

Artificial Intelligence in Kidney Transplantation: A Comprehensive Scientometric Analysis

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Abstract

Purpose of Review The integration of artificial intelligence (AI) has profoundly influenced kidney transplantation, enhancing the ability to predict graft survival, diagnose rejection, and improve post-transplant care. This study aims to provide an overview of AI research in kidney transplantation, identifying major contributors, research patterns, and key areas of focus. The data collection and retrieval process involved a systematic search conducted on September 28, 2023, using the Web of Science database. The search resulted in the identification of 269 scholarly articles exclusively focused on AI in kidney transplantation. These articles formed the basis of our comprehensive bibliometric analysis.

Recent Findings Analysis reveals a notable increase in publications since 2017, peaking at 87 in 2022. Machine learning (ML) emerged as the predominant AI subtype, with leading institutions including the Medical University of Vienna, Hannover Medical School, and the University of Alberta. The United States led in publications and citations. Primary research areas include graft outcome, survival, immunosuppressive treatments, and rejection.

Summary The growing integration of AI, particularly ML, underscores the importance of interdisciplinary collaboration and international cooperation in shaping the field. Further research is needed to address current challenges and fully exploit AI's potential in kidney transplantation.

Keywords Artificial Intelligence \cdot Kidney Transplantation \cdot Machine Learning \cdot Bibliometric Analysis \cdot Predictive Modeling

Introduction

Artificial intelligence (AI) has emerged as a transformative force in healthcare, revolutionizing medical practices by integrating intelligent systems capable of mimicking human cognitive functions [1]. Beyond its influence in many different fields of medicine, AI has left a significant impact on the kidney transplant field [2]. It has greatly improved

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our capacity to precisely match donors and recipients [3, 4], predict graft survival with unprecedented precision [5], diagnose rejection, optimize the dose of immunosuppression, and improve post-transplant care [6], enabling a more comprehensive and predictive approach to patient care throughout the transplant process [7, 8].

Further emphasizing the transformative role of AI, the kidney transplant field has become a prominent example of how AI can be effectively incorporated into the practice of solid organ transplantation medicine in general. The rapid growth of data in the field, combined with the powerful ability of AI algorithms to aggregate and interpret large datasets, has accelerated the implementation of AI in systems for supporting clinical decisions in the field [8].

Understanding the complex data framework encompassing kidney transplantation, AI and its specialized subset specifically, Machine Learning (ML)—have emerged as influential tools, assisting in analyzing and refining processes and management through these enormous amounts

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of data [6, 9]. These technologies have significantly contributed to a transformative era in understanding and managing various aspects of transplant processes. ML has emerged as a dominant methodology in the field of predictive modeling, outperforming traditional statistical approaches [9]. Its ability to efficiently analyze large and complex medical datasets has made it crucial in the development of superior prediction models. This capability allows for a more comprehensive and predictive patient profiling approach that is specifically tailored to the intricate requirements of kidney transplantation [10]. This technological advancement not only improves our ability to analyze data but also represents a future in which complex medical information transforms into practical insights that prioritize the patient, leading to significant changes in strategies and decision-making for kidney transplant care and outcomes [11].

In order to gain a comprehensive understanding of the evolving landscape of AI research in the domain of kidney transplantation, a meticulous bibliometric analysis is imperative. The present study offers an in depth analysis for gaining insights into the dynamic research landscape of AI in the field of kidney transplantation. This study analyzes research patterns, identifies notable contributors, and determines key areas of focus within this discipline. Through the identification of trends, it facilitates researchers, clinicians, and policymakers in shaping subsequent research endeavors and aligning their efforts with the pressing requirements and obstacles encountered in the field of kidney transplantation.

Methods

Data Collection and Retrieval

On September 28, 2023, a systematic search was conducted using the Web of Science database to identify scholarly articles related to AI in kidney transplantation. The search strategy employed a combination of key phrases: "artificial intelligence" or "machine learning" or "deep learning" or "neural networks" or "natural language processing" (All Fields) and "kidney transplant*" or "renal transplant"(All Fields).

Upon the initial search, a total of 674 documents were retrieved. To ensure the precision and accuracy of the collected data, an exhaustive screening process was applied, leading to the exclusion of documents that addressed topics other than kidney transplantation. This rigorous exclusion methodology resulted in the identification of 269 scholarly articles that exclusively focused on the application of AI in kidney transplantation. These meticulously curated articles formed the basis of our comprehensive bibliometric analysis.

It is important to note that this research was exempt from gaining approval from the international review board because it was focused on bibliometric analysis and didn't involve the extraction of patients' data.

Data Analysis

This bibliometric analysis encompassed a range of pivotal bibliometric variables, comprising the articles themselves along with their corresponding citation counts, number of publications per year, authors, countries, institutions, journals, and the prevalence of co-occurring keywords. The bibliographic information of the selected articles was analyzed using the "bibliometrix" library in R statistical language (version 4.2.2) and Microsoft Excel Office 365. To create visual representations of the data, VOSviewer (version 1.6.19) was used.

Results

Trends and Research Focus

Table 1 displays the main characteristics of the resulting documents. The publications ranged between 1999 and September 28, 2023. The data clearly shows a consistent upward trend in the quantity of publications pertaining to AI in the field of kidney transplantation, especially in recent years where there has been a significant surge. The annual growth rate was found to be 16.73%, an average of 3.2 years. Over the past seven years, the overall number of publications has risen significantly, culminating in its peak in 2022 with a total of 87 publications. In 2012, the

Table 1 Main information about the documents
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Main information	
Timespan	1999:2023
Number of Documents	269
Average citations per doc	7.81
Total References	5,721
Authors of single-authored docs	6
Authors Collaboration	
Single-authored docs	6
Co-Authors per Doc	7.87
International co-authorships %	33.46%
Documents type	
Article	153
Review	15
Meeting abstract	58
Proceedings paper	32
Correction	3
Editorial material	6
Letter	2

average number of citations per article was the highest, accounting for 43.67 citations. The total number of citations was 2132, with a mean (SD) of 7.81 ± 17.7 citations per article. The annual number of publications through the past 13 years is represented in Fig. 1.

A comprehensive set of 888 keywords was employed across the 269 documents that examined the application of AI in the context of kidney transplantation. The keywords such as "kidney transplantation," "renal transplantation," and "kidney" were omitted, along with any other superfluous keywords. The most frequently observed keywords were "Machine Learning" (n = 58), "Outcomes" (n = 24), "Recipients" (n = 24), "Survival" (n = 23), "Rejection" (n = 20), and "Artificial Intelligence"" (n = 19). The primary research emphasis was directed towards the evaluation of graft outcome and immunosuppressive treatments, including tacrolimus and cyclosporine. Figure 2 illustrates a network visualization map of the most frequently occurring keywords, presented in four clusters.

Overview of Authorship, Institutional Contributions, Country Trends, and Journal Impact

Among the 269 documents analyzed, six were found to have a single author, while the average number of authors per document was 7.87. Out of the 1441 authors who have contributed to the field of AI in the context of kidney transplantation, David Briggs has garnered the highest number of citations (n = 174) across eight documents. Following closely behind were Dorry L. Segev (n = 135) across five documents and Alexandre Loupy (n = 110) across eight documents. Wisit Cheungpasitporn and Charat Thongprayoon ranked with the top number of publications (n = 13), each accounting for (n = 48) citations. Table 2 displays the top 20 authors who have received the highest number of citations.

The Medical University of Vienna in Austria was identified as the top-cited institution (n = 189), followed by Hannover Medical School in Germany (n = 181) and the University of Alberta in Canada (n = 169). Mayo Clinic in the United States ranked as the top publishing institution (n = 24), followed by the University of Mississippi in the United States (n = 12) and Phramongkutklao College of Medicine in Thailand (n = 12). Table 3 presents the top 20

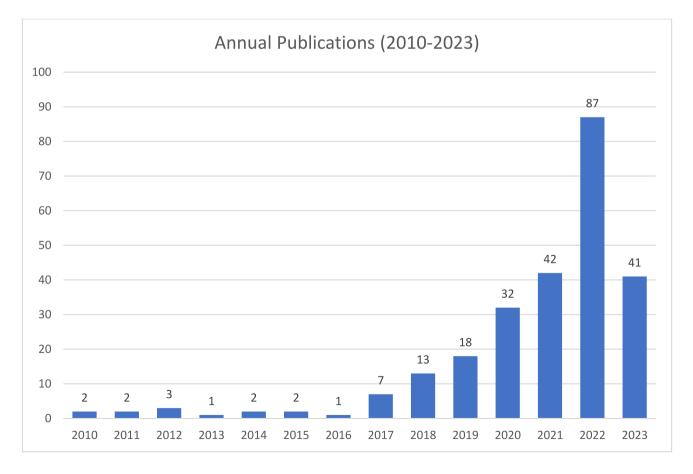


Fig. 1 Annual publications of AI in kidney transplantation (2010-2023)

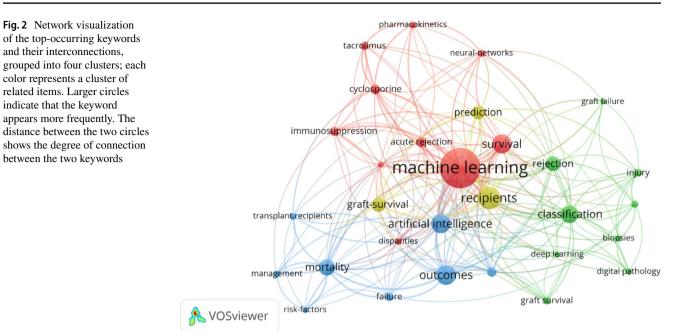


Table 2 Top 20 cited authors

Author	Citations	Documents	Total Link Strength
David Briggs	174	8	16
Dorry L. Segev	135	5	19
Alexandre Loupy	110	8	57
Carmen Lefaucheur	107	7	52
Wei Zhang	92	4	0
Gaurav Gupta	82	4	9
Marc Labriffe	63	5	11
Pierre Marquet	63	5	11
Jean-Baptiste Woillard	63	4	10
Ayman El-Baz	61	8	38
Mohamed Shehata	61	8	38
Mohamed Abou El-Ghar	60	7	33
Fahmi Khalifa	51	5	24
Amy C. Dwyer	49	5	26
Wisit Cheungpasitporn	48	13	124
Charat Thongprayoon	48	13	124
Napat Leeaphorn	48	12	117
John P. Dickerson	42	4	0
Mohammed Ghazal	37	5	25
Wisit Kaewput	36	11	109

cited institutions that have published in the field of AI in kidney transplantation.

The United States ranked as the top publishing country (n=119) and top-cited country (n=955). Germany follows as the second most commonly cited country (n=288), and

People's Republic of China follows as the second most publishing country (n=30). Table 4 presents the top 20 cited countries. Figure 3 a presents a network visualization illustrating the top publishing countries that have engaged in the highest levels of collaboration and connectivity. Figure 3 b presents the countries collaboration based on the corresponding author's countries, presenting the number of multiple country publications (MCP) and single country publications (SCP). We calculated the MCP ratio: the USA had an MCP ratio of 33.7%, China had 17.2%, France had 41.7%, and Germany had 50%. Ireland, the Netherlands, Switzerland had a 100% MCP ratio. This ratio represents the proportion of articles in the dataset that involved collaborations between researchers from different countries. A higher MCP_Ratio indicates a higher prevalence of international collaboration in the research publications.

In terms of journals, among the 143 sources examined, Scientific Reports led with 163 citations, followed by PLOS One (n = 118) and the American Journal of Transplantation (n = 116). The American Journal of Transplantation was not only highly cited but also the foremost publishing journal in the field. Transplantation and Transplant International followed in citations with 15 and 13, respectively. Figure 4 presents the network visualization of the top-contributed journals in the field of AI and kidney transplantation. Table 5 presents the top 20 cited journals.

Top cited documents

Table 6 represents the top ten cited documents in the field of AI and kidney transplantation. "Decision tree and random forest models for outcome prediction in antibody **Table 3** The top 20 citedinstitutions

Institution	Country	Citations	Documents	Total Link Strength
Medical University of Vienna	Austria	189	7	38
Hannover Medical School	Germany	181	7	19
University of Alberta	Canada	169	5	14
Johns Hopkins University	United States	155	6	29
Hôpital Necker-Enfants Malades	France	112	8	48
St. Louis Hospital	France	107	5	38
Virginia Commonwealth University	United States	82	4	15
Mayo Clinic	United States	71	24	100
University of Limoges	France	63	5	9
University of Louisville	United States	63	9	20
University of Pittsburgh	United States	51	5	8
University of Mississippi	United States	48	12	55
University of Valencia	Spain	46	4	0
Centre Hospitalier Universitaire de Limoges	France	42	4	9
Abu Dhabi University	United Arab Emirates	39	6	15
Northwestern University	United States	39	6	21
Universidade Federal de São Paulo	Brazil	37	7	36
Phramongkutklao College of Medicine	Thailand	36	12	60
Mansoura University	Egypt	35	7	13
University of Mansoura	Egypt	34	4	10

Table 4 Top 20 cited countries

Country	Citations	Documents	Total Link Strength
USA	955	119	93
Germany	288	26	39
England	217	17	15
Canada	212	13	16
France	198	20	36
Austria	189	7	24
Peoples R China	138	30	8
Italy	121	16	12
Egypt	102	11	15
Belgium	95	15	29
Australia	91	11	9
Spain	90	16	24
South Korea	60	7	1
United Arab Emirates	60	7	13
Thailand	57	15	15
Brazil	56	12	17
Netherlands	50	12	22
Poland	43	5	8
India	28	4	1
Saudi Arabia	28	4	2

incompatible kidney transplantation" published by Shaikhina, Torgyn et al. in the Biomedical Signal Processing and Control journal, was the most cited article (n = 172) [12], followed by "Assessing rejection-related disease in kidney transplant biopsies based on archetypal analysis of molecular phenotypes" published by Reeve, Jeff et al. in JCI Insight journal (n=91)[13] and "Application of Machine-Learning Models to Predict Tacrolimus Stable Dose in Renal Transplant Recipients" published by Tang, Jie et al. in the Scientific Reports journal (n=89) [14].

Discussion

As the number of publications addressing the application of AI in kidney transplantation continues to grow, it becomes increasingly necessary to dig through the existing robust academic output. In doing so, we hope to provide a critical overview of research contributions and highlight the need for more systematic evaluation and scrutiny of the rapidly expanding body of scholarly knowledge in the field. Bibliometric studies, which employ statistical methods to examine authorship trends, citation patterns, and other academic indicators [14], are more than just assessment instruments; they are essential lenses that enable the scope, significance, and development of scientific publications within particular

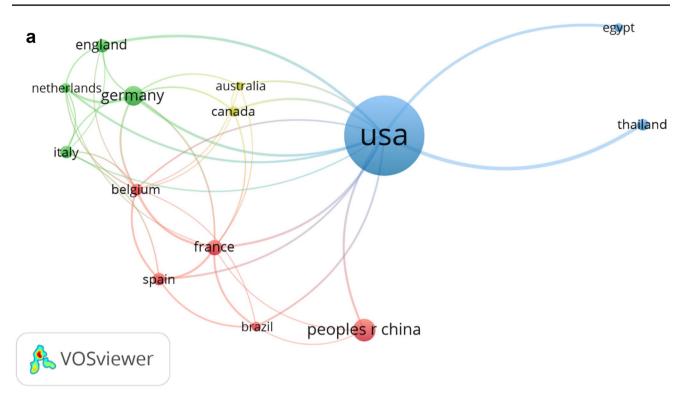
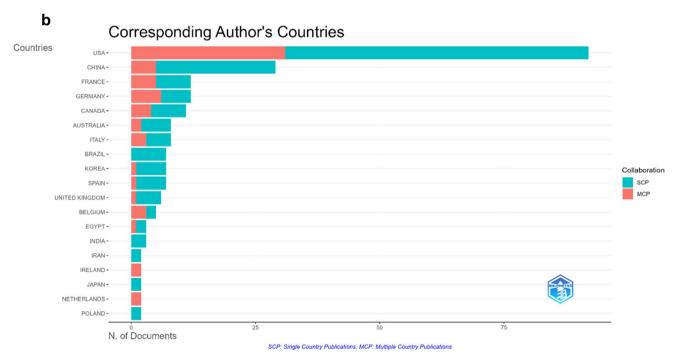


Fig. 3 a Visualization of the top-published countries and their interconnection, grouped into four clusters. The countries included in each cluster are displayed in the same color. Larger circles indicate that the country had a greater number of publications. The distance between the two circles shows the degree of connection between the two countries. (b) Collaboration between countries according to the corresponding author's countries



*MCP multiple Country Publications. SCP Single Country Publication

Fig. 3 (continued)

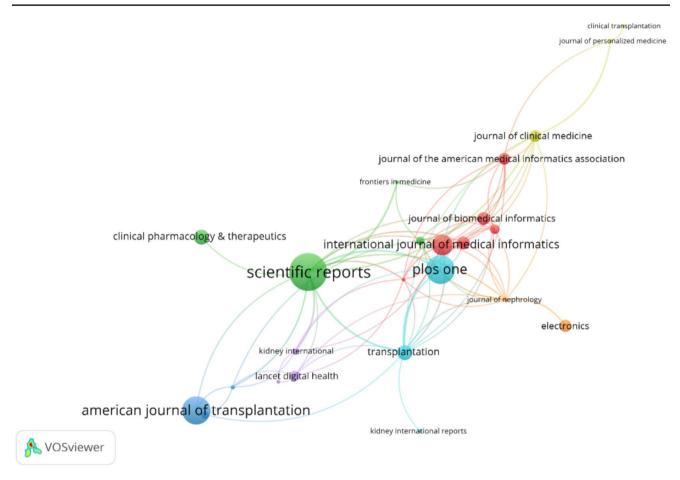


Fig. 4 Network visualization of the top-contributed journals according to citations. The same color displays journals included in the same cluster. The larger circles indicate that the journals had more

citations. The distance between the two circles shows the degree of connection between the two journals

academic domains to be closely examined and reviewed [14, 15].

Our analysis revealed that since 2017, the number of academic papers discussing the application of AI for kidney transplantation has dramatically increased. There was a noticeable increase, with twice as many publications in 2019 as in 2017. Moreover, a significant upsurge was noticed in 2022, as indicated by 88 publications that highlighted the noteworthy advancements made in this field of research during this time. This trajectory not only demonstrates the growing interest in AI applications in kidney transplantation, but also shows how quickly these technologies are being integrated and acknowledged in order to address the intricate, multiple challenges that are inherent to the field.

The importance of international collaboration in the field of AI research for kidney transplantation cannot be overstated. The findings of our study, as demonstrated in Table 1, reveal that a significant proportion of publications, specifically 33.4%, exhibit the presence of international co-authorship. International collaborations play a crucial role in facilitating a wide range of perspectives, expertise, and the ability to reach diverse patient populations [16, 17]. These factors are essential in the development of strong and universally applicable AI models. Furthermore, kidney transplantation, a life-saving medical intervention, has regional variations due to genetic, racial, environmental, and healthcare system differences [12, 13, 18, 19]. Through international collaboration, researchers can ensure that AI models exhibit inclusivity, cultural sensitivity, and effectiveness when applied to a wider range of patients. More importantly, our research serves as a crucial point of reference for prominent institutions and authors in the discipline, offering a standard for identifying the field of collaboration and fostering additional international efforts. We believe that international collaboration can play a crucial role in enhancing the quality and breadth of research, while also expediting the progress and worldwide applicability of AI innovations within the field of kidney transplantation.

Figure 2 clearly highlights the significance of particular keywords in the current trajectory of AI applications in the kidney transplant field. The keywords that were most frequently identified in the analysis are "prediction,"
 Table 5
 Top 20 cited journals

Journal	Citations	Documents
Scientific Reports	163	8
PLOS One	118	6
American Journal of Transplantation	116	32
International Journal of Medical Informatics	80	2
Clinical Pharmacology & Therapeutics	54	2
Transplantation	54	15
Frontiers in Immunology	50	7
BMC Medical Informatics and Decision Making	45	2
Journal of Biomedical Informatics	45	2
Electronics	43	2
Journal of Clinical Medicine	42	5
IEEE Transactions on Biomedical Engineering	41	2
Journal of the American Medical Informatics Association	41	2
Lancet Digital Health	36	2
Transplant International	33	13
Transplantation Proceedings	28	5
Journal of the American Society of Nephrology	24	2
Kidney International	21	4
Current Opinion in Organ Transplantation	14	3
Journal of Nephrology	13	2

"outcome," "survival," and "rejection." These terms demonstrate the crucial role of artificial intelligence in predicting the outcome of transplantation, assessing the patient's survival, and identifying patterns indicative of organ rejection. Moreover, the frequent mention of the keywords "immunosuppression," "cyclosporin," and "tacrolimus" highlights the clear focus on immunosuppression treatment in AI applications. This demonstrates the use of AI applications to refine post-transplant immunosuppressive protocols, with the goal of improving patient outcomes and minimizing complications [20]. This synthesis of AI-driven insights and clinical expertise predicts an innovative era in which technological advancement comes together with medical precision, significantly enhancing the prognosis for kidney transplant recipients and supporting their post-transplant journey.

Furthermore, our analysis; as shown in Fig. 2, uncovered some interesting patterns in the application of AI, with ML, a subset of AI, predominating in the majority of the articles on the subject. "Machine Learning" keyword emerged as a prominent and notable term, surpassing numerous other artificial intelligence techniques in terms of significance and frequency of mention. This highlights the critical significance and widespread utilization of ML in the domain of kidney transplant research, positioning it as a cornerstone in comparison to alternative artificial intelligence applications in this specific field [2, 11, 21]. Going into more detail, our research identified a number of ML models that are specifically employed in kidney transplant AI studies. For example, the utilization of Decision Trees and Random Forests has played a pivotal role in the prediction of recipient survival and outcomes in antibody-incompatible kidney transplantation [22–24]. In the field of kidney graft survival prediction, Bayesian Models and Artificial Neural Networks (ANNs) have garnered significant praise for their exceptional performance [25-27]. In addition to being highly effective at accurately identifying recipients with delayed graft function (DGF), support vector machines (SVM) also improve the prediction accuracy of graft survival [6, 28]. Other ML Models have been employed for predicting stable immunosuppressive doses, a critical aspect of post-transplantation care [29, 30]. The diverse range of models and their corresponding applications highlight the extensive interdisciplinary nature of AI in the field of kidney transplantation [9]. Furthermore, the utilization of advanced methodologies, such as Deep Learning, has played a crucial role in various domains, including the evaluation of histopathologic images for kidney transplant biopsies [31], the categorization of kidney transplant pathology [32], and the early identification of acute renal transplant rejection through a computer-aided diagnostic system that employs diffusion-weighted MRI [33].

Our geographic analysis revealed that, as indicated by the greatest number of publications and citations, the United States is a leader in AI research pertaining to kidney transplantation. Remarkably, the leading journals that published on the topic were transplantation journals, including Transplant International, Transplantation, and the American Journal of Transplantation. This highlights the recognition and

Table 6 Top ten cited articles				
Authors	Article Title	Publication Year	Source Title	Total Citations
Shaikhina, Torgyn; Lowe, Dave; Daga, Sunil; Briggs, David; Higgins, Robert; Khovanova, Natasha	Decision tree and random forest models for outcome prediction in antibody incompatible kidney trans- plantation	2019	Biomedical Signal Processing and Control	172
Reeve, Jeff; Boehmig, Georg A.; Eskandary, Farsad; Einecke, Gunilla; Lefaucheur, Carmen; Loupy, Alexandre; Halloran, Philip F	Assessing rejection-related disease in kidney transplant biopsies based on archetypal analysis of molecular phenotypes	2017	JCI Insight	16
Tang, Jie; Liu, Rong; Zhang, Yue-Li; Liu, Mou-Ze; Hu, Yong-Fang; Shao, Ming-Jie; Zhu, Li-Jun; Xin, Hua-Wen; Feng, Gui-Wen; Shang, Wen-Jun; Meng, Xiang-Guang; Zhang, Li-Rong; Ming, Ying-Zi; Zhang, Wei	Application of Machine-Learning Models to Predict 2017 Tacrolimus Stable Dose in Renal Transplant Recipients	2017	Scientific Reports	88
Marsh, Jon N.; Matlock, Matthew K.; Kudose, Satoru; Liu, Ta-Chiang; Stappenbeck, Thaddeus S.; Gaut, Joseph P.; Swamidass, S. Joshua	Deep Learning Global Glomerulosclerosis in Trans- plant Kidney Frozen Sections	2018	IEEE Transactions on Medical Imaging	83
Topuz, Kazim; Zengul, Ferhat D.; Dag, Ali; Alme- hmi, Ammar, Yildirim, Mehmet Bayram	Predicting graft survival among kidney transplant recipients: A Bayesian decision support model	2018	Decision Support Systems	67
Grams, Morgan E.; Kucirka, Lauren M.; Hanrahan, Colleen F.; Montgomery, Robert A.; Massie, Allan B.; Segev, Dorry L	Candidacy for Kidney Transplantation of Older Adults	2012	Journal of the American Geriatrics Society	63
Reeve, Jeff; Boehmig, Georg A.; Eskandary, Farsad; Einecke, Gunilla; Gupta, Gaurav; Madill-Thomsen, Katelynn; Mackova, Martina; Halloran, Philip F	Generating automated kidney transplant biopsy reports combining molecular measurements with ensembles of machine learning classifiers	2019	American Journal of Transplantation	58
Yoo, Kyung Don; Noh, Junhyug; Lee, Hajeong; Kim, Dong Ki; Lim, Chun Soo; Kim, Young Hoon; Lee, Jung Pyo; Kim, Gunhee; Kim, Yon Su	A Machine Learning Approach Using Survival Sta- tistics to Predict Graft Survival in Kidney Trans- plant Recipients: A Multicenter Cohort Study	2017	Scientific Reports	57
Decruyenaere, Alexander; Decruyenaere, Philippe; Peeters, Patrick; Vermassen, Frank; Dhaene, Tom; Couckuyt, Ivo	Prediction of delayed graft function after kidney transplantation: comparison between logistic regression and machine learning methods	2015	BMC Medical Informatics and Decision Making 46	46
Lin, Ray S.; Horn, Susan D.; Hurdle, John F.; Goldfarb-Rumyantzev, Alexander S	Single and multiple time-point prediction models in kidney transplant outcomes	2008	Journal of Biomedical Informatics	45

awareness of the significance of this subject within the discipline. Moreover, these transplant journals have emerged as prominent platforms for disseminating pioneering advances in the convergence of AI and kidney transplantation. Nevertheless, despite the greater number of publications found in the transplant journals, the citations for these publications are surpassed by those originating from sources outside the transplantation journals, as illustrated in Table 5. This disparity demands consideration and additional conversation.

Despite the considerable progress made in the integration of AI into the field of kidney transplantation, there remain noteworthy obstacles that restrict its widespread implementation [2, 8]. These challenges include issues related to data management, ethical considerations, legal issues, and technical complexities [6]. The data pertaining to kidney transplantation frequently exhibits a wide range of variations, lacks a standardized structure, and incorporates subjective elements. Healthcare professionals express skepticism towards ML algorithms due to their limited transparency, which hinders their understanding of how these algorithms operate [6]. In addition, the availability of real-time applications for matching donor grafts with recipients is limited. These applications have the potential to optimize the advantages of transplantation by considering factors such as age, donor type, and the medical history of both the donor and potential recipient. Furthermore, the field currently exhibits a deficiency in long-term outcome predictions, which necessitates future studies to address this gap.

Our research has a number of limitations. Web of Science is the primary input data source for the bibliometric analysis software described in this article. For technical issues related to the limitation of the VOSviewer application, we did not employ several search engines (e.g., Scopus, Ovid, and Google Scholar). Only English-language papers were retrieved, which may have affected the results. However, most publications are published in English and cited through Web of Science, so these limitations are negligible.

Conclusion

The global utilization of AI is experiencing rapid growth in various domains. Clinicians working within the domain of kidney transplantation will inevitably encounter AI in their routine professional activities. Nevertheless, it is crucial for this community to possess a comprehensive understanding of this technology. AI possesses the capacity to fulfill what is missing within the field, enabling precise predictions and proficient data analysis that surpass the limitations of traditional statistical methods. This is especially relevant in the current era of abundant data, as AI can effectively unlock complicated connections among huge databases containing numerous variables. Our comprehensive bibliometric analysis not only provides a detailed overview of the evolving landscape of AI research in kidney transplantation but also underscores the critical role of interdisciplinary collaboration. By incorporating various AI and machine learning models, researchers in the field continue to advance the management of kidney transplantation, paving the way for innovative solutions and improved patient outcomes. This study serves as a foundational resource, guiding future research efforts and encouraging further exploration of AI's vast potential in the realm of transplantation.

Author Contribution B.R. conceived the study, provided overall supervision, and wrote the manuscript. H.A. conducted the data analysis, contributed to the interpretation of results, and participated in writing the manuscript. R.H. contributed to the literature review, provided critical feedback, and helped revise the manuscript. B.T., E.A., C.M., and T.D. substantially contributed to the intellectual content, provided expert guidance, and critically revised the manuscript for important intellectual content. All authors reviewed and approved the final version of the manuscript for submission.

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Data Availability Data is available upon request.

Declarations

Conflict of Interest The authors declare no competing interests.

Human and Animal Rights and Inform Consent This article does not contain any studies with human or animal subjects performed by any of the authors.

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