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Artificial Intelligence in Kidney Transplantation: A Scoping Review

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Abstract: Artificial Intelligence (AI) technologies are increasingly being used to enhance kidney transplant outcomes. In this review, we explore the use of AI in kidney transplantation (KT) in the existing literature. Four databases were searched to identify a total of 33 eligible studies. AI technologies were used to help in diagnostic, predictive and medication management purposes for kidney transplant patients. AI is an emerging tool in KT, however, there is a research gap exploring the limitations associated with implementing AI technologies in the field. Research is also needed to recognize clinical educational needs and other barriers to promote adoption and standardization of care for KT patients amongst clinicians.

Keywords: Artificial Intelligence, Machine Learning, Deep Learning, Kidney Transplant.

1. Introduction

About 9.1% of the world's population suffer from chronic kidney failure requiring dialysis or a kidney transplant [1]. Kidney transplantation (KT) is the preferred intervention as it allows patients a better quality of life while being cost effective compared to long-term dialysis [2]. The development and use of artificial intelligence (AI) in medicine, and clinical applications is evolving in several fields, including the field of kidney disease and KT [3-6]. AI appears to be a promising tool in healthcare and clinical decision support, providing personalized diagnostics, therapeutic solutions, and predictions of future events such as hospitalization and patient's survival [3].

A review of collective evidence exploring the use of AI in KT is limited. We came across two reviews; Burlacu et al. (2020), reviews AI in nephrology, including in KT [6]. The search for the review was conducted in August 2019, omitting evidence related to KT during the pandemic. The review also does not report the types of AI technologies and algorithms observed. Seyahi et al. (2021) also explores AI used in KT [7]. The authors use only one data source to conduct their study and solely address AI applications. Our scoping review cover these gaps while combining the latest evidence to help keep clinicians informed and recognize future research opportunities.

The aim of this scoping review is to explore: 1) How is AI being used in KT? and, 2) What are the characteristics of AI technologies utilized for kidney transplant purposes?

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2. Methods

The scoping review is in line with PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analyses) Extension for Scoping Reviews guideline [8]. We searched four databases between 1st till 5th March 2021. While manually checking citations on Google Scholar, only the first 40 citations were relevant to the subject of interest. Hence, the top 40 hits are included. The search engine is known to retrieve many hundreds of citations in order of relevance to the search terms. This method can be seen in another scoping review [9]. Table 1 displays details of the search strategy used.

Only primary studies conducted in English between the years 2018 till 2021 were included in this scoping review. Three reviewers independently screened the articles using Rayyan System Inc. In case of conflict, discussion was held among reviewers to come to a mutual consensus. The reviewers independently extracted data using a data extraction form. The findings are synthesized narratively, then classified and described in terms of their purpose and characteristics.

3. Results

Only 32 studies met the criteria and are included in this review. One additional study was added by backward citation of the reference list of the included studies. Most studies were published between 2020-2019 (n=28) and conducted in the United State of America (n =11). Table 2 displays the common AI branch and models observed in the studies.

The use of AI technologies for KT found in included studies can be categorized into three – diagnoses, prediction, and prescription.

3.1 AI to Diagnose Kidney Transplant Patients

A total of 18 studies investigated usefulness of AI models for diagnostic purposes in kidney transplant patients [10,11,20-27,12-19]. For example, Kanzelmeyer et al. (2019) investigated use of AI in early diagnoses of chronic active antibody mediated rejection (cABMR) in kidney transplant patient [23]. Another example, study by Shehata et al. (2019) used AI to distinguish between diagnoses of non-rejection and acute rejection in transplant patients [19]. Majority of the models were based on RF [20,21,24,25] and SVM (Support Vector Machine) [18,21,23] models. Most data sources used to train and test the AI models were based on clinical setting such as hospitals (n =12). Clinical data such as blood, and biopsies (n =13) were the most used data type.

3.2 AI as a Prediction Tool in Kidney Transplantation

A total of 12 studies used AI as a prediction tool [28,29,38,39,30-37]. Algorithms and datasets were used to predict survival of graft tissue, rejection, and delayed graft function. Studies also explored AI facilitated prediction for critical clinical decisions of weighing benefits of receiving an available kidney over waiting for a 'better offer'. Information of patients and donors are used to predict suitable match and weigh risks of undergoing the procedure or receiving a certain quality of kidney.

Table 1. Search Strategy

Database/ # Citations	Search Strategy
Embase 349 Citations	('artificial intelligence'/exp OR 'machine learning'/exp OR 'deep learning'/exp OR 'neural network*' OR 'supervised learning'/exp OR 'unsupervised learning'/exp OR 'natural language' OR 'data mining'/exp) AND ('kidney transplant*':ti,ab,kw OR 'renal transplant*':ti,ab,kw OR 'kidney graft*':ti,ab,kw OR 'kidney allograft':ti,ab,kw)
CINAHL 25 Citations	('kidney transplant*' OR 'renal transplant*' OR 'kidney graft*' OR 'kidney allograft*') AND ('artificial intelligence' OR 'machine learning' OR 'deep learning' OR 'neural network*' OR 'supervised learning' OR 'unsupervised learning' OR 'natural language' OR 'data mining') 2018 – 2021
Pubmed 91 Citations	("Artificial intelligence"[Title/Abstract] OR "Machine learning"[Title/Abstract] OR "Deep learning"[Title/Abstract] OR "Neural network*"[Title/Abstract] OR "Supervised learning"[Title/Abstract] OR "Unsupervised learning"[Title/Abstract] OR "Natural language processing"[Title/Abstract] OR "Data mining"[Title/Abstract]) AND ("Kidney Transplant*"[Title/Abstract] OR "Renal Transplant*"[Title/Abstract] OR "Kidney Graft*"[Title/Abstract] OR "Kidney Allograft*"[Title/Abstract])
Google Scholar 40 Citations	("Kidney Transplant*" OR "Renal Transplant*" OR "Kidney Graft* OR "Kidney Allograft*") AND ("Artificial intelligence" OR "Machine learning" OR "Deep learning" OR "Data Mining")

Table 2. Most common features of AI-based techniques used for kidney transplantation

Features	Studies (N=33)
AI branch [a]	
Deep Learning	8
Machine Learning	25
Natural Language Processing	1
AI models / algorithm [b]	
Random Forest	11
Logistic Regression	6
Gradient Boosting	4
Support Vector Machine	4
Artificial Neural Network	3

[a] Numbers do not add up as some studies were based on more than one AI branch
[b] Numbers display only the most common models/algorithm used.

3.3 AI used as a Prescription Tool in Kidney Transplantation

AI techniques were used to manage appropriate dosage of immunosuppressants and other medications [40-42]. The models used included fuzzy logic [42], RF [40], and ANN [41]. All studies used clinical setting as the form of data to test and train their models. Genetic data was used in 2 studies. AI was used to manage immunosuppressant dosage to improve efficiency in KT patients. One study used a different approach by using ANN to understand the relationship between genetic factors and tacrolimus dose [41].

5. Discussion

With the increasing adaption of electronic health record, there is an abundance of patient data providing AI technologies the platform to improve multiple aspects of KT care. Clinicians and their input are a big part of integrating any system to enhance the health experience of patients, however, none of our included studies studied the clinician's perspective of using AI or the challenges and the ethics that need to be considered. Moreover, clinicians may not fully understand the technical explanations of these algorithms or performance metrices. Training programs and other resources catered towards healthcare providers are necessary. AI could be the answer to the shortage of solid organs as it provides the answer to many of the complications and challenges attached to it. Therefore, proactiveness to include stakeholders is needed, while also exploring barriers and facilitators of integrating AI technologies in the clinical setting.

5. Conclusion

Kidney transplantation is a complex intervention requiring patients and clinicians to undergo multiple processes and critical decision making. AI is proving to be an important tool to support clinicians and patients to make the best decision for their needs. AI is being used for diagnoses, making predictions, and prescribing personalized care plans for KT patients. More research is required to promote AI adoption within the field.

References

[1] Carney EF. The impact of chronic kidney disease on global health. Nat Rev Nephrol 2020 165 [Internet]. 2020 Mar 6;16(5):251–251.
[2] Klarenbach S, Manns B. Economic evaluation of dialysis therapies. Semin Nephrol [Internet]. 2009 Sep [cited 2022 Jan 21];29(5):524–32. Available from: https://pubmed.ncbi.nlm.nih.gov/19751898/
[3] Chaudhuri S, Long A, Zhang H, Monaghan C, Larkin JW, Kotanko P, et al. AI enabled applications in kidney disease. Semin Dial. 2021;34(1):5–16.
[4] Hannun PGC, Andrade LGM. The future is coming: promising perspectives regarding the use of machine learning in renal transplantation. J Bras Nefrol. 2019;41(2):284–7.
[5] Becker JU, Mayerich D, Padmanabhan M, Barratt J, Ernst A, Boor P, et al. Artificial intelligence and machine learning in nephropathology. Kidney Int. 2020;98(1):65–75.
[6] Burlacu A, Iftene A, Jugrin D, Popa IV, Lupu PM, Vlad C, et al. Using AI Resources in Dialysis and KT Patients: A Literature Review. Vol. 2020, BioMed Research International. Hindawi Limited; 2020.
[7] Seyahi N, Ozcan SG. AI and KT. World J Transplant. 2021 Jul 1, 11(7).
[8] Tricco AC, Lillie E, Zarin W, O'Brien KK, Colquhoun H, Levac D, et al. PRISMA Extension for Scoping Reviews (PRISMA-ScR): Checklist and Explanation. Ann Intern Med. 2018 Sep;169(7):467–73.
[9] Abd-alrazaq AA, Alajlani M, Alalwan AA, Bewick BM, Gardner P, Househ M. An overview of the features of chatbots in mental health: A scoping review. Int J Med Inform. 2019 Dec 1;132:103978.
[10] Zubke M, Katzensteiner M, Bott OJ. Integration of Unstructured Data into a Clinical Data Warehouse for Kidney Transplant Screening - Challenges & Solutions. Stud Heal Technol Inf. 2020;270:272–6.
[11] Shehata M, Shalaby A, Switala AE, El-Baz M, Ghazal M, et al. A multimodal computer-aided diagnostic system for precise identification of renal allograft rejection: Preliminary results. Med Phys. 2020;47(6).
[12] Vittoraki AG, Fylaktou A, Tarassi K, Tsinaris Z, Petasis GC, Gerogiannis D, et al. Patterns of 1,748 Unique Human Alloimmune Responses Seen by Simple ML Algorithms. Front Immunol. 2020;11.
[13] Costa SD, Andrade LGM, Barroso FVC, Oliveira CMC, Daher EDF, Fernandes PFCBC, et al. The impact of deceased donor maintenance on delayed kidney allograft function: A ML analysis. PLoS One. 2020;15(2).
[14] Abdeltawab H, Shehata M, Shalaby A, Khalifa F, Mahmoud A, El-Ghar MA, et al. A Novel CNN-Based CAD System for Early Assessment of Transplanted Kidney Dysfunction. Sci Rep. 2019;9(1):5948.
[15] Zacharias HU, Altenbuchinger M, Schultheiss UT, Samol C, Kotsis F, Poguntke I, et al. A Novel Metabolic Signature To Predict the Requirement of Dialysis or Renal Transplantation in Patients with Chronic Kidney Disease. J Proteome Res. 2019 Apr;18(4):1796–805.
[16] Zou Y, Zhang W, Zhou HH, Liu R. Analysis of long noncoding RNAs for acute rejection and graft outcome in kidney transplant biopsies. Biomarkers Med. 2019;13(3):185–95.
[17] Aubert O, Higgins S, Bouatou Y, Yoo D, Raynaud M, Viglietti D, et al. Archetype Analysis Identifies Distinct Profiles in Renal Transplant Recipients with Transplant Glomerulopathy Associated with Allograft Survival. J Am Soc Nephrol. 2019 Apr;30(4):625–39.
[18] Wittenbrink N, Herrmann S, Blazquez-Navarro A, Bauer C, Lindberg E, Wolk K, et al. A novel approach reveals that HLA class 1 single antigen bead-signatures provide a means of high-accuracy pre-transplant

risk assessment of acute cellular rejection in renal transplantation. BMC Immunol. 2019 Apr;20(1):11.
[19] Shehata M, Khalifa F, Soliman A, Ghazal M, Taher F, El-Ghar MA, et al. Computer-Aided Diagnostic System for Early Detection of Acute Renal Transplant Rejection Using Diffusion-Weighted MRI. IEEE Trans Biomed Eng. 2019;66(2):539–52.
[20] Friedewald JJ, Kurian SM, Heilman RL, Whisenant TC, Poggio ED, Marsh C, et al. Development and clinical validity of a novel blood-based molecular biomarker for subclinical acute rejection following kidney transplant. Am J Transplant. 2019;19(1):98–109.
[21] Reeve J, Böhmig GA, Eskandary F, Einecke G, Gupta G, Madill-Thomsen K, et al. Generating automated kidney transplant biopsy reports combining molecular measurements with ensembles of machine learning classifiers. Am J Transplant. 2019;19(10):2719–31.
[22] Archdekin B, Sharma A, Gibson IW, Rush D, Wishart DS, Blydt-Hansen TD. Non-invasive differentiation of non-rejection kidney injury from acute rejection in pediatric RT recipients. Pediatr Transplant. 2019;23.
[23] Kanzelmeyer NK, Zürbig P, Mischak H, Metzger J, Fichtner A, Ruszai KH, et al. Urinary proteomics to diagnose chronic active antibody-mediated rejection in pediatric KT. Transpl Int. 2019;32(1).
[24] Bae S, Massie AB, Thomas AG, Bahn G, Luo X, Jackson KR, et al. Who can tolerate a marginal kidney? Predicting survival after deceased donor kidney transplant by donor-recipient combination. Am J Transplant Off J Am Soc Transplant Am Soc Transpl Surg. 2019 Feb;19(2):425–33.
[25] Shaikhina T, Lowe D, Daga S, Briggs D, Higgins R, Khovanova N. Decision tree and RF models for outcome prediction in antibody incompatible KT. Biomed Signal Process Control. 2019;52:456–62.
[26] Rashidi P, Bagherzadeh J, Niazkhani Z, Pirnejad H. A dynamic model for predicting graft function in kidney recipients' upcoming follow up visits: A clinical application of ANN. Int J Med Inform. 2018;119:125–33.
[27] Marsh JN, Matlock MK, Kudose S, Liu T-C, Stappenbeck TS, Gaut JP, et al. DL global glomerulosclerosis in transplant kidney frozen sections. IEEE Trans Med Imaging. 2018;37(12).
[28] Kim S-K, Yang JJ, Hwang S-H, Sung H, Shin S, Ko S-Y, et al. Prediction of HLA-DQ in Deceased Donors and its Clinical Significance in Kidney Transplantation. Ann Lab Med. 2021 Mar;41(2):190–7.
[29] Wang D, Jing Z, He K, Garmire LX. Cox-nnet v2.0: improved neural-network based survival prediction extended to large-scale EMR data. Bioinformatics. 2021 Jan;
[30] Placona AM, Martinez C, McGehee H, Carrico B, Klassen DK, Stewart D. Can donor narratives yield insights? A NL processing proof of concept to facilitate kidney allocation. Am J Transplant. 2020;20(4).
[31] Luo Y, Tang Z, Hu X, Lu S, Miao B, Hong S, et al. Machine learning for the prediction of severe pneumonia during posttransplant hospitalization in recipients of a deceased-donor kidney transplant. Ann Transl Med Vol 8, No 4 (February 2020) Ann Transl Med (Focus "Intrauterine Adhes. 2020;
[32] Bae S, Massie AB, Caffo BS, Jackson KR, Segev DL. Machine learning to predict transplant outcomes: helpful or hype? A national cohort study. 2020;
[33] Kawakita S, Beaumont JL, Jucaud V, Everly MJ. Personalized prediction of delayed graft function for recipients of deceased donor kidney transplants with machine learning. Sci Rep. 2020 Oct;10(1):18409.
[34] Peng B, Gong H, Tian H, Zhuang Q, Li J, Cheng K, et al. The study of the association between immune monitoring and pneumonia in kidney transplant recipients through machine learning models. J Transl Med. 2020;18(1):N.PAG-N.PAG.
[35] Massie AB, Boyarsky BJ, Werbel WA, Bae S, Chow EKH, Avery RK, et al. Identifying scenarios of benefit or harm from KT during the COVID-19 pandemic: A stochastic simulation and machine learning study. Am J Transplant Off J Am Soc Transplant Am Soc Transpl Surg. 2020 Nov;20(11).
[36] Elihimas UF, Couto JP, Pereira W, Barros de Oliveira Sá MP, Tenório de França EE, Aguiar FC, et al. LR Model in a ML Application to Predict Elderly Kidney Transplant Recipients with Worse Renal Function One Year after KT: Elderly KTbot. Grosset J-F, editor. J Aging Res. 2020;2020:7413616.
[37] Atallah D, Badawy M, El-Sayed A. A new proposed feature selection method to predict kidney transplantation outcome. Health Technol (Berl). 2019 Nov;9:847–856.
[38] Rashidi P, Bagherzadeh M J, Niazkhani Z, Pirnejad H. Predicting the function of transplanted kidney in long-term care processes:Application of a hybrid model. J Biomed Inform. 2019 Mar;91:103116.
[39] Mark E, Goldsman D, Gurbaxani B, Keskinocak P, Sokol J. Using machine learning and an ensemble of methods to predict kidney transplant survival. PLoS One. 2019 Jan;14(1):e0209068.
[40] Cai N, Zhang X, Zheng C, Zhu L, Zhu M, Cheng Z, et al. A novel random forest integrative approach based on endogenous CYP3A4 phenotype for predicting tacrolimus concentrations and dosages in Chinese renal transplant patients. J Clin Pharm Ther. 2020;45(2):318–23.
[41] Thishya K, Vattam KK, Naushad SM, Raju SB, Kutala VK. Artificial neural network model for predicting the bioavailability of tacrolimus in patients with renal transplantation. PLoS One. 2018;13(4).
[42] Improta G, Mazzella V, Vecchione D, Santini S, Triassi M. Fuzzy logic–based clinical decision support system for the evaluation of renal function in post-transplant Patients. J Eval Clin Pr. 2020;26(4):1224.