

REVIEW ARTICLE

Artificial Intelligence and Nephrology

Muzafar Maqsood Wani¹, Jawad Iqbal Rather², Imtiaz Ahmad Wani³, M Ashraf Bhat⁴, Manzoor Parrray⁵, Rayees Yousuf⁶

Department of Nephrology, SKIMS

ABSTRACT

Artificial intelligence (AI) is an established branch of computer sciences that utilizes computer algorithms to solve problems that otherwise is done by humans. It is there in our daily routines be it in the form of search engines like Google or home assistants Alexa and, nowadays, OpenAI with its chatbot. AI utility in the field of Nephrology is immense, particularly in the areas of diagnosis, treatment, and prediction of prognosis in various kidney diseases. Instead of the human brain machine learning algorithms can help to identify early signs of kidney disease by recognizing patterns in patient demographic data, lab results, imaging, and medical history, and hence allow timely diagnosis and prompt initiation of treatment plans that ultimately improve patient outcome. AI holds the promise of advancing personalized medicine to new levels. It is mandatory to train nephrologists in the fundamentals of AI because time has come to shift from the traditional practice of decision-making in kidney diseases to AI-based tools to quickly analyse patients' information and come to a quick decision.

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INTRODUCTION

Artificial Intelligence (AI) is a field of computer science that focuses on creating systems and machines capable of performing tasks that typically require human intelligence. AI is aimed at mimicking human intelligence by using science and engineering to its best. It may appear complex, but it is not it is all around us. AI has found its way into every facet of our daily existence be it Google, Amazon, Tesla, Alexa, Siri, Roomba and nowadays Chatbot, ChatGPT or the DALL-E. One can generate text of any sort or create realistic images or art using AI gadgetry.

AI is also making huge strides in the field of medicine¹. The US Food and Drug Administration as well as the European regulatory authorities have approved for clinicians to incorporate AI into various medical domains. For instance, AI can now reliably identify diabetic retinopathy without requiring an ophthalmologist to verify the algorithm's diagnosis².

The fundamental tenet of AI revolves around machine learning (ML), a concept that entails the examination of

algorithms and statistical models utilized by computer systems to acquire knowledge from sample data and previous encounters, all without the need for explicit programming to execute a particular task. Generally, ML algorithms include support vector machines, random forests, gradient-boosting trees, and artificial neural networks (ANN)².

There are various ML techniques namely

Decision Tree: A decision tree serves as a tool for predictive modelling, featuring a hierarchical data structure employed in both classification and regression analysis. The process entails breaking down a dataset into subsets through recursive partitioning based on key features. A decision tree is like a flowchart that helps you make decisions based on a series of conditions or criteria. It starts with a decision or a problem and then branches out into possible outcomes or

Correspondence:

Dr Manzoor Parrray,
Assistant Professor,
Department of Nephrology, SKIMS
Email: maparry@gmail.com

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solutions based on the input or conditions at each node (Figure 1). The assignment of a sample subject to a particular segment is accomplished by identifying the features that effectively distinguish it and constructing a decision rule at each level of the division process to select the most appropriate division³.

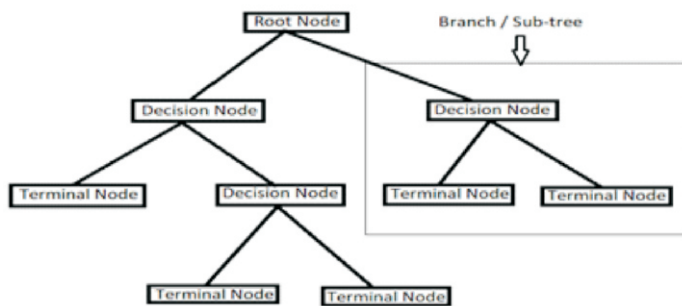


Fig. 1. Decision Tree³.

Artificial Neural Networks (ANNs). ANNs are a computational model inspired by the way biological neural networks in the human brain function. They consist of interconnected nodes, or artificial neurons, organized into layers. A node, often referred to as a neuron, serves as the fundamental computational unit within this framework. It accepts input data from external sources or other nodes. Layers are organizational units that group nodes. Nodes are interconnected through synapses, each carrying an associated weight known as a synaptic weight (Figure 2). The network's behaviour is ultimately shaped by the arrangement of these synaptic connections⁴.

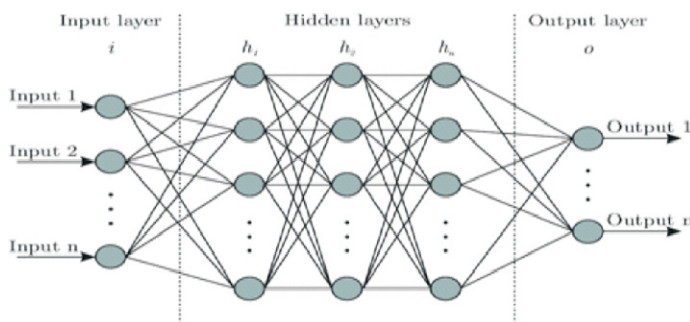


Fig. 2. Artificial Neural Networks (ANN)⁴.

Support Vector Machine (SVM). SVM is a supervised machine learning algorithm that can be used for classification or regression tasks. Its primary objective is to find a hyperplane that best separates data points of different classes in a high-dimensional space. In simpler terms, SVM tries to find the optimal decision boundary between

classes.⁵

UTILITY OF AI FOR RENAL DISEASES

AI can be utilized for diagnosis and outcome prediction and aid in the treatment of all kidney diseases. AI has been incorporated into various diagnostic tools that help to diagnose a particular disease. It aids, assists, and helps in analysing data as well as interpreting complex imaging and histological findings which finally will lead to a better outcome¹.

Early diagnosis of CKD in certain situations will be possible with AI. As an example, linking sphingomyelin ceramide and plasmalogen dysmetabolism to FSGS may predict an early diagnosis of CKD. Likewise, algorithms based on AI have been developed to estimate the total renal volume in ADPKD patients from the MRI scans and thus aid in seeing the response to interventions like long-term tolvaptan use. AI can also aid in the diagnosis of glomerular disease, especially by analysing the histopathological aspects of that glomerular disease. Diagnosis of hereditary disease can be improved using deep phenotyping of the clinical exome.

Many prediction scores/scales are in use for various kidney diseases as predictors of outcome, like the risk of developing CKD in IgA nephropathy. The traditional score utilizes various statistical methods on the available clinical risk factors and imaging/histological tests. With the integration of AI, this can be largely boosted even with the availability of limited data. Some examples like IgAN toolbox and IBox for IgA nephropathy prognosis, the post-op MAKE score for AKI in post-operative patients and the STARZ score in paediatric AKI¹.

On the treatment front individual patients (based on genetic, lifestyle and environmental factors) will need individual treatment in many situations which is called the tailored approach. AI can further help in tailoring the treatment which has been especially utilized in oncology to develop target therapy based on the molecular disease process which may improve the outcome. The day is not that far when ML will help in managing the treatment of most common kidney disorders^{1,2}.

AI IN ACUTE KIDNEY INJURY (AKI)

Contemporary acute kidney injury (AKI) research primarily centres on three key areas: risk prediction, early detection, and the implementation of automated electronic alerts, often referred to as E-alerts. One of the biggest

dilemmas in nephrology is to identify AKI at the earliest in patients admitted to hospitals. The commonest parameter of serum creatinine to detect AKI has its fallacies- it starts to rise once a reasonable reduction in glomerular filtration has already happened. To this date, no reasonable biomarker is available that foresees a patient admitted to the hospital to develop AKI. The reason for early and precise identification of AKI is of paramount importance for ascertaining the overall morbidity and mortality of a patient. AI can be helpful in this most important and reversible kidney disease.

In the study by Churpek et al, a total of 495,971 adult hospital admissions were examined across three medical institutions: the University of Chicago (UC) from 2008 to 2016 (comprising 48,463 cases), Loyola University Medical Center (LUMC) from 2007 to 2017 (encompassing 200,613 cases), and NorthShore University Health System (NUS) from 2006 to 2016 (including 246,895 cases). The study utilized a simplified version of a previously developed gradient-boosted machine AKI prediction algorithm. This algorithm was internally validated using patients from UC and externally validated using patients from NUS and LUMC. The primary outcome of interest in

this study was the prediction of Kidney Disease Improving Global Outcomes (KDIGO) serum creatinine-defined stage 2 AKI occurring within a 48-hour interval after admission. The AUCs for predicting at least stage 2 AKI in the next 48 hours were 0.86 (95%CI, 0.86-0.86) in the UC cohort, 0.85 (95%CI, 0.84-0.85) in the LUMC cohort, and 0.86 (95%CI, 0.86-0.86) in the NUS cohort. The AUCs for receipt of kidney replacement therapy within 48 hours were 0.96 (95%CI, 0.96-0.96) in the UC cohort, 0.95 (95%CI, 0.94-0.95) in the LUMC cohort, and 0.95 (95%CI, 0.94-0.95) in the NUS cohort⁶.

The active exploration of AI for optimizing Continuous Kidney Replacement Therapy (CKRT) is driven by the rising demand for critical care, the wealth of patient data available from electronic health records and CKRT machines, and the need to standardize CKRT practices, which currently exhibit considerable heterogeneity. AI offers the potential to streamline CKRT processes, enhance clinical decision-making, and ultimately improve patient outcomes in this critical care setting. Various potential areas of development are shown in Figure 3.

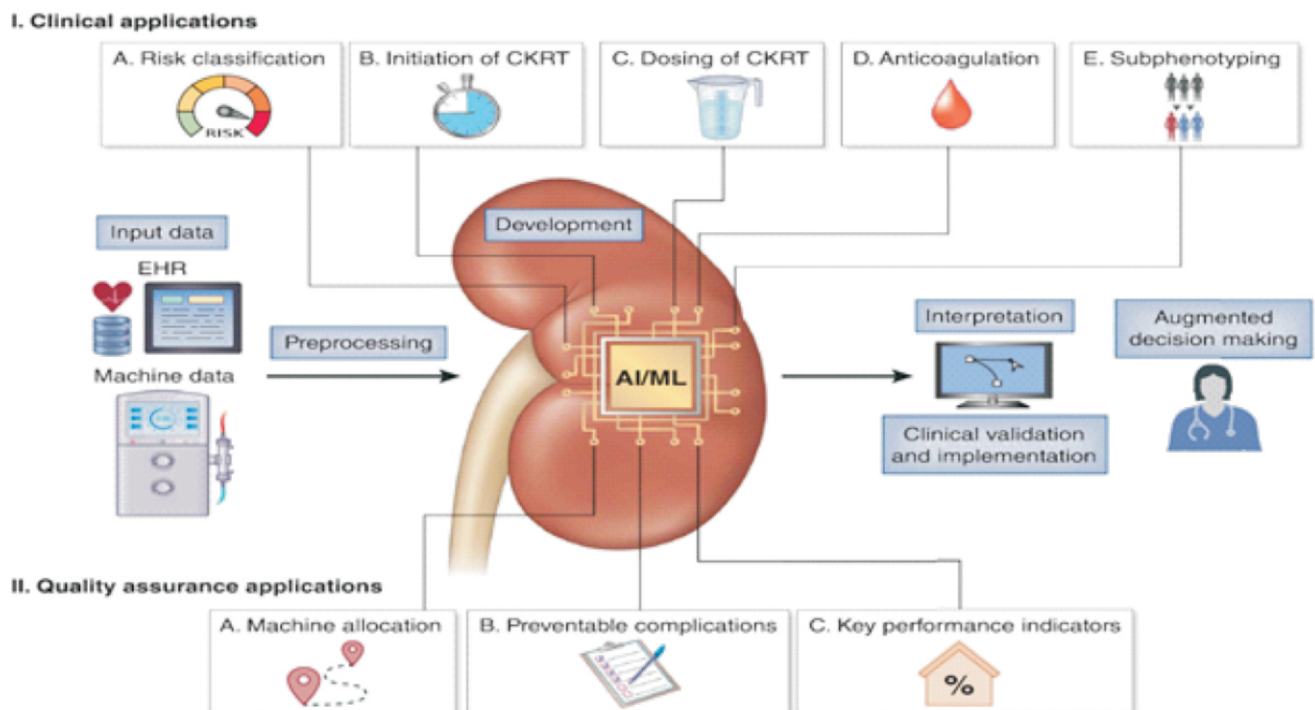


Fig. 3: Clinical and quality assurance applications of artificial intelligence (AI) in CKRT.⁷

AI IN NEPHRON-PATHOLOGY

The management and prognosis of most kidney diseases are based on pathological identification. However, many diseases are heterogeneous in clinical presentation as well on pathological evaluation. There are disease and observer-related discrepancies that have been a major hurdle in the proper evaluation of most kidney diseases. Lupus nephritis is a leading example of such a heterogeneous disease. AI can help limit this heterogeneity and bring in some homogeneity in such dilemmas. Computer algorithms possess a remarkable ability to discern subtle yet significant pathological alterations, these automated assessment algorithms can alleviate the laboriousness associated with visual evaluation.

The most extensively employed deep learning model for image analysis in the realm of kidney histopathology is the Convolutional Neural Networks (CNNs). Pre-trained neural networks can identify both glomerular and non-glomerular regions by analysing tissue characteristics. Bukowy et al., developed a CNN to identify glomeruli in trichrome-stained images, achieving an impressive average precision of 96.94% and a recall of 96.79%⁸. PathoSpotter-K is a computational system that works on the principle of Content-based Image Retrieval (CBIR) and is developed to identify nephrological lesions in digital kidney images, employing classical image processing and pattern recognition techniques to achieve an accuracy rate of around 88.3% (Figure-4)⁹. This system will assist pathologists in the fields of education and kidney disease research.

However, staining variability, the current lack of standard data sets and the time-consuming manual annotation by a highly trained neuropathologist are some of the obstacles faced when using AI in neuropathology.

AI IN GLOMERULAR DISEASES

AI has the potential to revolutionize the diagnosis, prediction, and treatment of glomerular disease by leveraging its ability to analyze large datasets and identify patterns. AI can be used to improve the accuracy and efficiency of kidney biopsy interpretation, predict the risk of disease progression, and identify potential new drug targets. While AI-powered tools for glomerular disease are still in their early stages of development, there is a growing body of scientific evidence to support their potential benefits¹⁰.

Chen et al developed a machine learning model designed to aid in risk prediction for immunoglobulin A nephropathy (IgAN), leading to the creation of the Nanjing IgAN Risk Stratification System. This system leveraged the power of eXtreme Gradient Boosting (XGBoost), an ensemble learning method that constructs a series of decision trees iteratively, each building upon the knowledge of the previous ones. Importantly, this approach enabled the system to directly discern patterns from a pool of 36 possible candidate features, eliminating the need for preliminary feature selection steps. The XGBoost method demonstrated exceptional predictive accuracy and the ability to generalize its predictions across a variety of risk prediction tasks. For instance, it achieved a C statistic of 0.84 when predicting the likelihood of end-stage kidney disease (ESKD) or a 50% reduction in estimated glomerular filtration rate within 5 years following the biopsy diagnosis. Utilizing this XGBoost system, a patient's baseline characteristics can be put into a risk calculator, which then automatically forecasts the patient's 5-year prognosis and categorizes them into high, moderate, or low-risk categories¹¹. Ginley et al. developed a computational segmentation and classification model of diabetic glomerulosclerosis. The digital classification results were

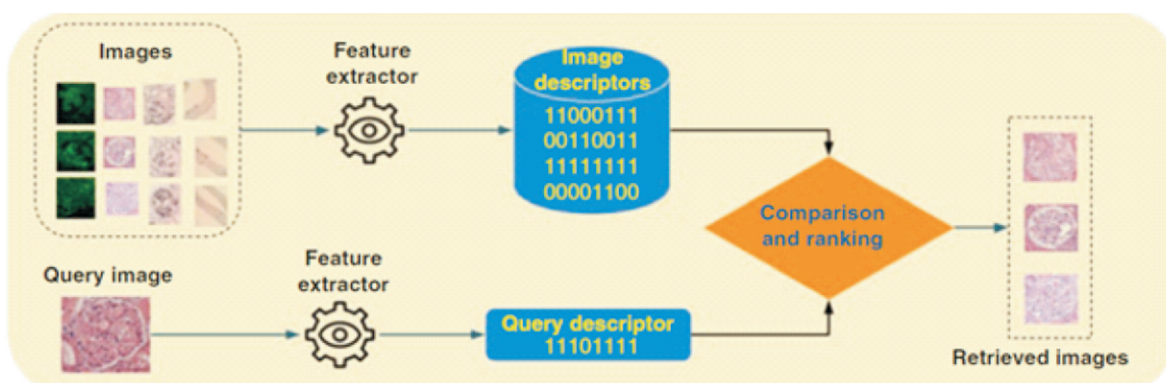


Fig. 4. Content Based Image Retriever⁹.

compared to the classifications provided by a senior pathologist, whose judgments were considered the ground truth, resulting in a moderate agreement indicated by Cohen's kappa (κ) of 0.55. Furthermore, two other renal pathologists also evaluated the digital classification results, showing a higher level of agreement with Cohen's kappa values of 0.68 and 0.48. The system successfully identified glomerular boundaries from whole slide images with an accuracy rate of 0.93. It demonstrated excellent sensitivity (0.94) and specificity (0.93) when detecting glomerular nuclei, and impressive sensitivity (0.95) and outstanding specificity (0.99) in identifying glomerular structural components¹².

AI IN CHRONIC KIDNEY DISEASE (CKD)

Although evidence-based guidelines and current treatment models can delay CKD progression and improve patient outcomes, the nephrology community recognizes that these approaches are insufficient to meet the growing needs of CKD patients. Due to the many risk factors and diagnostic tests involved, accurately diagnosing, predicting the course of, and optimally managing CKD can be challenging for clinicians. AI has been proposed as a potential solution to this complex problem¹³.

In a 2018 study conducted by Arianna et al, machine learning techniques were employed to predict complications related to Type 2 Diabetes Mellitus in a cohort of 1000 patients. The Random Forest (RF) model emerged as the top performer in terms of predictive accuracy, achieving an accuracy rate of 0.838¹⁴. Gastel et al. introduced an automated segmentation technique for measuring Total Kidney Volume (TKV) using a Deep Learning (DL) network on a dataset of 540 abdominal MRIs from individuals with Autosomal Dominant Polycystic Kidney Disease (ADPKD). The automated TKV measurements closely aligned with manually traced TKV measurements, displaying minimal bias and high precision¹⁵.

Chantaduly et al. conducted a retrospective analysis involving patients who had undergone one or more abdominal CT scans within 6 months before a kidney biopsy. The final dataset consisted of 152 CT scans from 92 patients, encompassing images of 300 native kidneys and 76 transplant kidneys. The study evaluated the performance

of two different convolutional neural networks: one operating at the slice level and the other at the voxel level, to distinguish severe kidney fibrosis ($\geq 50\%$) from mild/moderate fibrosis ($< 50\%$). The ground-truth for assessment was derived from interstitial fibrosis and tubular atrophy scores reported in kidney biopsy results. The results indicated that both ML models exhibited comparable positive predictive values (0.886 versus 0.935) and accuracy levels (0.831 versus 0.879). This suggests that both approaches were effective in distinguishing between severe and mild/moderate kidney fibrosis, showcasing their potential utility in clinical practice¹⁶.

AI IN DIALYSIS

Dialysis is a particularly attractive field for AI applications because of its large volume of documented data in electronic health records. AI can be used to help nephrologists develop personalized treatment plans for dialysis patients, considering their individual needs and preferences. Additionally, AI-powered monitoring systems can track patient vital signs and dialysis treatment parameters in real-time, providing early warning signs of complications and allowing for rapid intervention. One particularly promising area of AI innovation in dialysis is the development of wearable dialysis devices¹⁷.

Barbieri et al., evaluated the impact of an AI decision support system, the Anemia Control Model (ACM), on anaemia outcomes. The median darbepoetin consumption significantly decreased from 0.63 to 0.46 $\mu\text{g/kg/month}$, whereas on-target haemoglobin values significantly increased from 70.6% to 76.6%, reaching 83.2% when the ACM suggestions were implemented. Moreover, ACM introduction led to a significant decrease in haemoglobin fluctuation (intra-patient standard deviation decreased from 0.95 g/dl to 0.83 g/dl)¹⁸.

Zhang et al demonstrated that in peritoneal dialysis-related bacterial infections, AI-predicted pathogens correlate with actual pathogens responsible for bacterial infections¹⁹. ML Algorithms define pathogen-specific local immune fingerprints in peritoneal dialysis patients with bacterial infections.

AI IN KIDNEY TRANSPLANT

Kidney transplantation is the best treatment for end-stage renal disease (ESRD), but limited donor organs make it

inaccessible for many. To optimize organ allocation, researchers have developed complex e-health systems using data mining and neural network (NN) algorithms. AI can be used to develop personalized treatment plans, match donors and recipients more effectively, and predict which patients are at risk of rejection. AI is also being used to develop new diagnostic tools, treatment strategies, and predictive models, which could further improve patient outcomes^{20,21}.

In 2019, a study titled "Predicting Deceased Donor Kidney Transplant Outcomes: Comparing KDRI/KDPI with Machine Learning" conducted a comprehensive analysis of a decade's data encompassing numerous variables related to kidney transplants, harnessing the power of AI. The study's primary objective was to enhance the prediction of graft survival outcomes in deceased donor kidney transplantation (DDKT). The research compared MLM with the Kidney Donor Risk Index (KDRI) in their ability to forecast graft failure within 12, 24, and 36 months following DDKT. The MLM model employed an ensemble approach, consisting of thousands of randomly generated decision trees, and was trained using the same dataset initially utilized to develop KDRI. Remarkably, the MLM model, utilizing readily available recipient and donor variables, demonstrated significantly superior performance when it came to predicting graft failure during the post-DDKT follow-up period compared to KDRI/KDPI²².

Tacrolimus is frequently administered as part of post-transplantation immunosuppressive therapy. However, this medication presents a challenge due to its narrow therapeutic range and variations in patient responses. In clinical practice, it is crucial to identify the appropriate indications for tacrolimus therapy. Thishya et al. in their study, designed an enhanced Artificial Neural Network (ANN) to accurately estimate the initial tacrolimus dosage and approximate tacrolimus bioavailability. Their research demonstrated that the predicted tacrolimus bioavailability closely matched the actual values, signifying the potential of this approach to improve the precision of tacrolimus therapy²³.

CONCLUSION

Advancements in the integration of AI within clinical medicine are still in their early stages and hold the potential to evolve in several promising directions. The deployment

of AI in healthcare presents an expansive realm of possibilities that can benefit both patients and clinicians alike. Surely in the field of medicine, AI will not replace a professional/s by any means or measures but it will help them to make better informed decisions. AI will augment in decision making and should best be labelled as "Augmented Intelligence" once it comes to its role in medicine.

While AI has tremendous potential, there are also significant challenges that lie ahead of its implementation, including data access and quality, data privacy and security, ethical considerations, bias, trustworthiness, computing power, AI integration and legal issues. Tackling these challenges will be crucial as AI continues to shape the future of healthcare. The European Commission's proposed regulatory framework for AI technology will play a significant role in ensuring the safe and ethical implementation of these technologies in the healthcare industry.

To conclude there is no doubt that AI will be at the forefront and a leading means of improving the diagnosis and treatment of acute diseases affecting kidneys or in established kidney diseases.

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