Artificial Intelligence in Nephrology: Where Have We Reached?

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Artificial intelligence: An introduction

The impact of artificial intelligence (AI) in everyday life can now be felt more resoundingly than ever before.[1,2] Smartphones use facial recognition algorithms; Siri, Alexa, and Cortana are household names; autonomous cars are driving in streets, and human reigning world champions of strategy games have finally been defeated by computers.[2,3]

What exactly is AI? The father of the field, Mc-Carthy, defines AI as the science and engineering of creating intelligent machines that behave in a way that could be considered intelligent if it was a human being.[1] In essence, a computer mimics "intellectual processes characteristic of humans, such as the ability to reason, discover meaning, generalize, or learn from past experience" to achieve goals without being explicitly programmed for specific action.[3]

One of the things making AI different from classic computational approaches is integration of machine learning (ML), which is inherently a set of algorithms that have the ability to learn and improve from experience. Artificial neural networks (ANNs) and deep learning are renowned examples of ML algorithms.[2] ANN is a collection of artificial neurons organized in layers, that can approximate complex functions involved in classification or prediction processes.[2,4] Deep learning, on the other hand, uses convolutional neural networks (CNNs) that are artificial counterparts of the neural networks of the human brain, having multiple layers of nonlinear processing units for feature extraction and transformation. CNNs learn through exposure to examples of desired input–output behaviour and often specialize in image recognition.[2,4] In a befitting example, a CNN that is exposed to a sufficient number of correctly labelled pictures of cats and dogs will learn to discriminate between these two animal classes, in a process known as supervised learning.[4]

Artificial intelligence for augmenting clinicians' work in nephrology: Current advances

Medicine in the hands of a sophisticated machine? While the thought may superficially seem daunting, it is prudent to understand that AI intends to "augment" human intelligence and not replace it.[1] In nephrology, AI applications encompass diagnostics, predictions and treatment as well as patient care aspects of clinical nephrology, kidney transplantation, hemodialysis, as well as peritoneal dialysis.[2] Table 1 enumerates some of these current applications along with the AI method used.[1]

Diagnostics

In diagnostics, AI based deep learning can detect and classify lesions, as well as enable segmentation and quantification of structures.[4] Recently, the first-ever CNN for multiclass segmentation of stained nephrectomy samples and transplant biopsies was developed by Hermsen *et al*.[5] All major histological kidney compartments could automatically be segmented in whole-slide digital histopathological images of the kidney, with excellent segmentation results particularly for glomeruli (92.7% detection rate), interstitium and combined group of all classes of tubuli, as per the Banff classification system. Easily assessable quantitative data, such as the numbers of glomeruli and sclerotic glomeruli and the percentage of interstitial area, could be obtained that correlated well with scores assessed by expert nephropathologists. The results were validated using a cohort from a different centre.[5]

An AI-enabled digital classification of diabetic glomerulosclerosis was used by Ginley *et al*,[6] that could assess structural changes of glomeruli and classify the samples according to an existing diabetic nephropathy pathological classification scheme. Glomerular boundaries could be detected from whole slide images with

Table 1: AI applications in nephropathy

	Application	AI technique	Method
Diagnosis	Multiclass segmentation of digitized kidney tissue sections	Deep learning	CNN
	Segmentation and classification of diabetic glomerulosclerosis	Deep learning and unsupervised learning	CNN; unsupervised methods
Prediction	ESRD prediction for IgAN patients	Supervised learning	XGBoost algorithm
	Continuous prediction of AKI	Deep learning	RNN
Treatment/patient care	Recommendation of anemia therapy in hemodialysis patients	Deep learning	Reinforcement learning
	Clinical decision support for anemia management in hemodialysis patients	Deep learning	

Abbreviations: AI, artificial intelligence; CNN, convolutional neural network; ESRD, end-stage renal disease; IgAN, immunoglobulin A nephropathy; XGBoost, eXtreme Gradient Boosting; AKI, acute kidney injury; RNN, recurrent neural network

Adapted from: Xie G, Chen T, Li Y, Chen T, Li X, *et al*. Artificial intelligence in nephrology: How can artificial intelligence augment nephrologists' intelligence?. *Kidney Dis.* 2020;6(1):1-6.

0.93 ± 0.04 balanced accuracy, glomerular nuclei with 0.94 sensitivity and 0.93 specificity, and glomerular structural components with 0.95 sensitivity and 0.99 specificity. The classification results were comparable with those of expert nephropathologists and can thus offer improved precision in clinical decision workflows.

Prediction

Tomašev *et al*[7] recently used deep-learning methods to devise clinically applicable approach to continuous prediction of future acute kidney injury (AKI). A recurrent neural network (RNN) model was developed using sequential health record data of 703,782 veterans. The model was able to predict risk for 55.8% of inpatient AKI episodes and 90.2% of AKI cases requiring dialysis, with a lead time of 48 hours and a 2:1 false alert ratio. Furthermore, it could give a list of clinical features that were most salient to each prediction, alongside predicted future trajectories for clinically relevant blood tests. This would help identify patients at-risk of AKI with sufficient context and enough time for the clinician to impart early treatment.

In another study,[8] the previously validated AI-based preoperative MySurgeryRisk AKI model for postoperative AKI prediction was further improved with high sensitivity and specificity by dynamic incorporation of intraoperative data. Physiological time-series data was obtained intraoperatively for 2,911 patients undergoing surgery. The updated model correctly reclassified 40% of the high-risk patients who initially were considered to be low-risk.

AI has emerged as a powerful tool for predicting dry weight in hemodialysis patients. It was seen to outperform experienced nephrologists in correct dry weight estimation for most pediatric patients on chronic hemodialysis in a study by Niel *et al*.[9] Notably, collection of data required for prediction by the AI model was a non-invasive process, making it ideal for children. The neural network interface gave the added advantage of being user-friendly and could be accessed online through the Internet, on a computer or a smartphone.[9]

A prediction model using routinely available characteristics and based on the combination of a machine learning algorithm and survival analysis was developed to stratify risk for kidney disease progression in setting of Immunoglobulin A nephropathy (IgAN). Combined event of end-stage kidney disease or 50% reduction in estimated glomerular filtration rate (eGFR) within 5 years after diagnostic kidney biopsy could be predicted with significant risk stratification. An online calculator, the Nanjing IgAN Risk Stratification System, permitted easy implementation of this model.[10]

Patients with autosomal dominant polycystic kidney disease (ADPKD) exhibit different patterns of kidney function decline, neural network can be used to predict individual estimated glomerular filtration rate (eGFR) decline in patients with ADPKD.[11] Furthermore, artificial intelligence is also contemplated as fast, cheap, and clinically simple approach to estimate tacrolimus area under the concentration over time curve in renal transplant recipients, thus helping the clinicians to monitor such patients with an increased risk of inadequate tacrolimus dosing.[12]

Box 1: Summary of key advances

- A deep RNN model using data from electronic health records enables prediction of inpatient AKI episodes with lead times of up to 48 hours
- Intraoperative physiological signals can be integrated into an AKI risk model that integrates preoperative and intraoperative data to predict postoperative AKI
- A convolutional deep learning model enables non-invasive classification of CKD stage and eGFR using kidney ultrasound images
- A CNN that enables automated analysis of transplant biopsy and nephrectomy samples.

Abbreviations: RNN, recurrent neural network; AKI, acute kidney injury; CKD, chronic kidney disease; eGFR, estimated glomerular filtration rate, CNN, convolutional neural network

Adapted from: Rashidi P, Bihorac A. Artificial intelligence approaches to improve kidney care. *Nat Rev Nephrol.* 2020;16(2):71-72.

Treatment

Barbieri *et al*[13] established a decision support system, the Anemia Control Model (ACM), to recommend suitable erythropoietic stimulating agent doses based on a machine-learning model trained on about 170,000 clinical records, lending support to nephrologists in making decisions related to anemia treatment in hemodialysis patients. The system was clinically validated by a retrospective study that consisted of a 12-month control phase and a 12-month ACM-guided care phase in 752 hemodialysis patients. The primary outcomes of hemoglobin values and fluctuation improved significantly in the ACM phase. Median darbepoetin consumption significantly decreased from 0.63 to 0.46 mg/kg/month, whereas on-target hemoglobin values significantly increased from 70.6% to 76.6%, reaching 83.2% when ACM suggestions were implemented.

Thus, the capacity of AI algorithms to synthesize large volumes of data from multiple sources to undertake complex tasks is now well-established, and their application to nephrology has vast potential. Box 1 summarises the key advances in the field.[14] Further validation studies evaluating a range of machine learning strategies are merited in which AI models need to be objectively evaluated to finally enable FDA approval of AI algorithms in nephrology and bring this technology into routine clinical practice.

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