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Renal scintigraphy as an early and efficient method for detecting loss of renal function in a cat

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Abstract

Case summary A 6-year-old mixed-breed male cat was evaluated for a routine annual health assessment. No alterations on physical examination were observed other than mild pain on palpation of the right kidney. Complete blood count, serum biochemistry (including symmetric dimethylarginine), urinalysis and urine protein:creatinine ratio were within the reference intervals for the species. Abdominal ultrasonography showed the presence of asymmetric kidneys, decreased corticomedullary definition, presence of a cyst on the left kidney and moderate renal pelvis dilatation on the right kidney. Dynamic renal scintigraphy (technetium [^{99m}Tc]-diethylenetriamine pentaacetic acid) revealed a single functioning kidney on the left. Static renal scintigraphy (^{99m}Tc-dimercaptosuccinic acid) exhibited renal activity practically restricted to the left kidney (relative uptake was 99% for the left kidney and 1% for the right kidney). Results of renal scintigraphy showed that the left kidney was compensating for the lack of function of the right one. GFR was 2.17 ml/min/kg, which is considered subclinical renal insufficiency and is in accordance with the case, as the cat was asymptomatic and did not present alterations in laboratory parameters.

Relevance and novel information Renal scintigraphy was an important tool to determine the loss of renal function in one of the kidneys and mild reduction of global GFR. In this case report, renal scintigraphy proved to be more sensitive in the assessment of renal function than other tests routinely performed.

Keywords: Chronic kidney disease; glomerular filtration rate; abdominal ultrasonography; nuclear medicine

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Introduction

Chronic kidney disease (CKD) is defined as any functional or structural abnormality of one or both kidneys that has been continuously present for 3 months or longer.[1] Despite being a common disease in cats, its clinical manifestation varies individually and a single, simple and accurate marker for diagnostic evaluation does not exist. The diagnosis of CKD is based on the presence of azotemia (creatinine >1.6 mg/dl), associated or not with a low urine concentrating ability (urine specific gravity [USG] <1.035], over a period of weeks or months, or with a compatible clinical history.[2] However, not all cats will meet these criteria. Some have only structural

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alterations in kidney morphology, as evidenced by imaging studies.[2] Unfortunately, most of the time, CKD is present before the manifestation of clinical signs or the presence of alteration in renal function biomarkers. In general, azotemia only occurs when there is a ≥65% loss of renal function.[3]

Imaging examinations are important in the evaluation of patients with CKD.[2] Several structural changes are described in the abdominal ultrasonography and/or radiography of cats with CKD, including a decrease in kidney size, loss of corticomedullary definition, irregular renal contour, mineralization of the renal pelvis, and presence of neoplasia, renal cysts, areas of infarction and nephrolithiasis.[4–7] These changes can impair the normal renal parenchyma as they progress, resulting in loss of function.[7,8] There is no evidence that nephrolithiasis without ureteral obstruction is associated with CKD progression in cats.[9] Patients with International Renal Interest Society (IRIS) stage 1 CKD are not azotemic but present changes in kidney structure, such as abnormal renal imaging findings.[10]

Renal scintigraphy is a non-invasive imaging procedure that uses nuclear medicine tools to assess both renal function and morphology. It is performed through an intravenous (IV) injection of the radiopharmaceutical technetium (^{99m}Tc)-diethylenetriamine pentaacetic acid (^{99m}TcDTPA), which undergoes glomerular filtration,[11] and the radiopharmaceutical technetium (^{99m}Tc)-dimercaptosuccinic acid (^{99m}Tc-DMSA), which gradually accumulates in the proximal tubular cells, allowing for assessment of the size, shape and homogeneity of the tracer.[12] These ^{99m}Tc-labeled molecules are capable of emitting gamma rays, which can be detected by a gamma camera, forming the scintigraphic image. Therefore, it is possible to determine the total and individual glomerular filtration rate (GFR) of each kidney,[11] and qualitative and quantitative function (absolute [AU] and relative [RU] uptake).[12] Renal scintigraphy provides useful and unique information in most clinical settings, including regional and global kidney morphology and function, visualization of focal or diffuse functional lesions and the detection of obstructive disorders, which contributes to diagnosis, prognosis and follow-up treatment, or disease.[13]

This paper reports a case of an asymptomatic cat with loss of renal function detected exclusively by renal scintigraphy, emphasizing its value in the early diagnosis of CKD.

Case description

A 6-year-old mixed-breed male cat was evaluated for a routine annual health assessment at the Veterinary Teaching Hospital of the Federal University of Rio Grande do Sul, Brazil. The owner reported the absence of any clinical signs. No alterations on physical examination were observed other than mild pain on palpation of the right kidney. Systolic blood pressure, measured by a vascular Doppler device, was 140 mmHg.

A complete blood count, serum biochemistry, urinalysis, urine culture and urine protein:creatinine ratio were performed. The only relevant finding from the blood cell count was the presence of eosinophilia (2.600/µl). Serum creatinine was 1.5 mg/dl (reference interval [RI] <1.6 mg/dl)[10] and symmetric dimethylarginine (SDMA) (Catalyst SDMA; IDEXX Laboratories) was 6 µg/dl (RI <18 µg/dl),[10] both within the RI for the species. Urinalysis showed no alterations: USG was 1.060, urine protein:creatinine ratio was 0.05 (RI <0.2)[10] and urine culture was negative.

In the abdominal ultrasound evaluation (MyLab40; Esaote), the presence of asymmetric kidneys was observed, with a longitudinal axis measurement of 4.2 cm in the left kidney (LK) and 3.4 cm in the right kidney (RK; RI 3.0–4.5 cm).[7] The LK showed a slightly irregular contour, hyperechoic cortices and decreased corticomedullary definition. There was no dilatation of the renal pelvis, but there was a cyst containing anechoic fluid located within the cortex, measuring about 0.14 cm. The RK showed moderate dilatation of the renal pelvis, with anechoic liquid content, measuring 2.1 cm. The proximal ureter measured 0.96 cm, with anechoic content and, at a distance of 3.5 cm away from the kidney, the dilatation reduced to 0.5 cm. There was a reverberation artefact (gas in intestinal loops), impairing the proper assessment of the region. The ureters were normal, near the bladder. Abdominal radiography survey (HS40; Siemens Healthcare) did not show the presence of radiopaque urolithiasis.

Dynamic renal scintigraphy was performed with ^{99m}TcDTPA at a dose of 138 MBq (3.74 mCi) with a gamma camera (Sigma 410; Ohio Nuclear). For this procedure, the cat was sedated with tiletamine–zolazepam at a total dose of 5 mg/kg IV. Before starting the procedure, a static image was acquired, at a distance of 26 cm from the center of the gamma camera, to count the preinjection syringe. With the cat in dorsal recumbency and the detector positioned under the stretcher, the image field included the area from the 13th thoracic vertebra to the pubis. The ^{99m}Tc-DTPA radiopharmaceutical was applied IV, followed by 5 ml NaCl 0.9%. The image acquisition started immediately after the injection and 120 images were obtained, lasting 15 s each, giving a total of 30 mins for the examination. At the 15 min point of the examination, a diuretic stimulus was performed with 1 mg/kg furosemide IV. After completing the procedure, another static image was acquired at a distance of 26 cm from the center of the gamma camera, to count the residual activity within the syringe. Only one functioning kidney was observed, on the left, with evident concentration and excretion of the radiotracer within normal limits. In this LK, peak

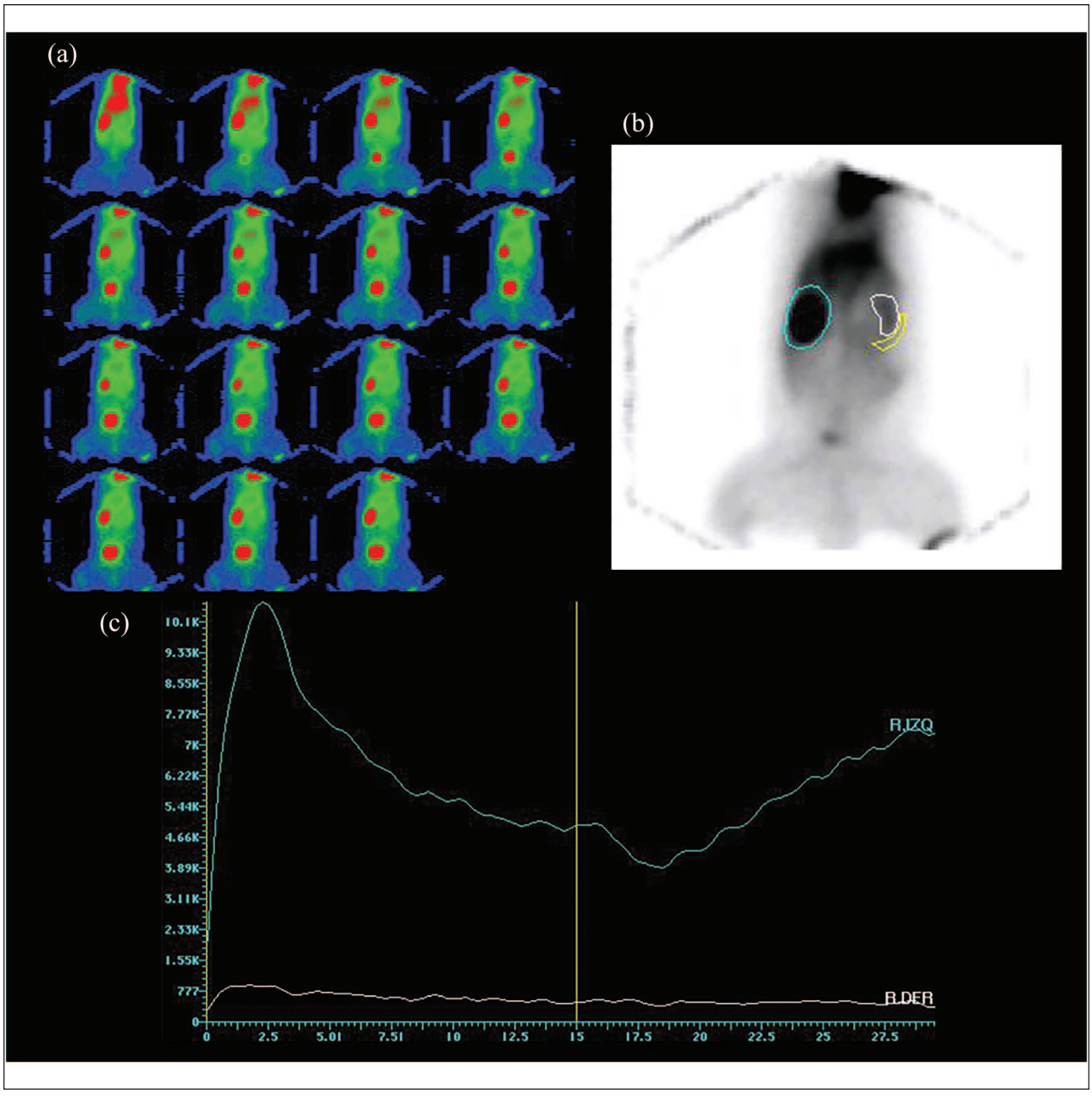

Figure 1 Dynamic renal scintigraphy of a 6-year-old cat with chronic kidney disease. (a) Images from acquisition after injection of technetium (99mTc)-diethylenetriamine pentaacetic acid. The images were acquired for 30 mins, at one frame every 15 s. (b) Regions of interest (ROIs) have been placed around the left (blue color) and right (white color) kidney, and around the region immediately caudal to the right kidney (yellow color) for background determination. (c) Renogram curves of the left (blue line) and right (white line) kidneys. The right kidney was small and had decreased function, showing a flat shape on the renogram curve. The global glomerular filtration rate was 2.17 ml/min/kg, of which 95% was derived from the left kidney. The yellow vertical line shows the timing of furosemide injection (15 mins after acquisition start)

renal activity was at 2.5 mins and the excretion half-time ($T_{1/2}$) was 9.75 mins. The absence of radiotracer uptake was observed in the topography of the RK. The GFR was 2.17 ml/min/kg, with a relative function of 5% in the RK and 95% in the LK (Figure 1).

The next day, static renal scintigraphy with ^{99m}Tc-DMSA was performed at a dose of 103 MBq (2.8 mCi) with a gamma camera. Before starting the procedure, the values of activity from the preinjection syringe were recorded. After IV administration of the radiopharmaceutical, the values of

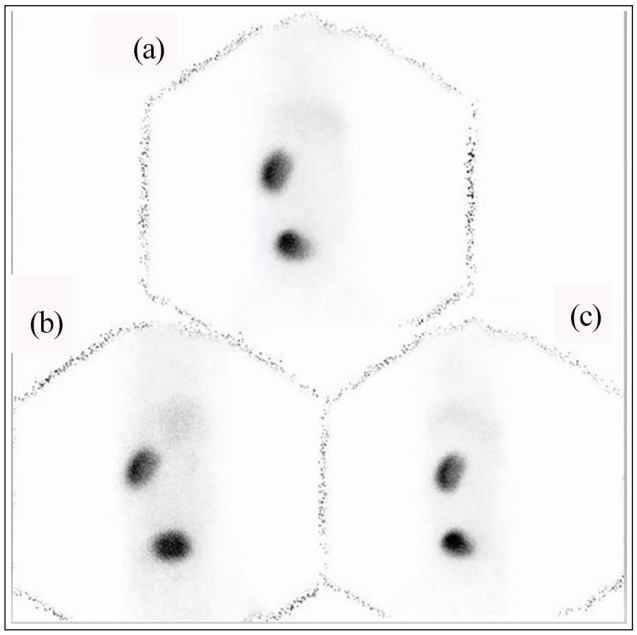

Figure 2 Static renal scintigraphy of a 6-year-old cat with chronic kidney disease. Images were obtained 5 h after the injection of technetium (^{99m}Tc)-dimercaptosuccinic acid on (a) dorsal recumbency, (b) right oblique dorsal recumbency and (c) left oblique dorsal recumbency. Note that the only activity is located in the left kidney and urinary bladder further down

activity from the empty syringe were also recorded. For this counting, a dose calibrator or curiometer (CRC15R; Capintec) was used. The waiting time between the application of the radiopharmaceutical and the acquisition of the images was 5 h. During this period, the cat remained isolated, with water and moist food provided ad libitum to ensure hydration. After this period, with the cat in dorsal recumbency and the detector positioned under the stretcher, the image field included the area from the 13th thoracic vertebra to the pubis. In this second examination, the patient was manually restrained and sedation was not necessary. Three images were acquired, each lasting 2 mins, in dorsal recumbency and right and left oblique dorsal recumbency, giving a total examination time of 6 mins. Static images were also taken in dorsal recumbency to calculate the relative and absolute renal function. Correction of tissue attenuation and radioactivity decay was performed. Renal activity was largely restricted to the LK (the RU of the LK was 99% and that of the RK was 1%; the AU of the LK was 32.6% and that of the RK was 0.3%), which showed an almost homogeneous concentration of the radiopharmaceutical in the parenchyma, with a small area of hypoactivity in the upper pole, which may represent previous focal parenchymal damage (Figure 2).

The cat was kept at home under observation, as no clinical signs or azotemia were detected. Ultrasonographic follow-up was performed after 3 weeks. The LK measured 3.9 cm in its longitudinal axis, in addition to the same alterations previously observed. The RK measured 3.2 cm and showed hyperechoic renal cortices, reduced corticomedullary definition and mild renal pelvis dilatation, measuring 0.32 cm (smaller compared with the previous examination), with anechoic liquid content. Ureters were not seen.

Discussion

The clinical manifestation of CKD occurs only after a substantial loss of renal function and includes polyuria, polydipsia, progressive weight loss, muscle wasting, decline in appetite, altered kidney size and dehydration.[1,2] In the early stages of CKD, patients show mild or absent clinical signs,[10] which can make it difficult for owners to identify. In this case, the cat was presented for an annual check-up and had no clinical signs of any disease, with the exception of mild pain on palpation of the RK during physical examination, emphasizing the need to perform periodic clinical check-ups in cats for the early diagnosis of CKD.

Asymmetric kidneys, an irregular contour, a reduction in corticomedullary definition, the presence of a renal cyst and pyelectasia on the RK were observed on ultrasonography, consistent with CKD.[4–7] Previous studies recorded that the magnitude of renal pelvic dilatation can range from 0.12 to 1.15 cm in cats with CKD,[14] from 0.17 to 1.24 cm in cases of pyelonephritis and from 0.12 to 3.91 cm in cases of urinary outflow obstruction.[15] In the present case, renal pelvic dilatation measured 2.1 cm, which could suggest obstruction. Although the pelvic diameter can be used as a guide, it should not be considered the only criterion to differentiate such conditions. Also, pyelonephritis was discounted based on the negative urine culture result and the lack of systemic signs.

Furthermore, abdominal ultrasonography and radiography examination did not reveal images compatible with ureterolithiasis. A previous study revealed a sensitivity of 90% in detecting ureterolithiasis when using a combination of survey radiography and ultrasonography, but small or radiolucent calculi may not be detected.[16] In addition, soft tissue plugs and solidified blood clots may be the cause of ureteral obstruction and are difficult to visualize during abdominal radiography and ultrasonography.[17,18] In this case, renal scintigraphy did not exhibit a renogram curve compatible with acute urinary flow obstruction, which is observed as a renal time–activity curve that reaches a plateau or shows continuous rise, even after the diuretic injection.[19] Hecht et al[19] reported a series of non-diagnostic tests, with a flat time–activity curve throughout the course of the diuretic renal scintigraphy in cats with ureteral obstruction, which was ascribed to decreased renal function, either due to underlying CKD or secondary to ureteral obstruction. The time–activity curve in this case report is similar to the non-diagnostic test results reported by Hecht et al.[19] Given the patient's history, the ultrasonographic

findings and the renogram curve, it is not possible to exclude the possibility of urinary flow obstruction that caused severe loss of renal function. In addition, the reduction in renal pelvis dilatation observed after 3 weeks is another factor that supports this possibility. The extent of renal damage is dependent on the degree and duration of the obstruction and on the presence of pre-existing renal disease, and may be irreversible.[20]

Abdominal ultrasonography and radiography assess renal morphology but are unable to determine renal function. Therefore, in the clinical setting, imaging tests are used in combination with indirect GFR biomarkers such as serum creatinine and SDMA.[2] However, those biomarkers carry some disadvantages. Serum creatinine is a relatively insensitive biomarker of GFR until a substantial reduction in overall kidney function has already occurred. It requires about a 65–75% reduction in GFR before serum creatinine values consistently exceed the upper limit of normal.[1] In contrast, serum SDMA is expected to be more sensitive than creatinine in detecting the early loss of renal function in cats with CKD.[21,22] In the present case, both serum creatinine and SDMA values were within the RI for the species.[10] Also, the USG showed adequate urine concentrating ability.[2] The cat was not hypertensive and not proteinuric, which are considered risk factors for CKD progression when present. The only alterations observed were mild pain on renal palpation and abnormalities on renal imaging. According to IRIS staging, the cat was classified as having stage 1 CKD.[10]

The alterations observed on abdominal ultrasound were clinically relevant, which led to the indication of further investigation of renal function and morphology through renal scintigraphy. Dynamic renal scintigraphy (^{99m}TcDTPA) was performed under zolazepam–tiletamine sedation, based on a previous study that showed no significant effect on GFR of cats a under dissociative anesthesia protocol.[23] Dynamic renal scintigraphy revealed a single functioning LK. Static renal scintigraphy (^{99m}Tc-DMSA) showed that the relative function was 99% in the LK and 1% in the RK. It also revealed that the absolute function of the LK was 32.6% and the absolute function of the RK was 0.3%. Normal values of absolute function reported for cats are 21.3% and 21.7% for the left and right kidneys, respectively, and 43% for both kidneys together.[12] These data show that the LK was compensating for the lack of function of the RK. With unilateral renal dysfunction, the contralateral kidney should undergo compensatory hypertrophy, presenting an individual GFR value of >1.5 ml/min/kg.[24] The kidneys adapt to loss of nephrons by recruitment of the surviving ones to recoup much of the function lost. However, this compensatory mechanism hinders the early diagnosis of CKD, in addition to contributing to the spontaneous progression of the disease.[1]

A GFR above 2.5 ml/min/kg is considered normal, while cats with subclinical renal insufficiency have GFR values between 1.2 and 2.5 ml/min/kg. Cats with azotemia may present GFR values between 1.0 and 1.3 ml/min/kg.[24] In this case, the GFR was 2.17 ml/min/kg, which is considered subclinical renal insufficiency, and is in accordance with the case, since the cat was asymptomatic and did not present alterations in laboratory parameters.

A limitation of this case report is the lack of a definitive diagnosis, as cytological or histopathological evaluation of the RK was not performed. Cytological evaluation is indicated to rule out neoplastic or infiltrative conditions and is not useful in the diagnosis of chronic interstitial nephritis;[25] for this reason, it was not indicated in this case. Also, the initial cause of the renal disease is unlikely to be determined by renal biopsy in cases of CKD in cats.[26] Furthermore, there is a possibility of complications occurring when performing a renal biopsy,[26] and the owner chose not to have invasive procedures performed.

Conclusions

Renal scintigraphy was an important tool in this case to determine the loss of renal function in one of the kidneys and mild reduction of global GFR. The lack of clinical signs compatible with CKD and the absence of alterations in laboratory parameters do not exclude the possibility of loss of renal function. In this case report, renal scintigraphy proved to be more sensitive to assess renal function than other tests routinely performed.

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Ethical approval The work described in this manuscript involved the use of non-experimental (owned or unowned) animals. Established internationally recognized high standards ('best practice') of veterinary clinical care for the individual patient were always followed and/or this work involved the use of cadavers. Ethical approval from a committee was therefore not specifically required for publication in *JFMS Open Reports*. Although not required, where ethical approval was still obtained, it is stated in the manuscript.

Informed consent Informed consent (verbal or written) was obtained from the owner or legal custodian of all animal(s) described in this work (experimental or non-experimental

animals, including cadavers) for all procedure(s) undertaken (prospective or retrospective studies). No animals or people are identifiable within this publication, and therefore additional informed consent for publication was not required.

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References

1 Polzin DJ. **Chronic kidney disease.** In: Bartges J and Polzin DJ (eds). Nephrology and urology of small animals. Ames, IA: Wiley-Blackwell, 2011, pp 433–471.
2 Sparkes AH, Caney S, Chalhoub S, et al. **ISFM consensus guidelines on the diagnosis and management of feline chronic kidney disease.** *J Feline Med Surg* 2016; 18: 219–239.
3 Lefebvre HP. **Renal function testing.** In: Bartges J and Polzin DJ (eds). Nephrology and urology of small animals. Ames, IA: Wiley-Blackwell, 2011, pp 91–96.
4 Seiler GS. **Kidneys and ureters.** In: Thrall DE (ed). Textbook of veterinary diagnostic radiology. St Louis, MO: Elsevier, 2018, pp 823–845.
5 Hecht S and Henry GA. **Ultrasonography of the urinary tract.** In: Bartges J and Polzin DJ (eds). Nephrology and urology of small animals. Ames, IA: Wiley-Blackwell, 2011, pp 128–145.
6 Cordella A, Pey P, Dondi F, et al. **The ultrasonographic medullary "rim sign" versus medullary "band sign" in cats and their association with renal disease.** *J Vet Intern Med* 2020; 34: 1932–1939.
7 Griffin S. **Feline abdominal ultrasonography: what's normal? What's abnormal? The kidneys and perinephric space.** *J Feline Med Surg* 2020; 22: 409–427.
8 Yu Y, Shumway KL, Matheson JS, et al. **Kidney and cystic volume imaging for disease presentation and progression in the cat autosomal dominant polycystic kidney disease large animal model.** *BMC Nephrol* 2019; 20: 259. DOI: 10.1186/s12882-019-1448-1.
9 Ross SJ, Osborne CA, Lekcharoensuk C, et al. **A case–control study of the effects of nephrolithiasis in cats with chronic kidney disease.** *J Am Vet Med Assoc* 2007; 230: 1854–1859.
10 International Renal Interest Society. **IRIS staging of CKD (modified 2019).** http://www.iris-kidney.com/pdf/IRIS_Staging_of_CKD_modified_2019.pdf (2019, accessed February 10, 2021).
11 Tyson R and Daniel GB. **Renal scintigraphy in veterinary medicine.** *Semin Nucl Med* 2014; 44: 35–46.
12 Vandermeulen E, Ham HR, Dobbeleir AA, et al. **(99m)Tc-DMSA absolute and relative renal uptake in cats: procedure and normal values.** *J Feline Med Surg* 2011; 13: 387–392.
13 Sfakianakis GN and Sfakianaki E. **Renal scintigraphy in infants and children.** *Urology* 2011; 57: 1167–1177.
14 Quimby JM, Dowers K, Herndon AK, et al. **Renal pelvic and ureteral ultrasonographic characteristics of cats with chronic kidney disease in comparison with normal cats, and cats with pylonephritis or ureteral obstruction.** *J Feline Med Surg* 2017; 19: 784–790.
15 D'Anjou M-A, Bédard A and Dunn ME. **Clinical significance of renal pelvic dilatation on ultrasound in dogs and cats.** *Vet Radiol Ultrasound* 2011; 52: 88–94.
16 Kyles AE, Hardie EM, Wooden BG, et al. **Clinical, clinicopathologic, radiographic, and ultrasonographic abnormalities in cats with ureteral calculi: 163 cases (1984–2002).** *J Am Vet Med Assoc* 2005; 226: 932–936.
17 Hardie EM and Kyles AE. **Management of ureteral obstruction.** *Vet Clin North Am Small Anim Pract* 2004; 34: 989–1010.
18 Westropp JL, Ruby AL, Bailiff NL, et al. **Dried solidified blood calculi in the urinary tract of cats.** *J Vet Intern Med* 2006; 20: 828–834.
19 Hecht S, Lawson SM, Lane IF, et al. **^{99m}Tc-DTPA diuretic renal scintigraphy in cats with nephroureterolithiasis.** *J Feline Med Surg* 2010; 12: 423–430.
20 Berent AC. **Ureteral obstructions in dogs and cats: a review of traditional and new interventional diagnostic and therapeutic options.** *J Vet Emerg Crit Care* 2011; 21: 86–103.
21 Hall JA, Yerramilli M, Obare E, et al. **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.
22 Reldford R, Robertson J and Clements C. **Symmetric dimethylarginine: improving the diagnosis and staging of chronic kidney disease in small animals.** *Vet Clin North Am Small Anim Pract* 2016; 46: 941–960.
23 Winter MD, Miles KG and Riedesel DH. **Effect of sedation protocol on glomerular filtration rate in cats as determined by use of quantitative renal scintigraphy.** *Am J Vet Res* 2011; 72: 1222–1225.
24 Daniel GB, Mitchell SK, Mawby D, et al. **Renal nuclear medicine: a review.** *Vet Radiol Ultrasound* 1999; 40: 572–587.
25 Borjesson DL. **Renal cytology.** *Vet Clin North Am Small Anim Pract* 2003; 33: 119–134.
26 Vaden SL. **Renal biopsy: methods and interpretation.** *Vet Clin North Am Small Anim Pract* 2004; 34: 887–908.