicates a noticeable shift in research emphasis, from early investigations into immunological mechanisms and therapies toward more recent focus on imaging-based profiling and emerging computational methods such as machine learning. These observed transitions offer tangible guidance for subsequent investigations. Future work should prioritize the integration of imaging data with immune profiles to establish non-invasive biomarkers for tolerance monitoring. Furthermore, the application of machine learning represents a promising direction for predictive model development and patient stratification. The sustained contribution of influential research groups also underscores the importance of international collaboration to harmonize data collection and validate findings across diverse cohorts.

Data Sharing Statement

All data generated or analyzed during this study are included in this published article.

Author Contributions

All authors made a significant contribution to the work reported, whether that is in the conception, study design, execution, acquisition of data, analysis and interpretation, or in all these areas; took part in drafting, revising or critically reviewing the article; gave final approval of the version to be published; have agreed on the journal to which the article has been submitted; and agree to be accountable for all aspects of the work.

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Disclosure

The authors declare that they have no competing interests in this work.

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