

INSIGHTS IN IMAGING

Ultrasonography for Diagnosing Chronic Kidney Disease in Dogs and Cats

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Chronic kidney disease (CKD) is a common diagnosis for dogs and cats; estimated prevalence in small animal general practice is approximately 0.5% to 1.5% among dogs and 1% to 3% among cats.¹ CKD is defined as a progressive and irreversible loss of structural renal integrity and function.² Although most prevalent among older patients, CKD can be identified in patients of all ages, from 9 months to 22 years.² Although for most patients a cause for CKD is often not identified, various inciting etiologies result in either tubulointerstitial nephritis, glomerulonephropathy, or amyloidosis. Of these, tubulointerstitial nephritis is most commonly reported in both dogs and cats.^{1,3}

During the early stages of CKD, patients are often asymptomatic and biochemical testing may not indicate

renal abnormalities. Over time, the progressive loss of functional nephrons is accompanied by azotemia and elevated levels of SDMA (symmetric dimethylarginine). Clinical signs become apparent after normal kidney function is reduced by two thirds.⁴ End-stage kidney disease is defined as the critical loss of kidney structure and function.³ Kidneys play a major role in endocrine and metabolic functions; loss of kidney function results in generalized systemic disturbances with possible detrimental clinical implications.⁵ Ensuing uremic syndrome may result in critical decline of clinical status.⁴

When nephrons are injured and the interstitium is concurrently damaged, the tissues are eventually replaced with fibrosis and mineralization.

Abstract

Chronic kidney disease (CKD) is a progressive condition that is commonly diagnosed in older dogs and cats. CKD may be part of the kidney's aging process or a sequela to an acute nephropathy; an inciting factor is often not recognized. A diagnosis is established by serial biochemical testing and diagnostic imaging. Ultrasonography plays a key role in identifying and staging CKD. Most patients are asymptomatic during the earlier stages of the disease process, and ultrasonographic abnormalities may be seen before renal biomarkers are elevated. This article reviews the reported ultrasonographic features of CKD in dogs and cats, with the goal of reducing morbidity of affected patients through early recognition.

Take-Home Points

- Chronic kidney disease (CKD) is prevalent among older cats and dogs.
- Early recognition and staging of CKD can prompt initiation of supportive care.
- Ultrasonography may help detect and stage CKD before abnormalities are detected with biochemical testing.
- Ultrasonography is valuable for excluding CKD sequelae or other renal disease, which may warrant more aggressive therapy, require other diagnostics, or alter prognosis.
- CKD is progressive, and serial ultrasonographic evaluations are valuable for monitoring longitudinal changes.

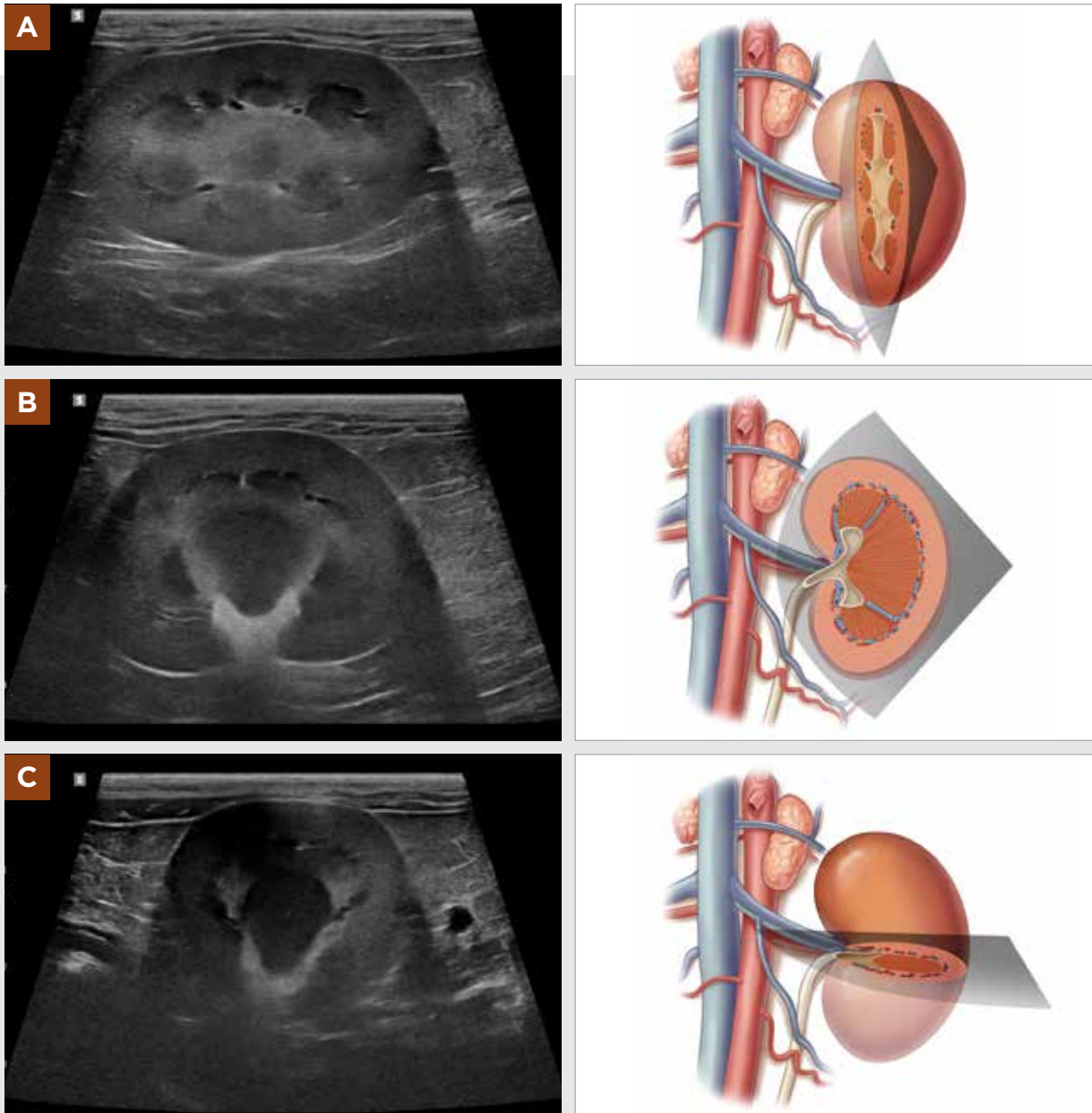


FIGURE 1. Ultrasonographic images of a normal kidney of a cat in (A) sagittal, (B) dorsal, and (C) transverse planes. Associated illustrations show the imaging planes.

The remaining nephrons will hypertrophy to compensate for the loss of function.³ The goal with therapy is to slow the progressive loss of nephrons and correct any sequelae (e.g., systemic hypertension, hyperphosphatemia, anemia).⁴ Successful long-term CKD therapy depends on early recognition and staging.⁶ For further evaluation of the kidneys in cats and dogs, the imaging modality of choice is ultrasonography due to its high resolution of the soft tissues, cost, and availability. Continual technologic advancements in ultrasonography systems enable detection of more subtle tissue alterations, and recognizing these changes is helpful for diagnosing and monitoring CKD in dogs and cats.

DIAGNOSTIC APPROACH

Patient Preparation and Machine Settings

Patient preparation is key for successful ultrasonography evaluation. For noncompliant patients, sedation may be indicated. Any fine needle or biopsy sampling should be performed with the patient under heavy sedation or anesthesia. The area of interest should be widely shaved, with alcohol and gel used as contact media to optimize image quality. The choice of probe is one with the highest frequency and enough penetration to enable visualization of the kidneys, which is best achieved with a linear transducer; however, a microconvex transducer may also be used if a smaller footprint or greater penetration is needed, such as in larger patients.

To optimize image quality, the following adjustments are recommended:

- **Depth:** Fill the field of view with the organ of interest.
- **Focal zone:** Place the probe at or just below the organ of interest. The focal zone represents the narrowest part of the ultrasonography beam, hence the region of highest spatial resolution and image quality.
- **Gain:** Adjust the overall brightness of the image so that there is good contrast between structures. In general, gain should be set lower to provide good contrast. Turning the gain up to compensate for a brightly lit room will make subtle lesions harder to find.
- **Time gain compensation:** Set the brightness at various depths within the field of view so that the overall image on the screen is uniform throughout, from near field to far field.

Normal Ultrasonographic Appearance

The normal ultrasonographic appearance of the kidney is well reviewed elsewhere,⁷ and this article focuses on CKD in cats and dogs. The kidneys should be imaged in 3 planes: sagittal, dorsal, and transverse (**FIGURE 1**).⁷ A hyperechoic outer medullary band in dogs, especially small-breed dogs, has been described and is seen with moderate prevalence in patients without renal disease (**FIGURE 2**).⁸ In cats, renal cortices may be homogeneously strongly hyperechoic with subsequently increased corticomedullary distinction, secondary to proximal tubular lipidosis (**FIGURE 3**).⁹ Fat deposition within the renal tubules is a consequence of obesity without impairment of renal function.¹⁰ In addition, an interrogation angle-dependent artefactual increase in renal cortical and medullary hyperechogenicity secondary to anisotropy is routinely seen in regions of the kidneys where the renal tubules are oriented perpendicular to the plane of sound. For example,



FIGURE 2. Sagittal image of a normal left kidney of a dog, showing a hyperechoic outer medullary band (**arrowheads**).



FIGURE 3. Sagittal image of a cat's left kidney, showing marked hyperechogenicity of the renal cortex, resulting in increased corticomedullary distinction, which is most compatible with tubular lipidosis. This finding in cats often makes the kidneys hyperechoic to the liver and/or spleen.

when imaging the kidney in a sagittal plane, echogenicity of the cranial and caudal poles will be focally and artefactually increased (**FIGURE 4**).¹¹ In the authors' experience, mild irregularity of the renal margins, especially in cats, can be seen where the renal vessels track along the renal capsule and should not be misinterpreted as a degenerative change (**FIGURE 5**). Color or power Doppler ultrasonography is useful for localizing these vessels.

Ultrasonographic Features of CKD

Ultrasonographic features of CKD have been reported with limited histopathologic correlation.¹² In addition, many ultrasonographic findings associated with CKD are nonspecific and are reported with other infectious, inflammatory, and neoplastic etiologies. Unfortunately, not all dogs and cats with CKD will exhibit renal ultrasonographic changes. However, ultrasonography is still valuable for supporting a diagnosis of CKD established with other routine diagnostics, evaluating CKD sequelae, and ruling out other diseases.

Ultrasonographic features of CKD are as follows:

Renal Cortical Hyperechogenicity

The most common abnormality seen in dogs and cats with CKD is a diffuse increase in renal cortical hyperechogenicity (**FIGURE 6**).^{12,13} Degeneration of the renal cortex has been speculated as an etiology; however, a distinct cause remains uncertain, mostly due to replacement of the tissues with fibrous tissues with/without mineralization resulting in nonspecific histopathologic changes, especially in more advanced cases.¹³ In studies by Banzato et al and Zotti et al, increased cortical echogenicity in dogs was associated with glomerulosclerosis, tubular atrophy, and fibrosis; in cats, interstitial nephritis/necrosis and fibrosis were most prevalent.^{10,13} Alterations in renal cortical echogenicity were more commonly correlated with histopathologic abnormalities in cats than in dogs.¹³ In the human literature, dehydration is a reported cause of increased renal cortical hyperechogenicity.¹⁴ A similar

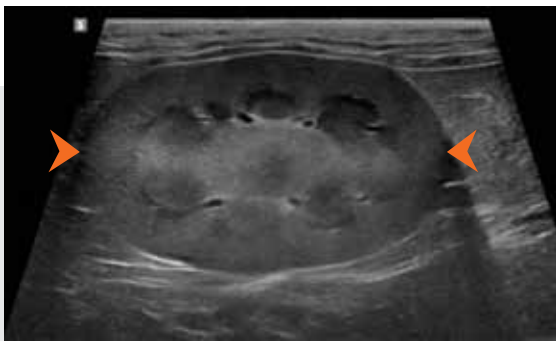


FIGURE 4. Sagittal image of the left kidney of a cat, showing with bilateral poorly demarcated regions of hyperechogenicity in the cranial and caudal poles (**arrow heads**), representing anisotropy.



FIGURE 6. Sagittal image of a dog's left kidney, showing a diffusely moderately hyperechoic cortex and containing poorly defined punctate and linear hyperechoic foci.



FIGURE 5. Power Doppler ultrasonography interrogation of the left kidney of a cat, showing evenly irregular margins at sites where the renal vasculature courses along the renal capsule (**arrowheads**).

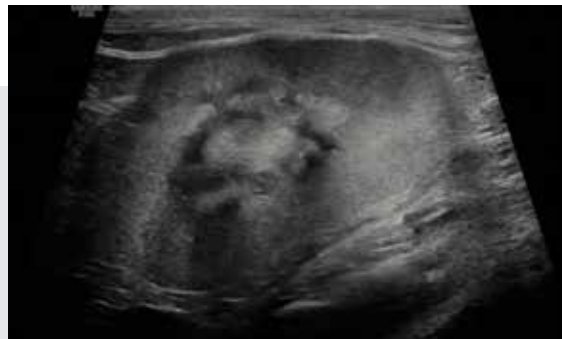


FIGURE 7. Sagittal image of a cat's right kidney, showing markedly reduced corticomedullary distinction, as well as renal cortical hyperechogenicity and irregular margins.

change could be expected in dogs and cats with CKD caused by loss of renal fluid retention as a result of diuresis, which may lead to increased renal cortical echogenicity resulting from collapse of the Bowman's space and tubule. Unfortunately, renal hyperechogenicity is a very nonspecific etiology with numerous other causes that include but are not limited to acute nephropathies (e.g., lily toxicosis in cats, leptospirosis in dogs).¹⁰

Reduced Corticomedullary Distinction

Good contrast is seen between the renal cortex and medulla due to higher cellular density within the renal cortex and fluid content within the medulla (FIGURE 7).¹⁵ With degeneration and loss of fluid retention in the medulla, medullary echogenicity progressively increases, leading to loss of corticomedullary distinction.¹⁵

Pyelectasia

Along with other processes, such as intravenous fluid administration or pyelonephritis, increased urinary secretion in patients with CKD is commonly associated with pyelectasia.¹⁶ Pyelectasia is the collection and subsequent dilation of the renal pelvis with fluid secondary to a nonobstructive process (FIGURE 8).⁸ In contrast, hydronephrosis is renal pelvic dilation secondary to urinary obstruction. Pyelectasia is most often symmetrical and bilateral; however, it may be unilateral or asymmetrically affect both kidneys.^{3,16} In patients with pyelectasia with renal insufficiency, renal pelvis height usually does not exceed 3.4 mm in dogs and 3 mm in cats.¹⁶ If renal pelvis dilation is higher, the urinary tract should be thoroughly evaluated for



FIGURE 8. Transverse image of the right kidney of a dog, showing mild fluid dilation of the renal pelvis (renal pelvic height denoted by cursors). No evidence of obstruction.

abnormalities to support the presence of other disease processes, such as pyelonephritis or hydronephrosis secondary to urinary tract obstruction.¹⁶

Irregular Renal Contour

Irregular renal margins (FIGURE 9) may be associated with one or more, often a combination, of fibrosis, sclerosis, atrophy, cyst formation, and infarction.¹² Irregular renal margins are commonly seen with more advanced stages of CKD and may be a poor diagnostic indicator.^{8,15,17}

Reduced Kidney Size

Ultrasonographic measurements of kidney size have been correlated with gross measurements at necropsy, although some underestimation of kidney length may be expected.¹⁸ Decreased kidney size (FIGURE 10) is expected with fibrosis; however, size may not directly

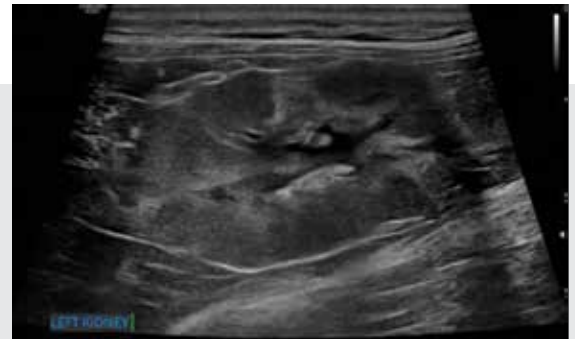


FIGURE 9. Sagittal image of the left kidney of a cat, showing severely irregular margins associated with the presence of renal cortical hyperechogenicity and chronic renal cortical infarcts. Mild pyelectasia is also present.

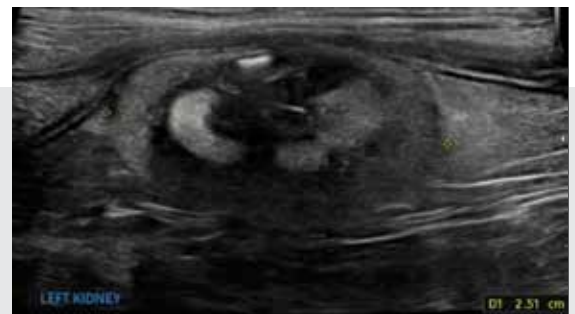


FIGURE 10. Sagittal image of a markedly small left kidney of a cat, associated with loss of normal renal morphology (e.g., thinning and hyperechogenicity of the renal cortex, loss of corticomedullary distinction, mineralization, irregular margination).

correlate with the degree of fibrosis in the presence of concurrent compensatory hyperplasia, renal cysts, and/or pyelectasia.^{8,17} Small kidneys may indicate a higher degree of fibrosis than compensatory hypertrophy, therefore indicating more advanced stages of CKD. Wide variability is seen with dog size; differences between breeds limit evaluation of kidney measurements.¹⁸ A kidney-to-aorta ratio was previously proposed in dogs, with normal kidney size ranging from 5.5 to 9.5 cm¹⁹; however, this measurement is not commonly used clinically. Variation is less among cats of different breeds, and normal kidney lengths have previously been described as ranging from 3 to 4.5 cm.⁸

Mineralization

Dystrophic mineral deposition within the nephrons and interstitium can occur secondary to renal damage and can be difficult to differentiate from fibrosis. Histologic correlation is limited; however,

mineralization (**FIGURE 11**) is speculated to primarily represent punctate and/or linear hyperechoic foci within the renal cortex, which are often too small to have distal acoustic shadowing.⁸ Hyperechoic streaks within the renal medulla, also thought to represent mineralization and/or fibrosis, are observed with more progressive renal disease.³ Although seen in dogs with and without CKD, a medullary rim sign has previously been correlated with possible mineralization of the renal tubular epithelium and basement membrane in dogs with a hypercalcemic nephropathy.^{9,20} Mineralization within the kidneys may be exacerbated by chronic hypercalcemia, resulting from parathyroid hormone elevation in response to decreased renal function. Although renal mineralization may be a response to CKD, it may also be a response to an

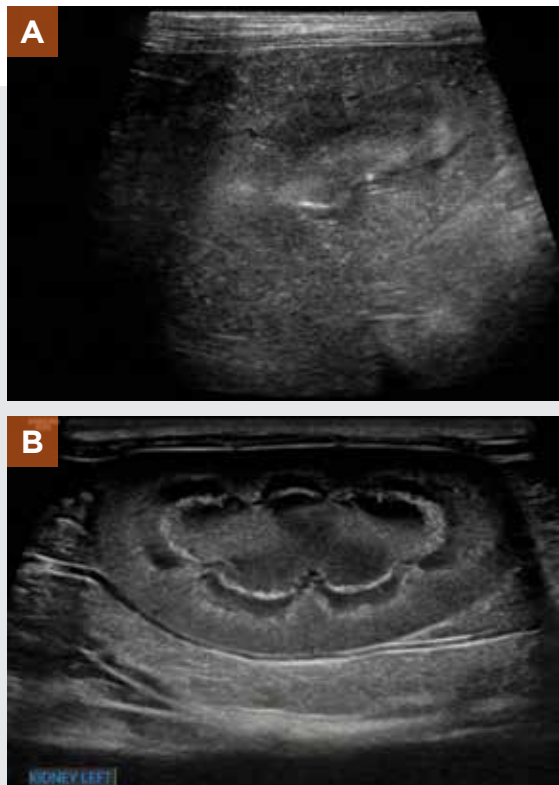


FIGURE 11. Sagittal images of the kidneys of a dog. **(A)** Right kidney, showing punctate and linear hyperechoic foci in the cortex, which may correlate with mineralization associated with chronic kidney disease. **(B)** Left kidney, showing a medullary rim sign, also previously correlated with mineralization secondary to a hypercalcemic nephropathy. A normal variant is also considered.

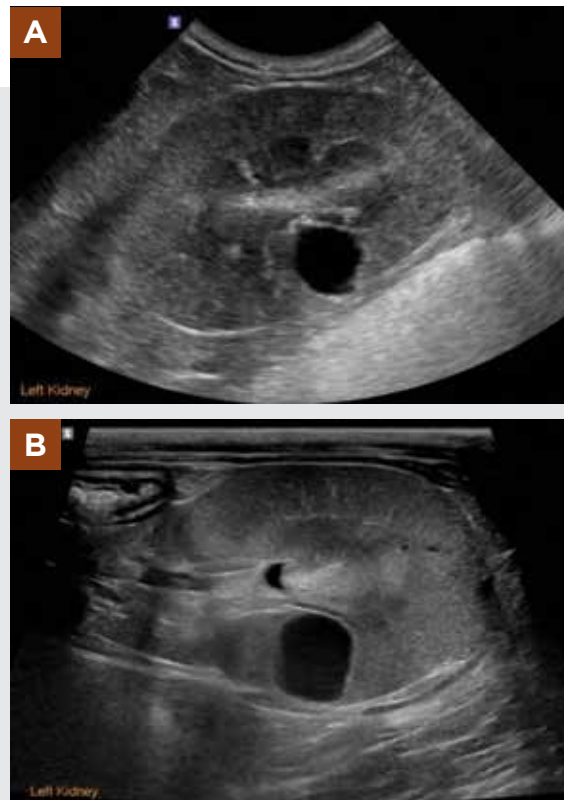


FIGURE 12. **(A)** Sagittal and **(B)** transverse images of the left kidney of a dog acquired by using microconvex and linear transducers, respectively. Centered on the renal cortex is a well-defined, smoothly margined, thin-rimmed, round, anechoic, and distally enhancing cyst. The renal cortices have poorly defined hyperechoic striation and reduced corticomedullary distinction. The mild pyelectasia (renal pelvis height <2 mm) was primarily considered to be secondary to diuresis (e.g., physiologic or secondary to intravenous fluid administration or renal insufficiency). The sagittal image also demonstrates the improved spatial resolution with higher-frequency linear transducers.

Hypovascularization has been described for all stages of CKD in cats but is reported to be a more severe and consistent change in cats with more progressed stages of CKD.²²

underlying endocrinopathy or other metabolic disturbances.^{8,17} In addition, mineralization of the renal diverticula may represent a chronic sequela to prior and/or chronic pyelonephritis.

Cysts

Renal cysts (**FIGURE 12**) occur more commonly in the cortex and can be acquired or congenital; therefore, without prior ultrasonographic examination for comparison, they are not a sensitive indicator of CKD in dogs.^{8,17} Renal cysts are common in dogs with CKD and most often do not affect renal function. They can distort the renal margins and may be a contributing cause of renal margin irregularity.^{8,12,21}

Infarcts

Renal infarcts (**FIGURE 13**) most commonly affect the renal cortex and can vary in number and size.^{8,17} They are associated not only with CKD but with other causes, including underlying coagulopathy, sepsis, or neoplasia.⁸ Correlation with serologic testing is often warranted.³ Renal cortical infarcts also contribute to renal margin irregularity and rarely affect more than two-thirds of the renal parenchyma; therefore, they are often not the only clinically significant cause of renal function loss.¹⁷ Ultrasonographic features of renal infarcts may vary depending on whether acute or chronic.²² After experimental focal occlusion of a branch of the renal artery, focal swelling and hypoechogenicity of the renal cortex occurred within 24 hours and persisted for 5 to 7 days.²¹ In that study, after 7 days, echogenicity of the affected region progressively increased, and a gradually shrinking wedge-shaped lesion with a concave defect along the capsular margin was seen by day 17.

Additional Uses of Ultrasonography for Evaluation of CKD

In dogs with more advanced stages of CKD, increased severity and numbers of ultrasonographic abnormalities are seen.¹² However, dogs and cats may have CKD without apparent ultrasonographic renal abnormalities.¹² Although currently of limited use for diagnosing CKD, evaluating the kidneys with color and/or power Doppler ultrasonography, measuring resistive and pulsatility indices, shear wave elastography, and contrast-enhanced ultrasonography may help support a diagnosis in the absence of other ultrasonographic findings.

Color/Power Doppler Ultrasonography

Color/power Doppler ultrasonography is used to demonstrate the presence and/or reduction of intrarenal arterial flow to assess renal function. Hypovascularization has been described for all stages of CKD in cats but is reported to be a more severe and consistent change in cats with more progressed stages of CKD.²² In addition, color/power Doppler ultrasonography is useful for identifying renal infarcts, especially in the acute stages as swelling of the infarcted cortical region may resemble a nodule.^{8,17}

Resistive and Pulsatility Indices

Resistive and pulsatility indices may be valuable for evaluating renal parenchymal perfusion.^{23,24}

- **Resistive index** = (peak systolic velocity – end-diastolic velocity) / peak systolic velocity



FIGURE 13. Sagittal image of a cat's left kidney, showing a poorly defined and wedge-shaped region of increased echogenicity centered on the cortex and underlying a small concave defect along the capsular margin (**arrowhead**), consistent with a chronic cortical renal infarct.

**TABLE 1 Normal Reference Ranges for Resistive and Pulsatility Indices**

INDEX	ADULT DOGS	CATS
Resistive	0.56–0.67 Variations in upper limit reported as 0.7–0.72 ^{23–26}	0.62 ± 0.04
Pulsatility	1–1.3 Upper end of normal reported as 1.52 ²¹	1.02 ± 0.02

■ **Pulsatility index** = (peak systolic velocity – end-diastolic velocity) / mean systolic velocity

These indices are unitless measurements of the pulsed-wave Doppler signal used to assess vascular resistance. Measurements are obtained near the hilus to evaluate the segmental or interlobar arteries or the corticomedullary junction to evaluate the evaluation of the arcuate arteries.^{23,24}

As described in the literature for human medicine, these measurements are affected by sedation, underlying heart disease, and/or abnormal blood pressure.²⁵ Veterinary studies have found no correlation between resistive index and creatinine levels in cats and dogs, making this index of uncertain clinical reliability.^{25,26} In addition, a large overlap in resistivity index is reported for dogs with and without CKD.²⁵ On the other hand, an elevated pulsatility index may represent a more dependable measurement of renal perfusion in dogs and cats when elevated renal markers in blood support a diagnosis of CKD.²³ Normal reference ranges are shown in **TABLE 1**.^{15,20}

Shear Wave Elastography

Shear wave elastography qualitatively and quantitatively measures tissue stiffness. Elevated renal stiffness in human patients with CKD, possibly resulting from fibrosis, has been reported.²⁷ A similar change has been observed in the renal cortex of cats and dogs with CKD.²⁸ However, using renal cortical stiffness measurement to diagnose CKD remains of limited reliability, and the need for special software restricts the availability of shear wave elastography in everyday veterinary practice.²⁹

Contrast-Enhanced Ultrasonography

In the United States, availability of contrast-enhanced ultrasonography is limited and cost prohibitive. To evaluate renal perfusion, a contrast agent composed of microbubbles is injected intravenously. The most repeatable measurements of renal perfusion have been

reported to be time to peak enhancement and rise and fall enhancement times.³⁰ Long time to peak and shorter mean transit times may be observed for cats and dogs with CKD; however, interpretation may be affected by variations in ultrasonography settings, stability of the contrast media, and inherent patient factors (e.g., abnormal blood pressure, presence of heart disease, motion).^{28,30,31}

Ultrasonographic Features of Advanced CKD

As CKD progresses, normal renal architecture may be lost. The kidneys become severely small and irregular. The kidneys appear exceedingly hypovascular on color and power Doppler ultrasonography interrogation and may be hard to identify with standard B-mode ultrasonography. If one of the kidneys is more severely affected, the contralateral kidney may enlarge as its nephrons enlarge as a compensatory response to increase functional capacity of remaining nephrons.³ As a consequence of severe CKD in dogs and cats, multisystemic complications of chronic uremia may develop,³ most commonly soft tissue mineralization. Proposed underlying etiologies, which may occur in combination, are metastatic mineralization caused by hypercalcemia from secondary hyperthyroidism and dystrophic mineralization caused by replacement of inflamed tissues with minerals in response to circulating toxins in uremic patients.^{32,33} A recent study

As a consequence of severe CKD in dogs and cats, multisystemic complications of chronic uremia may develop,³ most commonly soft tissue mineralization.

by Cardoso et al identified the kidneys as the most common site of mineralization; however, other affected sites evaluated during abdominal ultrasonography are gastric mucosa, aorta, and intestine.³² Nephrotic syndrome may result from excessive urinary loss of proteins, with ensuing hypercoagulability and thromboembolization. Multisystemic evidence of infarction observed with ultrasonography should be correlated with serologic testing to support a diagnosis.³ Other possible observations are peritoneal effusion secondary to portal hypertension from underlying thromboembolism or third spacing of fluid as a direct response to the hypoproteinemia. These syndromes are serious conditions that should be recognized to direct therapeutic recommendations and improve prognosis.

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SUMMARY

Ultrasonography plays a key supportive role in identifying, staging, and monitoring CKD in dogs and cats. Ultrasonographic abnormalities may be observed before serologic abnormalities are evident, therefore prompting early management of CKD in affected patients. However, ultrasonographic appearance of the kidneys may remain normal in patients with CKD. Therefore, a diagnostic work-up of CKD is most complete if combined with serologic testing. In addition, ultrasonography may guide further diagnostic and treatment recommendations if other or non-CKD-related lesions are seen, such as neoplasia, pyelonephritis, or evidence of proximal urinary obstruction. Ultrasonography is also useful for screening for the clinical manifestations of CKD sequelae, such as uremic or nephrotic syndrome, which are signs of more advanced CKD, requiring more extensive medical support. **TVP**

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	503A	503B
Type of Facility	Traditional Compounding Pharmacy	FDA Registered Manufacturer
Product Purpose	Customized prescriptions for individual patients	Manufactured drugs in bulk quantities for hospitals
Regulatory Oversight	State Boards of Pharmacy	FDA
Regulations	USP (United States Pharmacopeia)	cGMP (current Good Manufacturing Processes)
Product Dating	Beyond-Use Date (limited)	Expiration Date (proven)

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