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Relationship between ultrasonographically determined renal dimensions and International Renal Interest Society stages in cats with chronic kidney disease

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Abstract

Background: The correlation between renal dimensions and renal function in cats with chronic kidney disease (CKD) is unclear.

Hypothesis/Objectives: To investigate the relationship between renal dimensions and CKD severity in cats using ultrasound examination.

Animals: Nineteen healthy cats and 30 cats with CKD.

Methods: Renal ultrasound images obtained between 2012 and 2016 were reviewed. Severity of CKD was determined using the International Renal Interest Society CKD staging system. Renal length, cortical thickness, medullary thickness, and corticomedullary ratio were measured, and the relationship between these renal dimensions and serum creatinine concentrations as well as differences in dimensions between the control and disease groups was investigated. The sensitivity and specificity of the renal dimensions for differentiation of the CKD also were evaluated.

Results: The disease group was subdivided into stage I to II (15 cats) and stage III to IV (15 cats) groups. Cortical thickness was significantly decreased in both disease groups and negatively correlated with disease severity. Compared with other renal dimensions, cortical thickness had a stronger linear correlation with the reciprocal of the serum creatinine concentration and superior diagnostic performance (Youden index: left kidney, 90.0% sensitivity and 94.7% specificity for a cutoff of 4.7 mm; right kidney, 83.3% sensitivity and 94.7% specificity for a cutoff of 4.5 mm).

Conclusions and Clinical Importance: Decreased renal cortical thickness is observed in cats with loss of renal function. Measurement of cortical thickness using ultrasonography could be a useful method to evaluate the progression of CKD in cats.

KEYWORDS
corticomedullary ratio, renal cortical thickness, renal length, renal medullary thickness

Abbreviations: AUROC, area under the receiver operating characteristic curve; C/M, corticomedullary; CKD, chronic kidney disease; GFR, glomerular filtration rate; ICC, intraclass correlation coefficient; ROC, receiver operating characteristic.

Gong-Yi Yan and Kuan-Yo Chen contributed equally to this study.

1 | INTRODUCTION

Chronic kidney disease (CKD) is a long-term disease characterized by structural or functional abnormalities or both in 1 or both kidneys. The disease course generally is 3 months or longer.[1] Although CKD can develop at any age, its prevalence is higher in older cats than in younger cats,[2-4] with a previous study reporting prevalences of 62.5% and 39.1% in cats aged >10 years and <10 years, respectively.[2]

In clinical practice, serum creatinine concentration is a widely used surrogate marker for glomerular filtration rate (GFR). However, it has several limitations and can be affected by nonrenal factors.[5] Furthermore, a previous study found no significant linear association between serum creatinine concentration and GFR in cats ($P < .001$, $r^2 = 0.25$).[5] The same study, however, found that the reciprocal of the serum creatinine concentration had a strong linear association with GFR ($P < .001$, $r^2 = 0.43$).[5]

In clinical practice, ultrasound examination is used for initial evaluation of renal structure in patients with CKD. It can be used to facilitate the diagnosis of potentially reversible causes (eg, postrenal obstruction), to evaluate the risk and necessity of ultrasound-guided renal biopsy, and to measure renal dimensions as prognostic factors.[6,7] In the last decade, many studies have evaluated the usefulness of renal cortical thickness measured by ultrasonography as an indicator of renal function loss in human patients with CKD.[8-10] Results of these studies indicated that a decrease in renal cortical thickness was significantly associated with loss of renal function (estimated GFR) in the early stages of CKD, whereas a decrease in medullary thickness only was associated with renal function loss in later stages of the disease.[8-10] Furthermore, thinning of the renal cortex showed stronger correlation with renal function than did renal length, which suggested that renal function loss in human patients with CKD is better predicted by renal cortical thickness than by renal length.[8-10]

To date, no published study in veterinary medicine has evaluated the correlation between renal cortical thickness and renal function in cats with CKD. We hypothesized that the relationship observed in humans also would be observed in cats, and that ultrasonography would be a reproducible and noninvasive method for renal function prediction and monitoring in cats with CKD. Therefore, our aim was to evaluate the relationship between renal function and ultrasonographically determined renal dimensions, including renal length, cortical thickness, medullary thickness, and corticomedullary (C/M) ratio in cats with CKD.

2 | MATERIALS AND METHODS

This study was approved by the Institutional Animal Care and Use Committee (approval No. 105-065) at National Chung Hsing University.

2.1 | Control group

Twenty-eight cats (13 spayed females, 13 neutered males, 1 intact male, and 1 intact female) aged 1 to 8 years and weighting 3.4 to 7.5 kg were recruited with their owners' consent as a control group. Characteristics, such as sex, age, body weight, and breed, were recorded for all cats, all of which also underwent physical examination, blood pressure measurement, hematocrit measurement, serum biochemical and electrolyte measurements, ultrasound examination of the urinary system, and ultrasound-guided cystocentesis for routine urinalysis. Exclusion criteria based on the results of these examinations were as follows: serum creatinine concentration > 1.6 mg/dL, anemia (hematocrit < 30%), proteinuria (urine protein : creatinine ratio > 0.2), suspected urinary tract infection (>5 white blood cells/high power field or bacteria seen in the urinary sediment), systolic blood pressure > 180 mm Hg, or renal abnormalities on ultrasound examination (irregular renal margins, cysts, nephrolithiasis, nephrocalcinosis, pyelectasia, loss of the C/M demarcation, or some combination of these). Nine cats were excluded because of serum creatinine concentration >1.6 mg/dL.

2.2 | Disease group

The medical records database of the hospital was retrospectively reviewed to retrieve the records of cats that were clinically diagnosed with CKD between January 2012 and December 2016. Cats with at least 2 stable serum creatinine concentration (<25% differences from the previous result) obtained within a 30-day period were considered eligible. If the serum creatinine concentration showed marked changes indicating instability, the cats were excluded. Other exclusion criteria included renal structural abnormalities (eg, hydronephrosis, neoplasia, polycystic kidney disease, solitary cysts with diameter >5 mm), hyperthyroidism (serum thyroxine concentration > 4 μg/dL), diabetes mellitus (persistent hyperglycemia [>300 mg/dL] combined with glucosuria), or other systemic diseases.

The cats enrolled in the CKD disease group were staged according to the International Renal Interest Society (IRIS) CKD guidelines. Stage I disease was defined by a serum creatinine concentration <1.6 mg/dL and the presence of 1 of the following: urine specific gravity <1.035, renal abnormalities on diagnostic imaging (eg, cysts, irregular margins), and proteinuria. Stages II, III, and IV were defined by serum creatinine concentrations of 1.6 to 2.8 mg/dL, 2.9 to 5.0 mg/dL, and >5.0 mg/dL, respectively. On the basis of stage, the cats in the CKD disease group were subdivided into stage I to II and stage III to IV groups.

2.3 | Ultrasound examination

All images and cine loop clips were acquired using an ultrasound machine (Xario SSA-660A, Toshiba Medical Systems Corporation, Japan) with a 7.2 to 14 MHz linear transducer (PLT-1204 BT, Toshiba Medical Systems Corporation, Otawara-shi, Japan), and retrieved from the Picture Archiving and Communication System in the teaching hospital. In the control group, cine loop clips of complete scans of each kidney in the dorsal, longitudinal, and transverse planes were obtained by a first-year radiology resident with 1 year of experience in ultrasonography. The scanning technique used has been described previously.[11] In the true dorsal view, the renal pelvis is visible at the medial aspect of the kidney in the long axis. In the longitudinal plane, the central renal sinus is not visible, but 2 hyperechoic lines formed by cross-sectioned renal pelvic diverticula can be seen. The size of the cranial and caudal poles of the kidney should be similar in the dorsal and longitudinal planes. The transverse plane is at an angulation of 90° to the longitudinal and dorsal planes at the level of the renal hilus, and includes the V- or U-shaped renal crest at the apex of the renal medulla. Each plane included cine loop clips of the real-time B-mode and color Doppler mode. In the disease groups, ultrasonography was performed during a period when serum creatinine concentration was stable. At least 2 planes of still renal images (longitudinal/dorsal and transverse) or cine loop clips of both kidneys were evaluated for all included cases.

2.4 | Measurement and evaluation of renal dimensions

All renal dimensions for the cats in the control group were measured by 2 observers, a radiologist and a second-year graduate student of radiology with a 1.5 years of experience in diagnostic imaging. Neither of these investigators participated in the ultrasound examinations performed by the first-year resident. Both observers used the same digital imaging and communications in medicine viewer software Horos (v.2.0.2; The Horos Project) for obtaining the measurements. Renal length was measured from the cranial pole to the caudal pole in the largest longitudinal plane (Figure 1A), where the cranial and caudal poles of the kidney were similar in size. Renal dimensions in the dorsal and transverse planes of each kidney also were measured for statistical analysis (Figure 1B,C). The arcuate blood vessel was used for identification of the C/M junction between the renal cortex and medulla. Renal cortical and medullary thickness were measured in the dorsal and transverse planes at the mid-kidney level. The cortex was measured from the lateral margin (not including the hyperechoic renal capsule) to the margin of the arcuate blood vessel (not including the vessel), and the medulla was measured from the arcuate blood vessel (including the vessel) to the V- or U-shaped renal crest. All of the measurements were performed by each observer individually. The observers determined the frames that showed the true longitudinal, dorsal, or transverse views for performing measurements from the cine loop clips individually. Each renal dimension was measured 3 times and averaged. The C/M ratio was calculated as the thickness of the cortex divided by that of the medulla.

In the disease groups, the 2 observers were blinded to the patient's clinical information and status and measured bilateral renal dimensions. The measurement methods and variable (renal length, cortex thickness, and medullary thickness) were the same as those used for the control group. However, if the renal margins were irregular, the longest renal length was measured from the longitudinal view (Figure 2A). Cine loop clips with color Doppler were used to locate the arcuate blood vessel if it was not well defined (Figure 2B), and the cortical and medullary measurements included the thickest and thinnest points and the values were averaged (Figure 2C). All measurements of renal dimensions in the control and disease groups were performed twice at 2-day intervals with each observer evaluating the same still images and cine loop clips.

Pyelectasia was evaluated from the transverse plane in the disease and control groups. Any fluid visible in the renal pelvis with the pelvic diameter >0 mm was considered pyelectasia.[12] The percentages of patients with pyelectasia in the disease and control groups were calculated.

2.5 | Statistical analysis

Commercially available software, SAS (version 9.4, SAS Institute, Inc, Cary, North Carolina) and GraphPad Prism (version 5.01, GraphPad Software, Inc), were used for data analysis and graphing. The normality of all continuous variables was tested using the Shapiro-Wilk normality test; all variables passed the test. Therefore, all continuous variables are presented as mean ± analysis of variance (ANOVA [SD and range]). Differences in the proportional distribution of categorical variables among groups were evaluated using the Chi-square

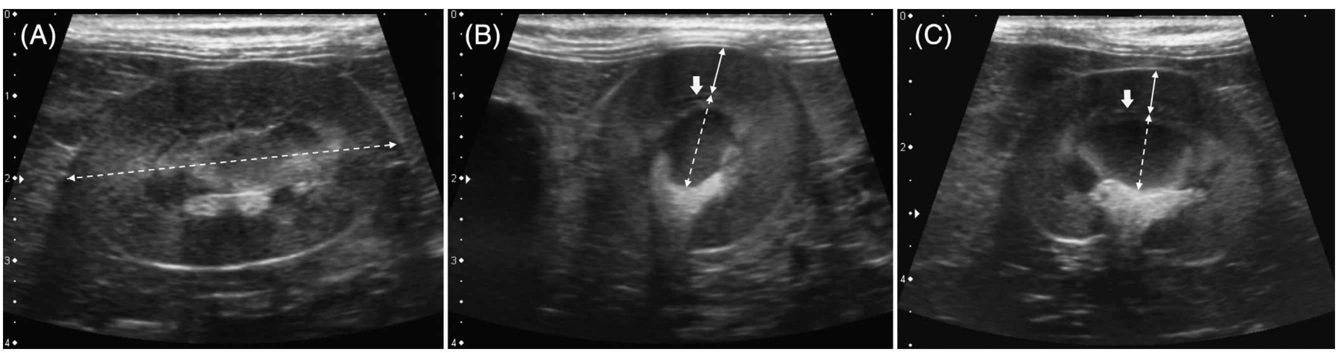

FIGURE 1 Ultrasound measurement of the renal length, cortical thickness, and medullary thickness in the, A, longitudinal, B, transverse, and, C, dorsal planes for cats in the control group. A, The double-headed dashed arrow shows the measurement of the renal length. B,C, The double-headed dashed arrow shows the measurement of the renal medullary thickness. The solid double-headed arrow shows the measurement of the cortical thickness. The arrow indicates the arcuate blood vessel for identification of the corticomedullary junction

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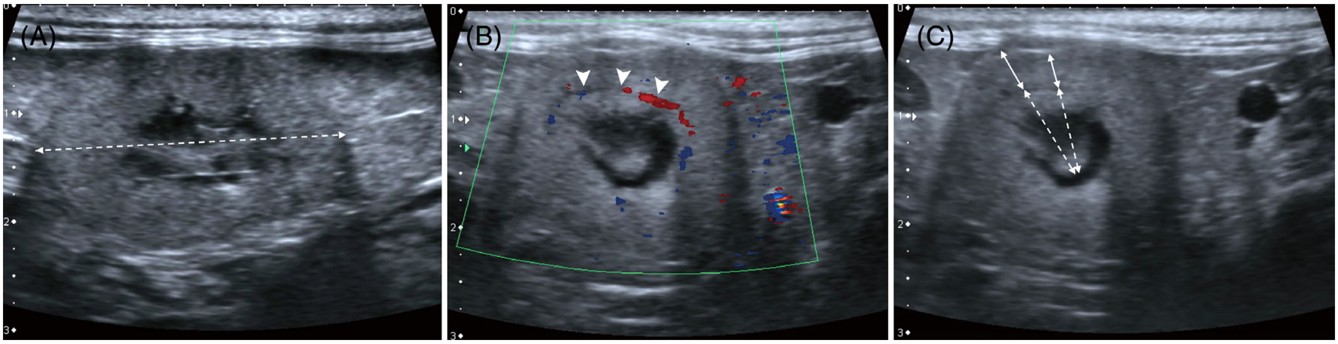

FIGURE 2 Illustration of ultrasound measurement of renal dimensions in a CKD cat with irregular renal margins. A, The longest renal length (double-headed dashed arrow) is measured in the longitudinal plane. B, The arcuate blood vessels (arrowheads) are identified using color Doppler to locate the corticomedullary junction in the transverse plane. C, The cortical (solid double-headed arrows) and the medullary thickness (double-headed dashed arrows) measured from the thickest and thinnest points were averaged (similar plane to B). CKD, chronic kidney disease; P, pyelectasia

TABLE 1 Signalment and serum creatinine of cats with (stage I-II and stage III-IV groups) or without CKD (control group)

	Control group n = 19	Stage I-II n = 15	Stage III-IV n = 15	*P* value
Age (y), mean ± SD (range)*	3.9 ± 1.73[a] (2-8)	11.2 ± 4.6[b] (4-17)	11.0 ± 4.1[b] (5-20)	<.001
Female ratio	0.56	0.60	0.27	.15
Body weight (kg), mean ± SD (range)*	4.88 ± .97[a] (3.4-6.7)	4.29 ± 1.43[a,b] (2.2-7.0)	3.62 ± 1.13[b] (2.1-6.1)	.01
Serum creatinine (mg/dL), mean ± SD (range)*	1.44 ± .12[a] (1.2-1.6)	1.84 ± .58[a] (.7-2.7)	4.63 ± .93[b] (3.0-6.0)	<.001
Species	DSH	DSH	DSH	.16
	(14/19, 73.7%)	(9/15, 60%)	(9/15, 60%)	
	ASH	ASH	Persian	
	(3/19, 15.7%)	(1/15, 6.7%)	(1/15, 6.7%)	
	BSH	Persian	Chinchilla	
	(1/19, 5.3%)	(2/15, 13.3%)	(5/15, 33.3%)	
	Chinchilla	Chinchilla		
	(1/19, 5.3%)	(3/15, 20%)		

Abbreviations: ASH, American shorthair, BSH: British shorthair; CKD, chronic kidney disease; DSH, domestic shorthair.
*Significant difference (P < .05) as per the Kruskal-Wallis test. Different letters indicate significant differences (P < .05) in the same row (Dunn's post-hoc test).

test or Fisher's exact test. Intra- and interobserver agreements for bilateral renal cortical thickness, medullary thickness, and renal length measurements were evaluated by calculation of intraclass correlation coefficients (ICCs). Two measurements were performed by each observer for calculation of the intraobserver ICC; these measurements were averaged for calculation of the interobserver ICC in the control and disease groups. One-way ANOVA was used to determine the presence of significant differences in renal dimensions between the control group and the 2 disease groups. Multiple linear regression was used to analyze the correlation of each dimension with age, body weight, and sex in the control group. In addition, Pearson's linear correlation coefficients were calculated to determine the correlation of each dimension with the reciprocal of the serum creatinine concentration. The diagnostic performance of the renal dimensions in terms of differentiation between cats with CKD and control cats and among different dimensions was tested by receiver operating characteristic (ROC) curve analysis using IBM SPSS Statistics 19 (IBM Corporation, Somers, New York). Area under the ROC curve (AUROC) and various cutoffs also were calculated and expressed with 95% confidence intervals (CIs). Comparisons of AUROC among different renal dimensions were tested using DeLong nonparametric tests. The best cutoff for each dimension was determining by calculation of the Youden index (sensitivity + specificity − 1). A P value of <.05 was considered statistically significant.

3 | RESULTS

Nineteen clinically healthy cats (9 neutered males, 1 intact male, 8 spayed females, and 1 intact female) were enrolled in the control

TABLE 2 Intra- and interobserver agreements for renal dimensions measured using ultrasound for cats without CKD (control group)

	ICC (95% CI)	ICC (95% CI)	ICC (95% CI)
Transverse plane	Intraobserver 1	Intraobserver 2	Interobserver
LK cortex	0.87* (0.70-0.95)	0.88* (0.72-0.95)	0.86* (0.67-0.94)
LK medulla	0.94* (0.84-0.98)	0.74* (0.42-0.89)	0.67* (0.30-0.86)
LK C/M ratio	0.82* (0.58-0.93)	0.78* (0.52-0.91)	0.64* (0.27-0.85)
RK cortex	0.90* (0.75-0.96)	0.93* (0.82-0.97)	0.90* (0.75-0.96)
RK medulla	0.76* (0.46-0.90)	0.81* (0.56-0.93)	0.56* (0.14-0.81)
RK C/M ratio	0.92* (0.81-0.97)	0.86* (0.68-0.95)	0.61* (0.21-0.83)
Dorsal plane			
LK cortex	0.91* (0.77-0.96)	0.92* (0.80-0.97)	0.80* (0.55-0.92)
LK medulla	0.91* (0.78-0.97)	0.80* (0.54-0.92)	0.55* (0.13-0.81)
LK C/M ratio	0.86* (0.69-0.95)	0.82* (0.59-0.93)	0.34 (−0.13 to 0.69)
RK cortex	0.89* (0.72-0.96)	0.92* (0.80-0.97)	0.83* (0.60-0.93)
RK medulla	0.89* (0.73-0.96)	0.86* (0.66-0.94)	0.66* (0.30-0.86)
RK C/M ratio	0.82* (0.59-0.93)	0.86* (0.67-0.95)	0.77* (0.49-0.91)

Note: ICC: poor < 0.5, satisfactory 0.5 to 0.74, excellent > 0.75.
Abbreviations: C/M, corticomedullary ratio; CI, confidence interval; CKD, chronic kidney disease; ICC, interclass correlation coefficient; LK, left kidney; RK, right kidney.
*Statistical significance $P < .05$.

TABLE 3 Renal dimensions measured using ultrasound for cats without chronic kidney disease (control group) by the radiologist's measurements

Renal dimension	Transverse plane	Range
LK cortex (mm)	5.33 ± 0.43	4.28-5.8
LK medulla (mm)	12.33 ± 1.04	10.61-13.99
LK C/M ratio	0.43 ± 0.05	0.33-0.44
RK cortex (mm)	5.22 ± 0.56	4.30-6.47
RK medulla (mm)	12.42 ± 0.84	11.08-14.07
RK C/M ratio	0.42 ± 0.05	0.34-0.54
Dorsal plane		
LK cortex (mm)	5.28 ± 0.44	4.46-6.08
LK medulla (mm)	12.52 ± 1.35	9.41-14.66
LK C/M ratio	0.43 ± 0.05	0.33-0.54
RK cortex (mm)	5.33 ± 0.58	4.48-6.35
RK medulla (mm)	11.98 ± 1.15	9.58-13.51
RK C/M ratio	0.48 ± 0.06	0.36-0.57
Longitudinal plane		
LK length	37.78 ± 3.52	32.00-43.72
RK length	39.94 ± 3.30	34.67-46.12

Note: All data are presented as mean ± SD.
Abbreviations: C/M, corticomedullary ratio; LK, left kidney; RK, right kidney.

group (Table 1); these included 14 domestic shorthairs, 3 American shorthairs, 1 British shorthair, and 1 Chinchilla. Mean age was 3.9 ± 1.73 years (range, 2-8 years) and mean body weight was 4.88 ± .97 kg (range, 3.4-6.7 kg).

Eighty-two cats with CKD were reviewed from the medical record database. Cats with the following diseases and conditions were excluded: hydronephrosis (n = 8), polycystic kidney disease (n = 9), no stable serum creatinine concentration (n = 8), pre-existing systemic disease (n = 17), or neoplasms (n = 10). Thirty cats were included in the 2 disease groups (Table 1), with 15 cats in the stage I to II group (6 with CKD stage I and 9 with CKD stage II) and 15 cats in the stage III to IV group (8 with CKD stage III and 7 with CKD stage IV).

In the stage I to II group, there were 6 neutered males, 6 spayed females, and 3 intact females; these included 9 domestic shorthairs, 1 American shorthair, 2 Persians, and 3 Chinchillas. Mean age and body weight were 11.2 ± 4.6 years (range, 4-17 years) and 4.29 ± 1.43 kg (range, 2.2-7.0 kg), respectively.

In the stage III to IV group, there were 6 neutered males, 4 intact males, 4 spayed females, and 1 intact female; these included 9 domestic shorthairs, 1 Persian, and 5 Chinchillas. Mean age and body weight were 11.0 ± 4.1 years (range, 5-20 years) and 3.62 ± 1.13 kg (range, 2.1-6.1 kg), respectively. Fisher's exact test found no significant differences in the distribution of sex ($P = .2$), reproductive status ($P = .3$), and breed ($P = .2$) among the 3 groups.

3.1 | Reproducibility of renal dimension measurements in the control group

The intra- and inter-observer agreement of renal dimension measurements was evaluated in the control group (Table 2). Excellent intraobserver agreement (ICC > 0.75) was found for most renal measurements; agreement for left medullary thickness measured by the radiologist in the transverse plane showed satisfactory agreement

TABLE 4 Intra- and interobserver agreements for renal dimensions measured using ultrasound for cats with chronic kidney disease

	ICC (95% CI)	ICC (95% CI)	ICC (95% CI)
Transverse plane	Intraobserver 1	Intraobserver 2	Interobserver
LK cortex	0.81* (0.63-0.90)	0.76* (0.56-0.88)	0.85* (0.71-0.93)
LK medulla	0.85* (0.71-0.93)	0.86* (0.72-0.93)	0.88* (0.77-0.94)
LK C/M ratio	0.44* (0.09-0.69)	0.59* (0.29-0.78)	0.39* (0.04-0.66)
RK cortex	0.79* (0.60-0.89)	0.74* (0.51-0.87)	0.87* (0.74-0.94)
RK medulla	0.71* (0.47-0.85)	0.75* (0.54-0.87)	0.81* (0.64-0.91)
RK C/M ratio	0.64* (0.36-0.81)	0.52* (0.19-0.74)	0.36* (0.01-0.64)

Note: ICC: poor < 0.5, satisfactory 0.5 to 0.74, excellent > 0.75.
Abbreviations: C/M, corticomedullary ratio; CI, confidence interval; ICC, interclass correlation coefficient; LK, left kidney; RK, right kidney.
*Statistical significance *P* < .05.

TABLE 5 Results of multiple linear regression analysis for the correlation between renal dimensions and age, body weight, and sex in cats without chronic kidney disease (control group)

	Age		Body weight		Sex		
Renal dimensional indices	*P* value	*β* coefficient	*P* value	*β* coefficient	*P* value	*β* coefficient	r^2
LK length	**.02**	−.99	.27	.79	**.04**	−2.80	0.41
RK length	.11	−.56	.17	.84	**.003**	−3.87	0.51
LK cortex	.07	−.11	.23	.12	.27	−.21	0.20
RK cortex	.15	−.11	.16	.19	.21	−.32	0.19
LK medulla	.48	.11	.19	.36	.71	−.19	0.02
RK medulla	.19	.16	.31	.22	.73	−.14	0.05
LK C/M ratio	.18	−.01	.70	−.01	.57	−.02	0.01
RK C/M ratio	.08	−.01	.52	.01	.38	−.02	0.13

Note: Sex is a categorical variable. A negative value indicates that the dimension is smaller in female cats. The renal length was measured in the longitudinal plane while the other dimensions were measured in the transverse plane. *P* values < .05 are shown in bold.
Abbreviations: C/M, corticomedullary ratio; LK, left kidney; RK, right kidney.

(ICC = 0.74). These results indicated that the measurements in the transverse and dorsal planes were consistent for an individual observer. Excellent interobserver agreement was found for cortical thickness and right C/M ratio. Although the agreements for medullary thickness and left C/M ratio were lower than those for the other dimensions, they still were satisfactory. Only left C/M ratio measured in the dorsal plane did not exhibit satisfactory agreement. Measurement of each renal dimension in the control group also was measured by the 2 observers and showed no statistically significant difference between the observers (calculated by *t*-test, *P* > .05). Measurements of each renal dimension are presented in Table 3.

3.2 | Reproducibility of renal dimension measurements from the transverse plane in the disease group

The intra- and interobserver agreement of renal dimension measurements also was evaluated in the disease group (Table 4). Excellent intra- and interobserver agreement (ICC > 0.75) was found for most of the renal measurements, but poor intra- and interobserver agreement was found for measurement of the C/M ratio.

Multiple linear regression analysis showed that left renal length was significantly correlated with age (*P* = .02) and sex (*P* = .04), whereas right renal length was correlated only with sex (*P* = .003), indicating that the female cats had shorter renal length. Renal cortical thickness, medullary thickness, and C/M ratio on both sides showed no significant correlations with age, body weight, or sex (Table 5).

All renal dimensions are presented as mean ± SD (range) in Table 6. Left renal length was significantly different between the control and stage I to II groups (*P* = .01). No significant intergroup differences were found in left (*P* = .3) and right (*P* = .4) medullary thicknesses. Right renal length was comparable (*P* = .01) between the 2 disease groups. Both left and right cortical thicknesses and C/M ratios showed significant differences (*P* < .001) between the control group and the 2 disease groups. Right renal length was greater than left renal length for 16 of the 19 (84.2%) cats in the control group, but this difference was not statistically significant (*P* = .2). Pyelectasia was detected in the left (63.3% and 15.8%) and right kidney (50.0% and 5.3%) in the disease group and control groups, respectively.

Based on linear regression analysis (Figure 3), left and right cortical thicknesses showed moderate to strong linear association (left: $P < .001$, $r^2 = 0.36$; right: $P < .001$, $r^2 = 0.35$) with the reciprocal of the serum creatinine concentration. Left and right medullary thickness did

TABLE 6 Renal dimensions measured using ultrasound for cats with (stage I-II and stage III-IV groups) or without CKD (control group)

Renal dimension	Control group n = 19	Stage I-II n = 15	Stage III-IV n = 15	P value
LK length(mm)*	37.46 ± 3.44[a]	31.99 ± 3.78[bc]	34.86 ± 7.68[ac]	.01
RK length(mm)*	38.90 ± 3.09[ac]	34.82 ± 5.42[bc]	33.65 ± 7.78[b]	.02
LK cortex(mm)*	5.32 ± 0.39[a]	3.80 ± 0.86[b]	3.74 ± 0.70[b]	<.001
RK cortex(mm)*	5.27 ± 0.54[a]	3.90 ± 0.59[b]	3.614 ± 0.94[b]	<.001
LK medulla (mm)	12.71 ± 1.22	11.65 ± 2.13	12.02 ± 2.33	.23
RK medulla (mm)	12.47 ± 1.04	11.63 ± 2.00	11.58 ± 2.87	.37
LK C/M ratio*	0.42 ± 0.04[a]	0.33 ± 0.05[b]	0.316 ± 0.61[b]	<.001
RK C/M ratio*	0.44 ± 0.05[a]	0.34 ± 0.07[b]	0.313 ± 0.03[b]	<.001

Note: All values passed the Shapiro-Wilk test for normality and are presented as mean ± SD (range). The renal length is measured in longitudinal view and the other renal dimensional indices were measured in transverse view. Different letters indicate significant differences in the same row.
Abbreviations: C/M, corticomedullary ratio; CKD, chronic kidney disease; LK, left kidney; RK, right kidney.
*Significant difference < .05 was calculated with one-way analysis of variance test.

not show a significant linear association (left: $P = .23$, $r^2 = 0.03$; right: $P = .11$, $r^2 = 0.05$). Left ($P < .001$) and right ($P = .03$) renal lengths showed significant linear associations, but the association of right renal length was weak ($r^2 = 0.12$) whereas that of left renal length was very weak ($r^2 = 0.02$). Both left and right C/M ratios showed moderate linear associations (left: $P = .002$, $r^2 = 0.26$; right: $P < .001$, $r^2 = 0.30$).

The ROC curve analysis of each renal dimension (Figure 4) and the sensitivity and specificity for various cutoffs (Table 7) were calculated. Renal cortical thickness had superior diagnostic performance compared to other renal dimensions. Left (AUROC = 0.95, 95% CI = 0.84-0.99) and right (AUROC = 0.93, 95% CI = 0.81-0.98) cortical thicknesses showed excellent diagnostic performances. For the left kidney, the AUROC of renal cortical thickness was significantly higher than that of medullary thickness ($P < .001$) and length ($P = .001$), whereas the AUROC of the C/M ratio was significantly higher than that of medullary thickness ($P = .01$) and length ($P = .03$). For the right kidney, the AUROC of renal cortical thickness was significantly higher than that of medullary thickness ($P < .001$) and length ($P = .01$); the AUROC of the C/M ratio was significantly higher than that of medullary thickness ($P = .01$) whereas the AUROC of medullary thickness was significantly higher than that of renal length ($P = .04$). The optimal cutoff for left cortical thickness was 4.7 mm with 90.0% sensitivity and 94.7% specificity, and the optimal cutoff for right cortical thickness was 4.5 mm with 83.3% sensitivity and 94.7% specificity.

4 | DISCUSSION

We found that renal cortical thickness was associated with renal function in cats with CKD, a finding that is already has been established for human patients. Moreover, measurement of cortical thickness using ultrasonography was reproducible, with satisfactory to excellent intra- and interobserver agreements relative to those for the C/M ratio. In addition, although renal length is used clinically to evaluate the severity of CKD and renal atrophy in cats, our study showed that renal cortical thickness exhibits better correlation with disease severity than does renal length. The diagnostic performance of cortical thickness for cats with CKD also was better than that of the other renal dimensions, including renal length, similar to findings for human patients with CKD.[8-10]

Measurement of renal dimensions was feasible, particularly in the transverse plane, as evidenced by satisfactory to excellent intra- and interobserver agreement relative to measurements in the dorsal plane in the control group. Therefore, renal dimensions in the disease group were measured only from the transverse plane. Additionally, the longitudinal plane was not included for measurements of renal dimensions because the full thickness of the renal medulla could not be evaluated because the renal crest was not visible in this plane.

Measurement of medullary thickness was more difficult than was measurement of cortical thickness in both the transverse and dorsal planes, because the exact margin of the medulla adjacent to the renal sinus was not always distinct, as previously described.[13] Thus, interobserver agreement for medullary thickness measurements was not as good as that for cortical thickness measurements. In the disease group, intra- and interobserver agreement in the measurement of cortical thickness was slightly less than in the control group. This difference could be explained by indefinite locations of the arcuate blood vessels and irregular contours, rendering measurement of cortical thickness relatively difficult. However, intra- and interobserver agreement in the measurement of medullary thickness in the disease group was higher than in the control group. Because a higher percentage of patients with pyelectasia was found in the disease group (which could be caused by the diuretic effect of CKD), the margin of the renal crest might become more defined by fluid in the renal pelvis, possibly making it easier to measure medullary thickness in the disease group.

In the control group, left and right renal lengths were 3.74 ± 0.34 cm (range, 3.16-4.32 cm) and 3.89 ± 0.30 cm (range, 3.39-4.52 cm), respectively. Thus, both lengths were within the reported reference range (3.0-4.3 cm).[13-17] Some previous studies showed that right renal length is significantly higher than the left renal length.[14,17,18] However, we found no significant difference, although the mean value for right renal length was larger than that for left renal length, and most of the cats in the

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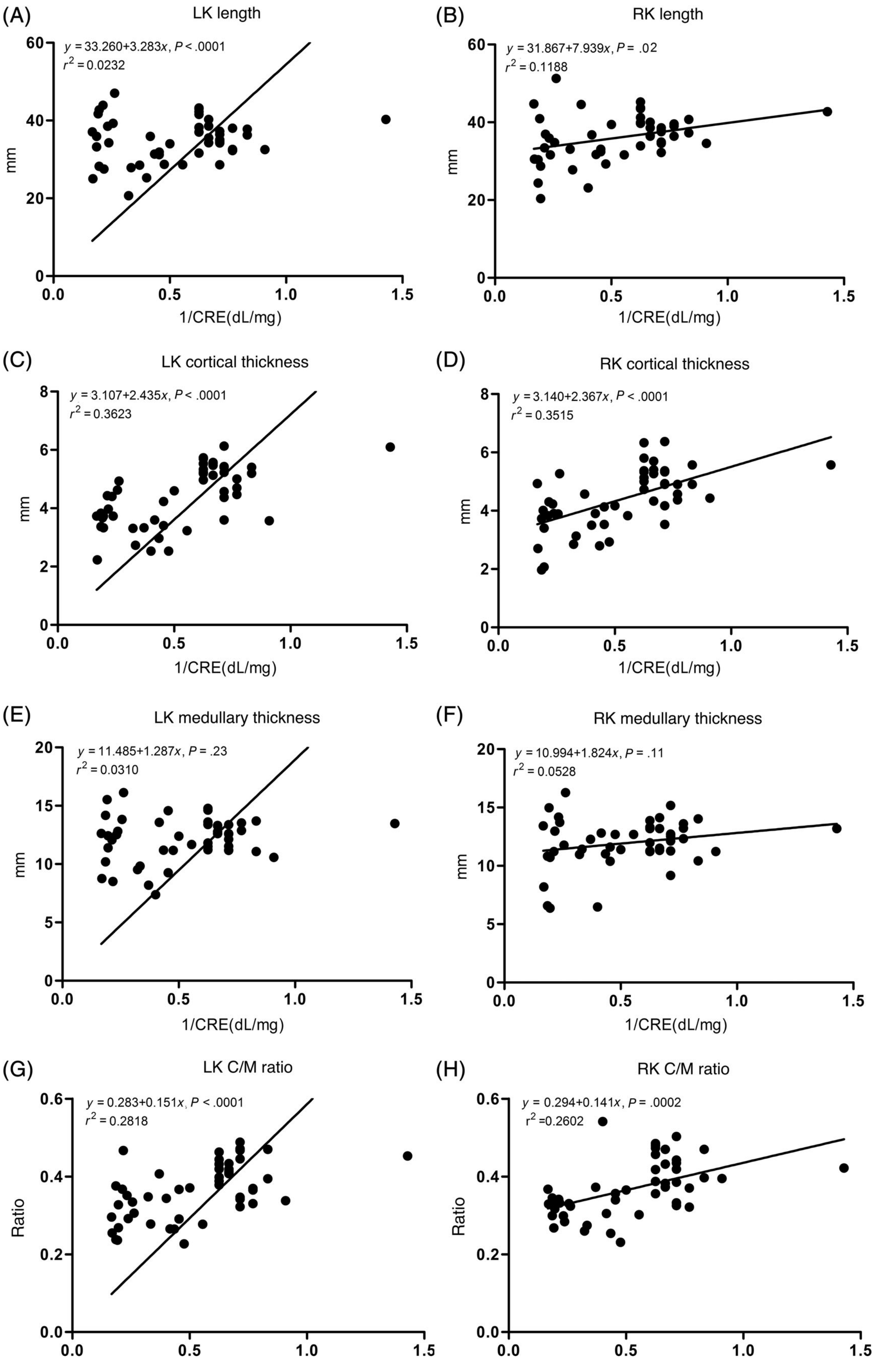

FIGURE 3 Legend on next page.

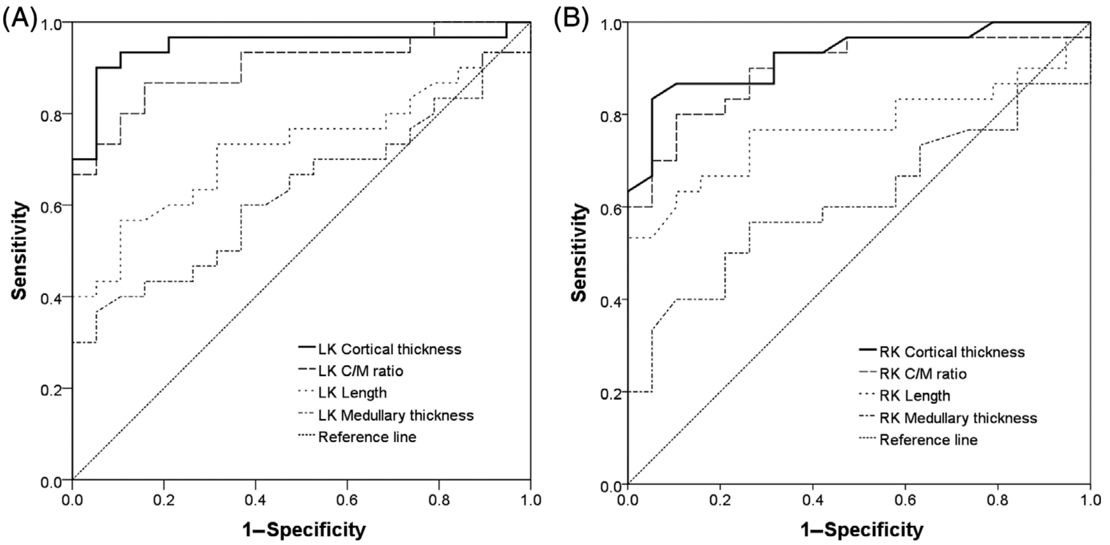

FIGURE 4 Receiver operating characteristic curve analysis of the, A, left and, B, right renal dimensions for renal function evaluation in cats. The AUROC of the left and right renal cortical thickness is 0.95 (95% CI = 0.84-0.99) and 0.93 (95% CI = 0.81-0.98), respectively. The AUROC of the left and right renal C/M ratio is 0.90 (95% CI = 0.78-0.97) and 0.90 (95% CI = 0.78-0.97), respectively. The AUROC of the left and right renal length is 0.73 (95% CI = 0.58-0.84) and 0.77 (95% CI = 0.63-0.88), respectively. The AUROC of the left and right renal medullary thickness is 0.63 (95% CI = 0.48-0.76) and 0.61 (95% CI = 0.46-0.75), respectively. The ROC curve of the left and the right renal cortical thickness is above and to the left of the other ROC curves at almost all values, indicative of superior sensitivity and specificity to other renal dimensions. AUROC: poor (0.60-0.70), fair (0.70-0.80), good (0.80-0.90), and excellent (0.90-1.00). AUROC, area under the receiver operating characteristic curve; C/M, corticomedullary ratio; CI, confident interval; LK, left kidney; RK, right kidney; ROC, receiver operating characteristic

control group (84.2%) exhibited higher right renal length. The reason for these different results could be the small sample size in our study, and a larger sample size could result in significant differences between the left and right kidneys.

The normal cortical thickness measured in the longitudinal plane in Korean domestic shorthair cats was reported as 0.47 ± 0.08 cm for the left kidney and 0.55 ± 0.30 cm for the right kidney.[16] These values are different from those obtained in our study because measurements were obtained in a different plane. Moreover, cortical thickness measured in the dorsal plane in 3 healthy cat breeds (Ragdoll, British Shorthair, and Sphynx) was reported as 0.71 ± 0.14 cm for the left kidney and 0.74 ± 0.14 cm for the right kidney, with no significant difference between the left and right kidneys.[17] Again, these values are larger than those found in our study because of differences in the method of identifying the C/M junction. In the previous study, the C/M junction was determined between the hyperechoic cortex and hypoechoic medulla. In our study, the level of the arcuate artery in the dorsal and transverse planes was used as the anatomical landmark for determination of the C/M junction.

Renal length, cortical thickness, medullary thickness, and C/M ratio have been found to be comparable among different breeds of cats.[17] In Ragdoll cats, renal length exhibited a significant positive correlation with body weight, age, and male sex, but the C/M ratio did not.[13] A negative correlation between age and renal length in cats also has been described.[19] Renal length in our study also was influenced by age and sex, whereas renal cortical thickness, medullary thickness, and C/M ratio showed no correlations with age, body weight, and sex. Thus, renal length may not be an appropriate index for evaluating the progression of CKD in cats.

In our study, renal cortical thickness and C/M ratio were significantly different between the control group and disease groups, but they were not significantly different between the stage I to II and stage III to IV groups. These results indicate that renal cortical thickness could facilitate detection of early changes in renal function in cats with CKD, as observed in a previous study in humans.[9] On the other hand, the difference in medullary thickness between our control and disease groups was not statistically significant, which indicated that medullary thickness may be relatively unaffected in the different stages of CKD in cats. Even in humans, medullary thickness was found to have no association with renal function until the late phase of dysfunction, during which it decreased.[9]

FIGURE 3 Plots for linear correlations between the reciprocal of the serum creatinine concentration and ultrasonographically determined renal dimensions in cats. The left and right cortical thickness have a strong (r^2 = 0.36) and moderate (r^2 = 0.35) linear association with the reciprocal of the serum creatinine concentration, respectively. The cortical thickness has the best linear correlation with the reciprocal of the serum creatinine concentration compared with other renal dimensions. $r^2 < 0.04$ very weak, $0.04 \le r^2 < 0.16$ weak, $0.16 \le r^2 < 0.36$ moderate, $0.36 \le r^2 < 0.64$ strong, $r^2 \ge 0.64$ very strong. C/M, corticomedullary ratio; CRE, creatinine; LK, left kidney; RK, right kidney

TABLE 7 Sensitivity and specificity of the renal dimension for predicting CKD

	Sensitivity % (95% CI)	Specificity % (95% CI)
LK cortical thickness (mm)		
<6.1	100 (88-100)	5.3 (1-26)
<5.2	97 (83-100)	79.0 (54-94)
<5.0	93 (78-99)	89.5 (67-99)
<4.7	90 (73-98)	94.7 (74-100)
<4.3	70 (51-85)	100 (82-100)
RK cortical thickness (mm)		
<5.6	100 (88-100)	21.1 (6-46)
<5.0	93 (78-99)	68.4 (44-87)
<4.7	87 (69-96)	89.47 (67-99)
<4.5	83 (65-94)	94.7 (74-100)
<4.2	63 (44-80)	100 (82-100)
LK C/M ratio		
<0.42	93 (78-99)	53 (29-76)
<0.40	90 (74-98)	63 (38-84)
<0.38	87 (69-96)	84 (60-97)
<0.36	73 (54-88)	95 (74-100)
<0.34	67 (47-83)	100 (82-100)
RK C/M ratio		
<0.43	97 (83-100)	53 (29-76)
<0.39	90 (73-98)	68 (43-87)
<0.37	80 (61-92)	89 (67-99)
<0.35	70 (51-85)	95 (74-100)
<0.33	60 (41-77)	100 (82-100)
LK length (mm)		
<38.6	80 (61-92)	32 (13-57)
<36.1	73 (54-88)	68 (43-87)
<34.1	57 (37-75)	89 (67-99)
<32.1	43 (25-62)	94 (74-100)
<31.5	40 (23-59)	100 (82-100)
RK length (mm)		
<41.1	87 (69-96)	21 (6-46)
<39.5	80 (61-92)	42 (20-67)
<37.1	77 (58-90)	74 (49-91)
<35.4	63 (44-80)	84 (60-97)
<33.7	53 (34-72)	100 (82-100)
LK medullary thickness (mm)		
<13.6	83 (65-94)	21 (6-46)
<12.6	60 (41-77)	63 (38-83)
<11.7	47 (28-66)	74 (49-90)
<11.2	37 (20-56)	95 (74-100)
<10.8	30 (15-49)	100 (82-100)
RK medullary thickness (mm)		
<13.8	87 (69-96)	16 (3-40)
<12.8	70 (51-85)	37 (16-62)
<11.9	58 (37-75)	74 (49-91)

(Continues)

TABLE 7 (Continued)

	Sensitivity % (95% CI)	Specificity % (95% CI)
<11.3	40 (23-59)	89 (67-99)
<10.4	20 (8-39)	100 (82-100)

Note: Optimal cut-off values were assessed using Youden index and shown in bold.
Abbreviations: C/M, corticomedullary ratio; CI, confidence interval; LK, left kidney; RK, right kidney.

Previously, it was demonstrated that the reciprocal of the serum creatinine concentration ($P < .001$, $r^2 = 0.43$) could explain 43% of the variability in GFR, a result better than that for serum creatinine concentration ($P < .001$, $r^2 = 0.25$).[5] Therefore, the reciprocal of the serum creatinine concentration was selected as an indicator of renal function in the regression analysis in our study. The results showed that renal cortical thickness was superior to the other renal dimensions in terms of the detection of changes in renal function in cats with CKD, similar to findings in previous studies of humans.[8-10]

We used AUROC curves for each renal dimension to evaluate their accuracy in differentiating healthy cats from those with CKD. Unlike renal length and medullary thickness, cortical thickness and C/M ratio showed excellent diagnostic performances. However, interobserver agreement was better for cortical thickness measurements than for C/M ratio measurements, thus the former may be a more useful indicator than the latter. In addition, the accuracy of cortical thickness showed statistical significance compared to that of medullary thickness and renal length in both kidneys, suggesting that measurement of renal cortical thickness is superior to measurement of other renal dimensions in the evaluation of CKD in cats.

The major limitation of our study was the 2-gate design. This design may exclude some samples in the gray zone between healthy and CKD groups, and lead to higher estimates of diagnostic accuracy. Another limitation was the small sample size with a relatively wide 95% CI of the measurements, which may increase the probability of type I error. Although excellent agreement was found in the measurements of renal dimensions between observers, these results may be overestimated because of the wide 95% CI. Moreover, cats with abnormal renal morphologies such as polycystic renal disease and hydronephrosis were excluded because of the difficulty in measurement of renal dimensions, which could have led to selection bias. All of the renal ultrasound images for the disease group were consistently recorded in the transverse and dorsal or longitudinal planes, but slight differences in the scanning angle for each plane among all kidneys were inevitable. In addition, symmetric dimethylarginine, which is sensitive for the determination of CKD stage I,[20] was not available in our animal hospital until June 2018. Therefore, stage I CKD might not be well classified in our study. Despite these limitations, we demonstrated an auxiliary and useful method to evaluate and monitor CKD using noninvasive ultrasound examination in cats.

In conclusion, our findings suggest that renal cortical thickness measured in the transverse plane using ultrasonography is a better variable than renal length, medullary thickness, and C/M ratio for evaluating and monitoring the progression of CKD in cats, exhibiting excellent diagnostic performance and excellent intra- and interobserver reproducibilities. Thus, similar to findings in humans, thinning of the renal cortex in cats with CKD reflects renal function loss. The optimal cutoffs of 4.7 mm and 4.5 mm for left and right cortical thicknesses showed sensitivities of 90.0% and 83.3% and specificities of 94.7% and 94.7%, respectively. In addition, renal cortical thickness was not influenced by age, body weight, and sex. These results should be carefully interpreted in combination with clinicopathological findings during routine clinical practice.

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CONFLICT OF INTEREST DECLARATION

Authors declare no conflict of interest.

OFF-LABEL ANTIMICROBIAL DECLARATION

Authors declare no off-label use of antimicrobials.

INSTITUTIONAL ANIMAL CARE AND USE COMMITTEE (IACUC) OR OTHER APPROVAL DECLARATION

This study was approved by the IACUC (approval No. 105-065) for healthy cats recruited at the Veterinary Medical Teaching Hospital, National Chung Hsing University with the consent from the owners.

HUMAN ETHICS APPROVAL DECLARATION

Authors declare human ethics approval was not needed for this study.

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REFERENCES

1. Bartges JW. Chronic kidney disease in dogs and cats. *Vet Clin North Am Small Anim Pract*. 2012;42:669-692.
2. Marino CL, Lascelles BD, Vaden SL, et al. Prevalence and classification of chronic kidney disease in cats randomly selected from four age groups and in cats recruited for degenerative joint disease studies. *J Feline Med Surg*. 2014;16:465-472.
3. O'Neill DG, Church DB, McGreevy PD, et al. Prevalence of disorders recorded in cats attending primary-care veterinary practices in England. *Vet J*. 2014;202:286-291.
4. White JD, Norris JM, Baral RM, et al. Naturally-occurring chronic renal disease in Australian cats: a prospective study of 184 cases. *Aust Vet J*. 2006;84:188-194.
5. Finch N. Measurement of glomerular filtration rate in cats: methods and advantages over routine markers of renal function. *J Feline Med Surg*. 2014;16:736-748.
6. Debruyn K, Haers H, Combes A, et al. Ultrasonography of the feline kidney. Technique, anatomy and changes associated with disease. *J Feline Med Surg*. 2012;14:794-803.

7. Drost WT, Henry GA, Meinkoth JH, Woods JP, Payton ME, Rodebush C. The effects of a unilateral ultrasound-guided renal biopsy on renal function in healthy sedated cats. *Vet Radiol Ultrasound*. 2000;41:57-62.
8. Yamashita SR, von Atzingen AC, Iared W, et al. Value of renal cortical thickness as a predictor of renal function impairment in chronic renal disease patients. *Radiol Bras*. 2015;48:12-16.
9. Takata T, Koda M, Sugihara T, et al. Left renal cortical thickness measured by ultrasound can predict early progression of chronic kidney disease. *Nephron*. 2016;132:25-32.
10. Beland MD, Walle NL, Machan JT, Cronan JJ. Renal cortical thickness measured at ultrasound: is it better than renal length as an indicator of renal function in chronic kidney disease? *Am J Roentgenol*. 2010; 195:W146-W149.
11. Widmer WR, Biller DS, Adams LG. Ultrasonography of the urinary tract in small animals. *J Am Vet Med Assoc*. 2004;1:46-54.
12. D'Anjou MA, Bédard A, Dunn ME. Clinical significance of renal pelvic dilatation on ultrasound in dogs and cats. *Vet Radiol Ultrasound*. 2011; 52:88-94.
13. Debruyn K, Paepe D, Daminet S, et al. Renal dimensions at ultrasonography in healthy Ragdoll cats with normal kidney morphology: correlation with age, gender and bodyweight. *J Feline Med Surg*. 2013; 15:1046-1051.
14. Barrett RB, Kneller SK. Feline kidney mensuration. *Acta Radiol Suppl*. 1972;319:279-280.
15. Walter PA, Feeney DA, Johnston GR, Fletcher TF. Feline renal ultrasonography: quantitative analyses of imaged anatomy. *Am J Vet Res*. 1987;48:596-599.
16. Park IC, Lee HS, Kim JT, et al. Ultrasonographic evaluation of renal dimension and resistive index in clinically healthy Korean domestic short-hair cats. *J Vet Sci*. 2008;9:415-419.
17. Debruyn K, Paepe D, Daminet S, et al. Comparison of renal ultrasonographic measurements between healthy cats of three cat breeds: Ragdoll, British Shorthair and Sphynx. *J Feline Med Surg*. 2013;15: 478-482.
18. Shiroma JT, Gabriel JK, Carter RL, Scruggs SL, Stubbs PW. Effect of reproductive status on feline renal size. *Vet Radiol Ultrasound*. 1999; 40:242-245.
19. Seyrek-Intas D, Kramer M. Renal imaging in cats. *Vet Focus*. 2008;18: 23-30.
20. Hall JA, Yerramilli M, Obare E, Yerramilli M, Jewell DE. Comparison of serum concentrations of symmetric dimethylarginine and creatinine as kidney function biomarkers in cats with chronic kidney disease. *J Vet Intern Med*. 2014;28:1676-1683.

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