



Artificial intelligence-aided ultrasound in renal diseases: a systematic review

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Background: The development of artificial intelligence (AI) techniques has provided a novel strategy for improving the performance of renal ultrasound. To reflect the development of AI methods in renal ultrasound, we aimed to clarify and analyze the state of AI-aided ultrasound research in renal diseases.

Methods: PRISMA 2020 guidelines have been used to guide all processes and results. AI-aided renal ultrasound studies (for both image segmentation and disease diagnosis) published up to June 2022 were screened through the databases of PubMed and Web of Science. Accuracy/Dice similarity coefficient (DICE), the area under the curve (AUC), sensitivity/specificity, and other indications were applied as evaluation parameters. The PROBAST was used to assess the risk of bias in the studies screened.

Results: Of 364 articles, 38 studies were analyzed, and could be divided into AI-aided diagnosis or prediction related studies (28/38) and image segmentation related studies (10/38). The output of these 28 studies involved differential diagnosis of local lesions, disease grading of, automatic diagnosis, and diseases prediction. The median values of accuracy and AUC were 0.88 and 0.96, respectively. Overall, 86% of the AI-aided diagnosis or prediction models were classified as high risk. An unclear source of data, inadequate sample size, inappropriate analysis methods, and lack of rigorous external validation were found to be the most frequent and critical risk factors in AI-aided renal ultrasound studies.

Conclusions: AI is a potential technique in the ultrasound diagnosis of different types of renal diseases, but the reliability and availability need to be strengthened. The use of AI-aided ultrasound in chronic kidney disease and quantitative hydronephrosis diagnosis will be a promising possibility. The size and quality of sample data, rigorous external validation, and adherence to guidelines and standards should be considered in further studies.

Keywords: Renal disease; ultrasound; artificial intelligence (AI); computer-aided diagnosis; image segmentation

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Introduction

In clinical practice, ultrasound has been essential for the noninvasive diagnosis and management of renal diseases as it provides information on anatomy and its condition. The main clinical application of renal ultrasound imaging includes chronic kidney disease (CKD), acute kidney injury, kidney stones, benign or malignant renal tumors, and urinary obstruction (1,2). Although conventional ultrasound is one of the most used imaging tools for renal disease screening and diagnosis, it confronts the challenges of low efficiency in separating regions of interest from the surroundings, as a result of speckle noise, low image quality, insufficient contrast, and inconsistent intensity profile. In addition, the adjacency of organs with high scattering tissues may cause shadows to partially occlude the organs, leading to incorrect decisions. The majority of these limitations are associated with the advancement of equipment or techniques and do not diminish with increased operational experience. Furthermore, as the workloads of physicians have increased dramatically, errors are inevitable (3,4).

In recent years, artificial intelligence (AI) techniques have improved the management of patients by healthcare professionals. Several reports have demonstrated the excellent accuracy of AI in the diagnosis of multiple fields, such as oncology (5), skin diseases (6), and epidemic prevention and control (7). AI-aided medical imaging analysis is one of the fundamental issues in the field of AI in medicine (8). Based on the assessment of characteristics from ultrasound images, AI techniques increase efficiency, reduce subjective errors, and achieve objectives with minimal manual input by providing trained radiologists with prescreened images and identified features (9). AI technology in medical imaging can be roughly divided into “non-deep” machine learning algorithms, based on handcrafted engineered features, and deep learning algorithms, with fewer manual preprocessing steps. Their key difference lies in the existence of explicit feature predefinition or selection (*Figure 1*). For a computer-aided diagnosis system based on machine learning, three main stages are required: image preprocessing, feature extraction (such as texture analysis), and analysis aimed at solving a particular task or application using classifiers (such as an artificial neural network) (10). According to a recently published study, AI-aided technique is valid for improving the diagnosis accuracy of urolithiasis, pediatric urology, renal transplant, and urologic neoplasms by computer-based prediction and decision support models, providing

quantitative diagnosis information, and overcoming substantial interobserver variability in ultrasound interpretation (10). However, according to search results, in the field of renal ultrasound, limited advances in AI have been made in the past 10 years. It is unclear whether AI-aided ultrasound is a reliable and valid technique in renal disease diagnosis in clinical practice. The application of AI-aided ultrasound to diagnose and predict renal diseases has not been reviewed previously. Therefore, this systematic review aimed to clarify the state of AI-aided ultrasound research associated with renal diseases, and further analyze the challenges that remain to be addressed in this area. We present the following article in accordance with the PRISMA reporting checklist (available at <https://qims.amegroups.com/article/view/10.21037/qims-22-1428/rc>).

Methods

We searched the publication databases PubMed and Web of Science systematically in June 2022. In the search strategy, the following terms were used for the search syntax: (I) ultrasound: *ultras**; (II) organs: renal, kidney; (III) artificial intelligence: *artificial intelligent**, *image segment**, *texture analysis*, *machine learning*, and *deep learning*. The complete search strategy was available from the authors. This study was conducted in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines (11). Two authors screened the titles and abstracts independently and deleted duplicate and irrelevant studies. Studies evaluating AI-aided ultrasound in renal disease diagnosis, detection, and prediction were eligible for inclusion in this study, and disagreements regarding the relevance of the studies were resolved by consensus. Animal studies, laboratory investigations, non-English studies, conference abstracts, and reviews were excluded. Because we mainly focused on the methods and efficiency of AI-aided ultrasound in disease diagnosis and prediction, the analyses of image registration and fusion (for ultrasound-guided kidney intervention) were excluded. Because of the heterogeneity of this review and the paucity of studies, a qualitative synthesis of the results used a narrative approach.

Checklists demonstrate the data obtained from the studies included in qualitative synthesis (*Table 1* for image segmentation and *Table 2* for AI-aided diagnosis). “Clinical parameters” included patient information and laboratory examination data. The performance considered in the studies was controversial depending on the study design. Therefore, we used accuracy/Dice similarity coefficient

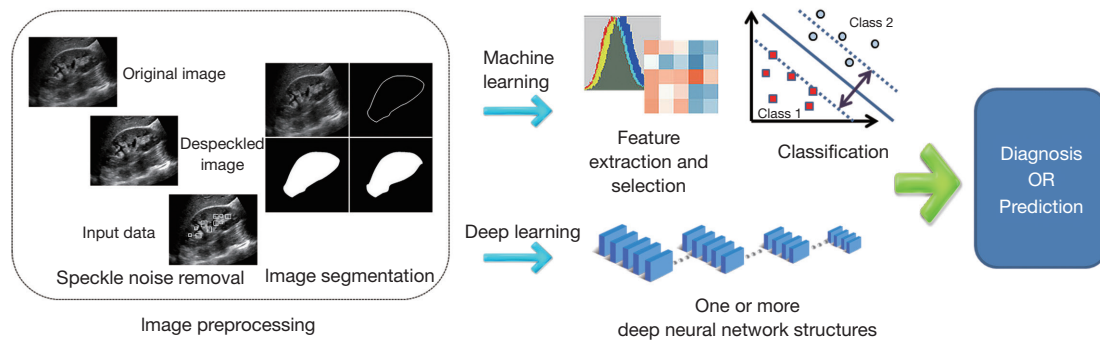


Figure 1 AI methods in medical imaging for disease diagnosis or prediction. AI, artificial intelligence.

(DICE) as an evaluation parameter for image segmentation, and accuracy, area under the curve (AUC), and sensitivity/specificity as evaluation parameters for AI-aided diagnosis, because most studies addressed these metrics. Herein DICE is a measure of the overlap between two structures or methods.

The Prediction Model Risk of Bias Assessment Tool (PROBAST) (47) was used to assess the risk of bias for all the AI-aided diagnosis studies. It includes 20 signaling questions across four domains including participants, predictors, outcome, and analysis. The risk of bias in the studies was classified as low, moderate, or high in each domain and overall. The applicability concerns were not considered in this study because of the uncertain subject.

Results

The number of publications on AI-aided ultrasound in renal diseases has increased rapidly from 2016 onwards (*Figure 2*). Database searches identified 364 studies, which included 168 from the Web of Science and 196 from PubMed. After excluding duplicates, 240 studies were screened by title and abstract, of which 167 studies were irrelevant or non-English articles. Following full-text access, a total of 38 studies were considered eligible for review, including 10 for ultrasound image segmentation and 28 for AI-aided ultrasound diagnosis or prediction. *Figure 3* summarizes the search strategy of this study.

Owing to the uncertain subjects and evaluation index, the studies included in the qualitative synthesis were divided into two parts: AI-aided diagnosis or prediction studies and image segmentation. For ultrasound image segmentation, the following indexes were summarized: author, year of publication, AI method, input, and number of patients, data augmentation methods, number of training

sets, validation and testing sets, and efficiency evaluation. For AI-aided diagnosis or prediction, author, year of publication, input, output, image preprocessing, feature extraction, classification/statistics methods, size of patients, data augmentation, and size of training and testing set were summarized.

In AI-aided diagnosis or prediction studies, most of the input data were two-dimensional (2D) ultrasound images (25/28), and three studies used value-based data from multiple ultrasound techniques such as Color Doppler flow imaging (CDFI) and elastography (3/28). Output (targeted diagnosis or prediction) was indicated as the aim of studies, including automatic differential diagnosis of kidney lesions, kidney stone detection, CKD diagnosis/grading, quantitative analysis of hydronephrosis in children, and automatic diagnosis of congenital abnormalities of the kidney and urinary tract (CAKUT). To improve the accuracy, image segmentation, speckle noise removal/de-speckling, and normalization were the most frequently used image preprocessing methods. Six out of 19 machine learning studies were published before 2019. The most frequently used machine learning algorithm for classification was the support vector machine (SVM), and other algorithms contained logistic regression, linear regression, artificial neural network (ANN), k-Nearest Neighbor (KNN), random forest, linear discriminant analysis (LDA), and fuzzy-neural network. Feature extraction was an imperative procedure of AI-aided ultrasound studies and most of the machine learning studies used texture analysis. Deep learning algorithm used studies (9/28) were all published after 2018, and the commonly used algorithm methods were convolutional neural network (CNN) and its optimization algorithms. Although conventional deep learning methods did not need feature predefinition or selection, four of the recent studies combined traditional (like texture analysis)

Table 1 Summary of “image segmentation” studies

Author	Objective	Year	AI methods	Input	No. of patients	Data augmentation	No. of training set	No. of validation set	No. of testing set	Efficiency evaluation
Wang <i>et al.</i> (12)	Kidney segmentation (parenchymal area)	2014	2-step level set (distance regularized level set, region-scalable fitting energy minimization method)	2D image	20	–	10	–	–	SN score >0.9
Yin <i>et al.</i> (13)	Kidney segmentation	2019	Boundary distance regression deep neural network	2D image	100	Transfer learning	105	80	–	DICE =94%, ACC =0.99
Yin <i>et al.</i> (14)	Kidney segmentation	2020	Boundary distance regression and pixel classification networks	2D image	152	Transfer learning	105	20	164	DICE =93–94%
Marsousi <i>et al.</i> (15)	Kidney detection	2014	Probabilistic kidney shape model, level set propagation	3D image	Nm	–	24	–	–	Detection accuracy =92.86%
Marsousi <i>et al.</i> (3)	Kidney segmentation	2017	Shape-to-volume registration, combined prior knowledge of training shapes with anatomical knowledge; a level set method	3D image	8	–	16	30	–	ACC =97.48%, Sensitivity/specificity =0.79/0.99
Chen <i>et al.</i> (16)	Kidney segmentation	2021	CNN (SDFNet)	2D image	Nm	–	450	50	–	Sensitivity/specificity =0.94/0.99
Torres <i>et al.</i> (17)	Kidney segmentation	2021	A hybrid energy functional that combines localized region- and edge based terms	3D image	Nm	–	57	–	–	DICE =81%
Kang <i>et al.</i> (18)	Kidney-hydronephrosis evaluation (child)	2013	ASM with image acquisition priors, intensity correction and anatomical priors	2D image	34	–	–	–	–	DICE =0.83–0.87
Cerrolaza <i>et al.</i> (19)	Kidney-hydronephrosis evaluation (child)	2015	Gabor-based appearance models, Graph-Cut Based method	3D image	19	–	–	–	–	DICE =0.86
Cerrolaza <i>et al.</i> (20)	Kidney-hydronephrosis evaluation (child)	2016	Active shape model	3D image	39	–	–	–	–	DICE =0.74–0.86

Nm, not mentioned; 2D, two-dimensional; 3D, three-dimensional; CNN, convolutional neural network; ASM, active shape models; ACC, accuracy; DICE, dice coefficient; SN, an author-defined index, the higher the SN score, the closer the segmentation result obtained by the method to the manual segmentation result.

or cutting-edge feature extraction methods (like transfer learning) with deep learning algorithms to further improve the evaluation efficiency.

The size of the dataset was generally small in these published studies. The largest dataset was 5,523 cases. Only

seven studies contained more than 1,000 images and over a third of the datasets (11/28) contained less than 100 images. With regards to the image source, the number of patients was not mentioned in nearly 25% of the studies (7/28). Nearly one in four studies used data augmentation methods

Table 2 Summary of “diagnosis and prediction” studies

Author	Year	Input	Output (diagnosis/prediction)	Image preprocessing	Feature extraction	Classification/statistic method	Size of patient	Data augmentation	Size of Dataset		ACC (%)	AUC	Sensitivity/specificity
									Training set	Testing set			
Bommanna <i>et al.</i> (21)	2008	2D image	Normal, medical renal diseases and cortical cyst	Segmentation and rotation	Texture analysis	Hybrid fuzzy-neural system	Nm	–	150	78	80–85	–	–
Subramanya <i>et al.</i> (22)	2015	2D image	Normal, medical renal disease, cyst	De-speckling	KNN	SVM	35	–	35	Internal validation	86.3	–	–
Bama <i>et al.</i> (23)	2016	2D image	Hydronephrosis, nephrocalcinosis, normal and multicystic dysplasia	Speckle noise removal and segmentation	Texture analysis	SVM	Nm	Multiple ROIs obtained from one image	40	Internal validation	88–92	–	0.88–0.92/–
Yu <i>et al.</i> (24)*	2020	2D image	Abnormal and normal cases of the kidney	Automatic recognition and location	–	DCNN	1460	–	2,922	400	94.67	0.96	0.98/–
Nithya <i>et al.</i> (25)	2019	2D image	Normal, kidney stone and tumor	Speckle noise removal and segmentation (K-Means)	Texture analysis-GLCM	ANN	Nm	–	80	20	93.45	–	1.00/0.90
Sudharson <i>et al.</i> (26)	2020	2D image	Normal, cyst, stone, and tumor	Speckle noise removal	Deep neural networks	SVM	Nm	Transfer learning	4,940	520	95–97	–	–
Sagreiya <i>et al.</i> (27)	2019	SWV, clinical information	Renal cell carcinoma, angiomyolipoma	–	–	SVM	51	–	52	Internal validation	94	0.98	–
Shin <i>et al.</i> (28)	2019	2D image	Wilms tumor, clear cell sarcoma and rhabdoid tumor of the kidney	Normalization	Texture analysis-GLCM, GLRLM	Subgroup analysis with 32 post hoc analysis	–	–	32	Internal validation	>76	>0.89	>0.7/1.0
Selvarani <i>et al.</i> (29)	2019	2D image	Kidney stone	Speckle noise removal and segmentation (K-Means)	Texture analysis-GLCM	SVM	Nm	–	100	Internal validation	98.8	–	–
Muller <i>et al.</i> (30)	2021	Video (2D image)	ESWL hit rate	Image Annotation	–	U-net	11	–	57	Internal validation	63.9	–	0.56/0.75
Kuo <i>et al.</i> (31)	2019	2D image	CKD	Image normalization	–	CNN (ResNet, XGBoost)	1299	Transfer learning, image shift, rotation, horizontal flip	4505	Internal validation	85.6	0.904	0.61/0.92
Hao <i>et al.</i> (32)	2020	2D image	CKD (classification and screening)	–	Texture analysis	CNN (ResNet)	226	Transfer learning, image rotation, shifting, random gray level transformation of pixels	226	Internal validation	96	0.97	0.99/0.82
Li <i>et al.</i> (33)	2021	2D, CDFI and SWE parameters	CKD-abnormal and normal cases	–	KNN	MLP-SVM	203	–	142	61	81	0.91	0.81/0.81
Zhang <i>et al.</i> (34)*	2021	2D image	CKD-Membranous nephropathy and IgA nephropathy	Segmentation	LASSO logistic regression	Random forest, logistic regression	68	–	470	153	76.5	0.76	0.75/0.89
Athavale <i>et al.</i> (35)*	2021	2D image	CKD	Speckle noise removal, segmentation (U-net)	Pretrained CNN	XGBoost	352	Transfer learning	5523	612	86.8	–	0.80/–
Chen <i>et al.</i> (36)	2019	2D image	CKD	Inpainting, median filter	Texture, standard deviation, area, and brightness analysis	SVM	205	–	798	Internal validation	77.9–83.7	–	–
Zhu <i>et al.</i> (37)	2022	2D, CDFI, SWE, clinical information	CKD (kidney fibrosis)	–	–	SVM	117	–	117	Internal validation	–	0.833	0.77/0.72
Ahmad <i>et al.</i> (38)	2021	2D image	CKD	De-speckling, cropping	Texture analysis-GLCM	LDA	Nm	–	308	Internal validation	96–100	–	–
Kim <i>et al.</i> (39)	2021	2D image	CKD	Histogram equalization, range filter preprocessing	Texture analysis-GLCM	ANN	Nm	–	741	Internal validation	95.4	–	–
Abbasian Ardakani <i>et al.</i> (8)	2017	2D image	Rejected and unrejected allografts	Segmentation	Texture analysis, LDA	Nearest neighbor classifier	61	–	61	–	98.36	0.975	0.91/1.00

Table 2 (continued)

Table 2 (continued)

Author	Year	Input	Output (diagnosis/prediction)	Image preprocessing	Feature extraction	Classification/statistic method	Size of patient	Data augmentation	Size of Dataset		ACC (%)	AUC	Sensitivity/specificity
									Training set	Testing set			
Abbasian <i>et al.</i> (40)	2020	2D image	Increased or decreased serum creatinine (sCr)	–	Texture analysis-LDA	KNN	40	–	40	–	93.5	0.974	0.95/0.91
Lin <i>et al.</i> (41)	2021	2D image	Hydronephrosis in children	Gray processing, normalization, segmentation (U-net)	–	Fluid-to-kidney area ratio, linear regression	699	–	1414	394	–	0.99	0.90/0.80
Smail <i>et al.</i> (42)	2020	2D image	Hydronephrosis in children	Speckle noise removal, cropping, normalization	–	CNN	673	Image rotation and shifting	2420	Internal validation	51–78	–	–
Cerrolaza <i>et al.</i> (43)	2016	2D image	Hydronephrosis in children	–	Quantitative image analysis algorithms	SVM, logistic regression	50	–	50	Internal validation	–	0.94–0.98	1.00/0.74–0.90
Zheng <i>et al.</i> (44)	2019	2D image	CAKUT	Segmentation (graph-cuts), normalization	Transfer learning (CNN), texture analysis	SVM	100	–	100	Internal validation	81–87	0.88–0.92	0.85–0.88/0.74–0.88
Yin <i>et al.</i> (45)	2019	2D image	CAKUT	–	–	CNN (GCN)	225	–	4933	Internal validation	85	–	0.86/0.84
Yin <i>et al.</i> (46)	2020	2D image	CAKUT (posterior urethral valves)	Normalization	Transfer learning (CNN)	Deep learning (VGG 16)	157	Image rotation, left-right flipping	157	Internal validation	92.5	0.96	0.87/0.98

*, low risk studies. Nm, not mentioned; 2D, two-dimensional; ACC, accuracy; AUC, area under the curve; KNN, k-nearest neighbor; SVM, support vector machine; ROI, region of interest; SWV, shear-wave velocity; SWE, shear-wave elastography; GLCM, grey level co-occurrence matrix; DCNN, deep convolutional neural network; CNN, convolutional neural network; GCN, graph convolutional network; VGG, visual geometry Group; ANN, artificial neural network; CDFI, color doppler flow imaging; CKD, chronic kidney disease; LASSO, least absolute shrinkage and selection operator; LDA, linear discriminant analysis; ESWL, extracorporeal shock wave lithotripsy; CAKUT, congenital abnormalities of the kidney and urinary tract.

to enlarge the dataset, and four of these used transfer learning. Regarding the evaluation performance, most of the studies used internal validation, only eight studies had performed external tests using independent datasets. The median values of accuracy and AUC of these studies were approximately 0.88 and 0.96, respectively.

The risk of bias evaluated by using PROBAST demonstrated that 86% of AI-aided diagnosis or prediction models were classified into a high-risk group (Figure 4). Most of the studies were classified as low risk in domains

of participants, predictors, and outcome (62%, 83%, and 90%, respectively). However, in domains of analysis, high risk accounted for a higher ratio (62%). High risk factors included the lack of appropriate data sources (1.1) and a reasonable number of participants (4.1), inappropriate handling method for missing data (4.4), using univariable analysis for predictor selection (4.5), ignorance of the complexities in data (4.6), inappropriate evaluation of relevant model performance measures (4.7), and model overfitting, underfitting, and optimism (4.8).

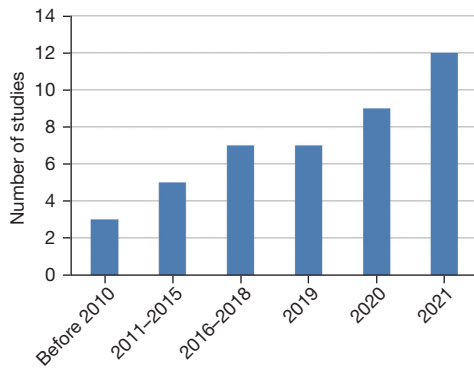


Figure 2 Studies on AI-aided ultrasound in renal diseases. AI, artificial intelligence.

Segmentation and detection

Image segmentation is often a first and essential stage for image analysis and further evaluation. In this qualitative synthesis, 10 studies of renal ultrasound image segmentation were identified. Five studies used 2D ultrasound images and five studies used three-dimensional (3D) ultrasound images. Only one of the studies evaluated the performance of the model using an individual testing set.

Seven studies focused on the innovation and efficiency of kidney segmentation algorithms (3,12-17). Wang *et al.* proposed a two-step level set method for segmentation of both the kidney boundary (distance regularized level set evolution) and kidney collecting system (region-scalable

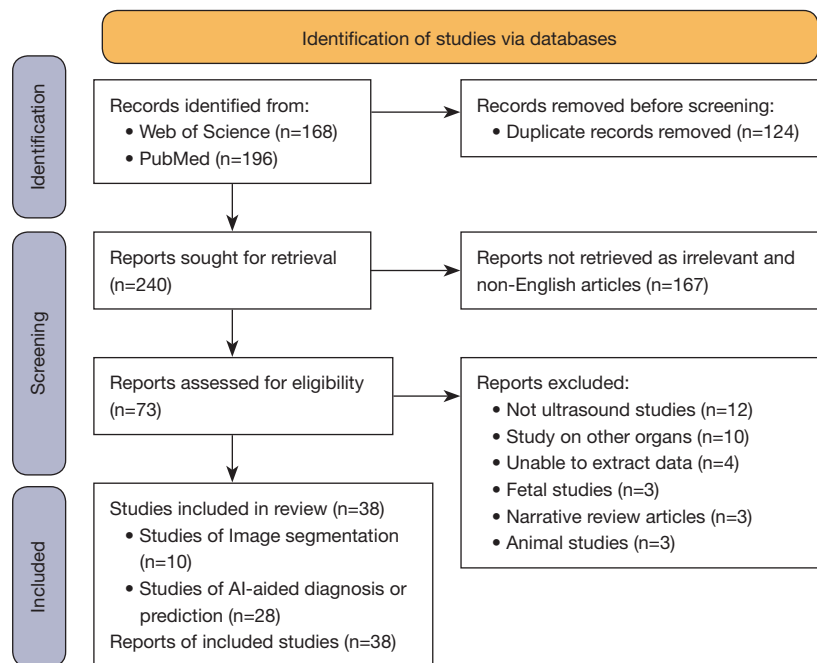


Figure 3 PRISMA flow diagram (flowchart presenting the selection process).

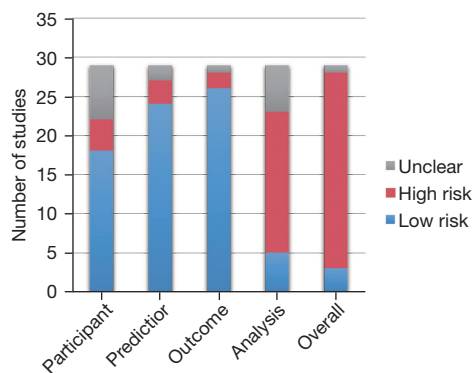


Figure 4 PROCAST risk of bias for AI-aided diagnosis or prediction studies. PROCAST, Prediction Model Risk of Bias Assessment Tool; AI, artificial intelligence.

fitting energy minimization) to determine the renal parenchymal area, and the SN score evaluated using ten cases was >0.9 (12). Yin *et al.* developed a boundary distance regression deep neural network for kidney segmentation, which extracted high-level image features using transfer learning (13). To improve the stability of kidney ultrasound image segmentation, Yin *et al.* found that the boundary detection strategy worked better than pixelwise classification techniques for segmenting clinical ultrasound images (14). The DICE score for these deep learning models achieved 0.93–0.94. Marsousi *et al.* combined prior knowledge of training shapes (shape-to-volume registration) and anatomical knowledge, to propose a detecting and segmenting method in 3D kidney ultrasound image segmentation. The detection accuracy was 92.86% (3,15).

Three studies focused on the segmentation of the kidney collecting (KS) system and quantitative kidney-hydronephrosis evaluation in children (18–20). Hydronephrosis index (HI) is a quantitative measurement of hydronephrosis severity, which was defined as the ratio of the collecting system area to the total area of the kidney collecting system and renal parenchyma (43). Kang *et al.* used a combination of improvements made to the active shape model framework and minimal user intervention to segment the KS system and computed the HI semi-automatically. The DICE score was >0.8 (18). Cerrrolaza *et al.* developed a variant of the popular active shape model considering brightness and contrast normalization, and positional prior information in 3D kidney image segmentation with a DICE score of 0.86 (19).

AI-aided renal ultrasound diagnosis and prediction

Differential diagnosis or identification of kidney diseases

In early studies, classifiers were trained for simple differential diagnosis among different lesions, or between normal and abnormal ultrasound performances. In this systematic review, 10 studies were identified for differential diagnosis or identification of kidney diseases (21–30). After image rotation, speckle noise removal, and normalization, AI methods could distinguish normal, cyst, kidney stone, tumor, hydronephrosis, nephrocalcinosis, and multicystic dysplasia rapidly with an accuracy range from 80% to 97% (21–25). Sudharson *et al.* introduced an ensemble of pretrained deep neural networks (DNNs) like ResNet-101, ShuffleNet, and MobileNet-v2 using transfer learning, and final predictions were done by using the majority voting technique. With an accuracy of 95–97%, it showed better classification performance than the individual models in the early and automatic diagnosis of kidney disorders (26). Sagreiya *et al.* used value-based SVM analysis to improve the ability of shear wave elastography in differentiating renal cell carcinoma from angiomyolipoma (27). The results of a study by Shin *et al.* indicated that texture analysis using features from the second-order statistics achieved an AUC greater than 0.89 for differentiating Wilms tumor from clear cell sarcoma and rhabdoid tumor (28).

CKD

CKD is defined as a chronic condition that causes kidney damage for more than three months or continuous kidney dysfunction. In clinical applications, CKD is usually identified through the glomerular filtration rate (GFR) test, especially when GFR is lower than 60 mL/min/1.73 m² for 3 months or more. Early and noninvasive detection is crucial to preventing or delaying the progression of CKD. In this systematic review, 12 studies were identified in this section, of which 10 referred to CKD and related diseases classification or screening (31–39,48) and two referred to complications after allograft renal transplantation (8,40). Iqbal *et al.* showed that texture feature obtained from the cortex region in ultrasound images was more significant than those obtained from the entire kidney or renal medulla in distinguishing between normal and CKD patients (48). Kuo *et al.* combined a deep neural network with a transfer learning technique to identify CKD status based on 4,505

kidney ultrasound images labeled using GFR. This AI-GFR estimation had reached a classification accuracy of 85.6% (31). Hao *et al.* proposed a novel approach named texture branch network containing both traditional texture features and deep features for CKD image screening. This scheme of fusing texture features and deep features combined with transfer learning was found to be suitable for an unbalanced small-sample dataset with an accuracy of 96% and a sensitivity of 99% (32). Li *et al.* used machine learning classifiers for the diagnosis of CKD based on value-based data of 2D, CDFI, and shear wave elastography (SWE). It showed that the elastic hardness parameter of the renal cortex was the most important, and the highest diagnostic accuracy of SVM was 80.98% (33). In a study by Zhang *et al.*, quantitative radiomics features based on kidney ultrasound images were associated with the histological classification of glomerulopathy, which could distinguish IgA nephropathy from membranous nephropathy (34). The ability of ultrasound-based prediction of kidney interstitial fibrosis and tubular atrophy using a deep learning framework was also demonstrated in a diagnostic evaluation of 6,135 images in a study by Athavale *et al.*, and the accuracy at the patient level was approximately 90% (35). In an assessment of kidney function after allograft transplantation, Abbasian *et al.* used 16 texture features extracted from 61 cases classified by the nearest neighbor classifier to identify the occurrence of transplant rejection, the AUC was 0.975 (8).

Pediatric application

The application of AI-aided renal ultrasound diagnosis in the pediatric domain mainly consisted of hydronephrosis in children (three studies) and CAKUT (three studies) (41-45,49,50). Lin *et al.* and Smail *et al.* used a deep learning approach to grade hydronephrosis ultrasound images and quantify the fluid and kidney areas automatically (41,42). Cerrolaza *et al.* introduced a semi-automated means which computed 131 morphological parameters (including size, geometric shape, and curvature) to define sonographic biomarkers for hydronephrotic renal units. As a consequence of a good performance (AUC 0.94–0.98), this method could potentially decrease the number of diuretic renograms in up to 62% of children (43).

Three studies of AI-aided CAKUT ultrasound diagnosis were identified, which were performed in the same single research center. CAKUT, including posterior urethral valves and kidney dysplasia, is the most common cause of end-stage renal disease in children (49). The diagnosis of

CAKUT is usually based on kidney size, hydronephrosis, abnormal kidney position, echogenicity of the kidney parenchyma, and ureter and bladder abnormalities (50). Zheng *et al.* developed a new model that combined pretrained deep features based on transfer learning with conventional imaging features to distinguish CAKUT from controls. The AUC of this approach achieved 0.92, which performed better than classifiers built on either the transfer learning features or the conventional features alone (44). Yin *et al.* introduced a multi-instance deep learning method for fast diagnosis of CAKUT with an AUC of 0.96, which was found to be better than classifiers built on either single sagittal images or single transverse images (45).

Discussion

In the clinical practice of renal ultrasound imaging, there are still some key problems that have not been resolved, such as quantitative analysis of CKD severity. In addition to improving the diagnosis efficiency of ultrasound, it is also significant to explore more image features, which could reflect the pathological type and features (46). In recent years, AI technology in medical imaging has involved the diagnosis of various diseases (51), and the use of AI technology in renal ultrasound has shown potential in addressing the problems above (52,53). In this systematic review, we have illustrated and analyzed the current status of AI-aided renal ultrasound from two important aspects: image segmentation and AI-aided diagnosis or prediction.

Image segmentation, which extracts regions of interest from the original image, helps characterize the tissue and further improves the efficiency of diagnosis; it is a reliable and essential procedure for ultrasound images (16,54,55). Speckle noise, acoustic shadow, and low contrast between kidneys and other tissues are problems in renal segmentation (12). Regardless of 2D or 3D images, because the kidney has a known shape and localization, the combination of prior knowledge of training shapes and anatomical knowledge proved superior in improving the accuracy of kidney detection and segmentation on ultrasound images (3). In kidney segmentation studies enrolled in this systematic review listed in *Table 1*, we found the studies using prior knowledge had great segmentation performance (3,19,20). In addition, image preprocessing using Gaussian filtering, wavelet-based filtering, etc. was reported to be effective in addressing the problems of speckle noises (15).

For AI-aided diagnosis or prediction studies, a serious

problem is whether the studies of AI-aided methods can be explainable and reliable for clinical application (56). The latest guidance on AI released by the World Health Organization in 2021 also defined “Ensure transparency, explainability, and intelligibility” as one of the six core principles (57). The systematic review shows that the focus of the research is switching to multicenter, big data studies, especially after 2019. Clinical problem-oriented research has become the focus of research involving AI technology in renal ultrasound. Nevertheless, based on the evaluation of PROBAST in the results, the unclear source of data, inadequate sample size, inappropriate analysis methods, and lack of rigorous external validation are found to be the most frequent and critical risk factors in AI-aided renal ultrasound studies. As known, overfitting is a common problem in studies with a small number of samples, which is caused by not only the small size of the dataset but also the small number of patients (58). However, in the period covered by the search, the number of patients was not mentioned in nearly a quarter of AI-aided renal ultrasound studies. From the aspects of data collected, the size and quality of sample data are both important in this kind of research. However, what sample size would be adequate for AI-aided ultrasound studies is still unclear and controversial. Some of the research followed the Widrow-Hoff learning rule, which suggested 10 data or patients for every image feature that would be used in the model, but this rule is very rough (59). In different clinical scenarios, the sample size estimate should take suitable crowd, the source of the data, data acquired equipment, and the type of sample into consideration, as well as data from the results of previous clinical studies. Furthermore, it suggested that prospective randomized data collected in hospital is preferred, rather than open-source data, which could help ensure generalization and repeatability of AI methods. Similarly, to avoid serious bias and overfitting, an effort should be made to perform AI-related clinical trials according to the requirement of the latest guidelines (60).

According to *Table 2*, we found only eight of 28 studies performed external tests using an independent dataset, and 17 of 28 studies performed an internal test. Although heat maps, feature visualization, prototypical comparisons, and other approaches or indicators have been used to illustrate the performance of AI techniques in medicine, it is difficult to avoid the influence of subjectivity (61). Based on highly validated performance requirements, rigorous internal and external validations are recommended for AI-

aided studies (62).

Abnormal and normal ultrasound image identification that can distinguish one lesion from another (such as computer-aided ultrasound diagnosis of normal, medical renal disease, and kidney cyst) automatically were popular in earlier studies (21-25). In general, the performance of the classification algorithms in these studies was impressive. However, because their ultrasound features were significantly different, these tasks were void of applicable clinical value. Since 2019, the evaluation of CKD using AI-aided ultrasound imaging has gradually become a hot topic. Although timely and effective treatment (like hemodialysis and kidney transplant) is the primary focus of CKD, of equal importance is the achievement of early detection (63). Still, it is difficult to make a quantitative diagnosis of CKD at an early stage; a GFR test based on blood serum creatine level (sCr) always changes significantly in CKD stages 3-5. In addition, the gold standard of CKD diagnosis is a biopsy, which is invasive with the risk of complications that hamper its general application (64). Texture features of renal ultrasound images, especially for the renal cortex, were various in different stages of CKD based on the changes in microstructure including fibrosis composition and lipid fraction (65). Thus, texture analysis has been widely reported as an effective approach to reducing interobserver variability. Unlike renal tumors, kidney stones, or other renal diseases, good performances of CKD evaluation using AI-aided renal ultrasound were demonstrated by studies that used different datasets. As for the future research trend in this field, according to the results of this systematic review, multicenter studies with big data should be considered for the evaluation of CKD using AI-aided renal ultrasound. For renal diseases with few reports, basic research on small and medium-sized samples should be performed to assess algorithm fitness and effectiveness.

There were also some limitations in this systematic review. First, the included studies in this review had high heterogeneity, which was caused by various clinical themes, AI methods, and the evaluation methods involved. Therefore, this systematic review only reflected the recent progress of the application of AI methods in renal disease, rather than any definite quantitative conclusion. Second, acute kidney injury was excluded in this review because the research involving the application of ultrasound in this disease is rarely reported. Last, although PubMed and Web of Science were selected as the databases in this review, a small number of AI studies published at preprint sites and

other databases were not included.

Conclusions

AI provides a novel efficient strategy for the evaluation and diagnosis of renal diseases. In this study, we conducted a systematic review to evaluate and analyze the trend in the application of AI techniques in renal ultrasound. The use of AI-based ultrasound systems in CKD and quantitative hydronephrosis diagnosis will be a promising possibility in the near future. It should be noted that to improve the stability and reliability, the sample size and image quality, rigorous external validation, and adherence to guidelines and standards should be carefully considered in future studies.

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Footnote

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Ethical Statement: The authors are accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

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