

FELINE COMORBIDITIES

Balancing hyperthyroidism and concurrent chronic kidney disease

Rebecca Geddes and Joana Aguiar

Introduction

Hyperthyroidism is the most common feline endocrinopathy, affecting up to 11.4% of cats over 9 years of age.^{1–5} Hyperthyroidism is a multisystem disorder that results from excessive production of thyroid hormones by the thyroid gland;^{1,3,5} thyroid growth and function become autonomous from hypothalamic and pituitary regulation.^{6,7} Most cats with hyperthyroidism are diagnosed with thyroid nodular hyperplasia, adenomatous hyperplasia or a thyroid adenoma, and approximately 2% of hyperthyroid cats have a thyroid carcinoma.^{1,3,5,8–13}

Despite the fact that feline hyperthyroidism was first described in 1979, its aetiology is still not fully understood.^{5,14,15} Since its first description, its worldwide prevalence has increased and the reasons for this are most likely multifactorial.^{5,12,16} Raised awareness of the condition, widespread availability of diagnostic tests and ageing of the cat population may all be playing a role; however, environmental, genetic, hereditary and goitrogenic risk factors, such as dietary components, additives and pollutants, could also be contributing factors.^{1,5,8,17–19}

Chronic kidney disease (CKD) is prevalent in older cats, with over 80% having evidence of the condition by 15 years of age²⁰ and over 30% of cats in this age group having azotaemic CKD.²¹ A number of risk factors for developing CKD have been identified, including frequent vaccination,²² the presence of dental disease,^{22,23} a thin body condition and a history of a cystitis episode or a general anaesthetic within the previous 12 months.²³ However, the cause of CKD in cats is often unclear, and in the majority of cases a renal biopsy reveals tubulointerstitial inflammation of unknown aetiology.²¹

Once a diagnosis of CKD has been made, the condition is considered to be progressive, but the time course for progression to end-stage disease is highly variable, with many cats demonstrating very stable disease and dying or being euthanased for an unrelated reason. Following a diagnosis of CKD,

Practical relevance: Both hyperthyroidism and chronic kidney disease (CKD) are common long-term conditions in older cats, which might be diagnosed concurrently or develop at different times. Hyperthyroidism may mask the presence of CKD, and vice versa, by various mechanisms that are described in this review. Hyperthyroidism treatment options should be carefully considered when CKD has also been diagnosed.

Clinical challenges: Although it can be difficult to diagnose hyperthyroidism and CKD simultaneously, given that one condition may mask the other, it is important to consider the presence of both diseases when examining an older cat presenting with vomiting, weight loss, polyuria/ polydipsia, anorexia or sarcopenia. The concurrent presence of hyperthyroidism and CKD requires careful monitoring of glomerular filtration rate biomarkers, and adequate and prompt support of kidney function when normal thyroid function is re-established. Iatrogenic hypothyroidism is a recognised complication of all of the treatment options for hyperthyroidism, and increases the risk of azotaemia. Therapy with levothyroxine is recommended for cats that are hypothyroid and azotaemic.

Evidence base: The information in this review draws on current literature and guidelines related to the pathophysiology, diagnosis and treatment recommendations for feline hyperthyroidism and CKD.

Keywords: CKD; glomerular filtration rate; GFR; azotaemia; goitre



Hyperthyroidism is the most common feline endocrinopathy, affecting over 10% of cats over 9 years of age.



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**CKD is prevalent in older cats,
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It is recommended that cats are staged using the International Renal Interest Society (IRIS) CKD staging system (iris-kidney.com), based initially on their serum creatinine concentration $\pm$ serum symmetric dimethylarginine (SDMA) concentration, and subsequently on systolic blood pressure and urine protein:creatinine (UPC) ratio.

CKD and hyperthyroidism are common comorbidities. It is important to consider both conditions together because they are both prevalent in older cats. Studies have found that 15–51% of cats with hyperthyroidism have underlying CKD.^{24,25} The two conditions will often appear on the same differential diagnoses lists because they share a number of historical findings and clinical signs.

Clinical signs and findings

Hyperthyroidism

Most cats diagnosed with hyperthyroidism are senior, although this condition can occasionally be diagnosed in cats under 10 years of age.^{2,5} Cats with hyperthyroidism may present with a number of clinical signs and blood work changes including a palpable goitre, weight loss, polyphagia, polydipsia/polyuria, sarcopenia, tachycardia, cardiac murmurs, hyperactivity and increased vocalisation, vomiting and diarrhoea, mild erythrocytosis and mild to moderately raised liver enzyme activities, particularly serum alanine transferase (ALT).^{2,5,17,26–28} Not all of these clinical signs and findings are present in all hyperthyroid cats, particularly if diagnosed early in the disease process.^{5,29} Moreover, some cats may present with atypical clinical signs such as lethargy and reduced appetite (termed ‘apathetic’ hyperthyroidism), making the diagnosis of hyperthyroidism less straightforward.⁵ Cats suffering from concomitant hypertrophic cardiomyopathy, usually as a result of increased metabolism and constantly raised cardiac rate, may present collapsed with dyspnoea and/or no palpable femoral pulses if this condition has led to congestive cardiac failure and/or aortic thromboembolism.⁸

Chronic kidney disease

CKD is unlikely to cause any clinical signs early in the course of the disease (particularly prior to the development of azotaemia), except perhaps for documentation of weight loss.³⁰ This possibility for underlying disease

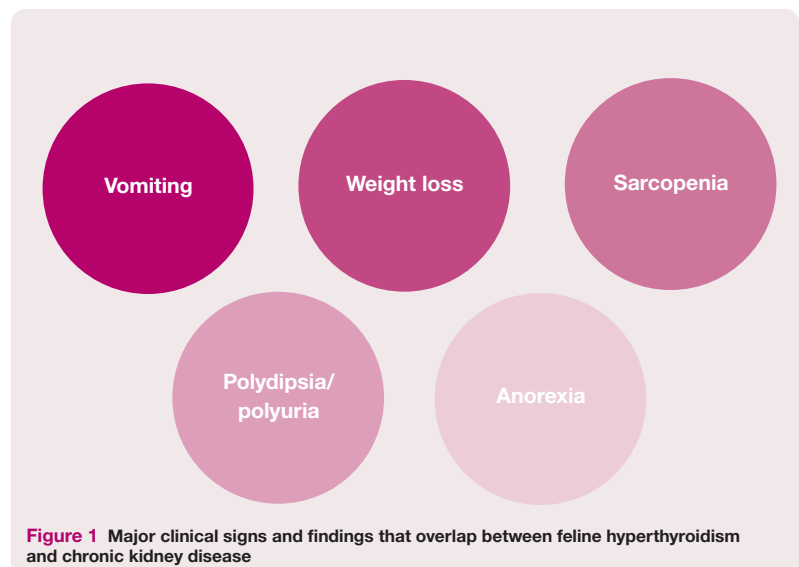


**Up
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in apparently healthy older cats is one of the main arguments for health screening in this patient population.³¹ As CKD advances a number of historical and physical examination findings can develop. Owners may report polydipsia and may also notice polyuria in cats that use a litter tray. Gastrointestinal signs, including a decreased appetite and nausea with or without vomiting, may develop. Cats may be more lethargic, although this can be difficult to assess in older cats that might also have osteoarthritis. On physical examination, pale mucous membranes may be apparent if anaemia has developed, the kidneys may be small or misshapen on palpation (though can feel normal), and loss of muscle mass and body condition may be documented.

Concomitant disease

Given that feline hyperthyroidism and CKD are diseases that affect older cats and that clinical signs and findings of one disease may mimic those of the other (see Figure 1), it is important to consider the possibility of the presence of both diseases when investigating a cat suspected of either hyperthyroidism or CKD. Clinical evaluation of cats with suspected hyperthyroidism and CKD can be all the more challenging given the potential for one disease to mask the presence of the other. For example, the presence of CKD may lead to mild to moderate suppression of thyroid hormone concentrations (non-thyroidal illness syndrome), masking the presence of hyperthyroidism.^{5,6,32} Similarly, hyperthyroidism may increase the cat's glomerular filtration rate (GFR) and decrease its muscle mass, thereby decreasing serum creatinine concentrations and masking the presence of CKD.³²



Diagnosis

Hyperthyroidism

The diagnosis of feline hyperthyroidism is most commonly made when cats present with one or more of the previously described clinical signs and findings, and have a concurrently raised serum total thyroxine (TT4) concentration.^{5,8,13,33} In some cases, definitive diagnosis might require additional diagnostic investigations including measurement of serum thyroid-stimulating hormone (TSH) and free thyroxine (fT4) concentrations and/or scintigraphy.⁵ Despite its higher sensitivity, fT4 measured after equilibrium dialysis is not considered on its own a good test for diagnosing hyperthyroidism in cats, as 3–17% of euthyroid cats will have high fT4 concentrations.^{34,35}

A systematic and categorical approach to the diagnosis of feline hyperthyroidism has been described in the 2016 AAFP Guidelines for the Management of Feline Hyperthyroidism.⁵ These guidelines are particularly helpful for the diagnosis of more challenging cases. In summary, cats with clinical signs and findings suggestive of hyperthyroidism, but a serum TT4 concentration within the reference interval (RI), are recommended to have serum TSH and/or fT4 concentrations measured or scintigraphy performed, as well as further investigations (ie, abdominal ultrasonography, routine urinalysis) carried out, with the aim of identifying the presence of any concurrent illness that might be lowering thyroid hormone concentrations.^{5,32,36} If all these investigations return results that are within normal limits, repeat measurement of serum TT4 concentration 3–4 weeks later is recommended.³² The presence of a goitre in the absence of clinical signs and a normal serum TT4 concentration should prompt ongoing monitoring by repeat serum TT4 concentration measurement at least 6 months later.³² A persistently raised TT4 concentration should prompt medical treatment for hyperthyroidism, even in the absence of clinical and physical examination findings.⁵

Chronic kidney disease

CKD can be diagnosed in a number of ways (see box), but diagnosis usually relies on documentation of a reduction in GFR. It is possible for GFR to be measured directly, but this can be expensive, time consuming and stressful for the cat. Biomarkers of GFR including urea, creatinine and SDMA are therefore commonly used in clinical practice. Azotaemic CKD is diagnosed following documentation of renal azotaemia on at least two occasions; that is, elevated serum creatinine and concurrent inappropriately dilute urine.

Diagnostic findings indicating CKD

- ❖ Reduced GFR on direct measurement.
- ❖ Renal azotaemia, indicated by elevated serum creatinine and low urine specific gravity (USG; <1.035), on at least two occasions.
- ❖ Persistently elevated serum SDMA concentration (>14 µg/dl).
- ❖ Increasing trend over time in serum creatinine or SDMA concentration.
- ❖ Abnormal kidney imaging.
- ❖ Persistent proteinuria, with a UPC ratio >0.4, after ruling out other causes of proteinuria.

An increasing trend over time in SDMA or creatinine concentration, or persistently elevated serum SDMA concentrations, are also recognised as diagnostic for early, non-azotaemic CKD (see iris-kidney.com). A checklist for initial diagnostics to perform when evaluating a cat suspected of CKD and hyperthyroidism is shown in Figure 2.

Challenges of diagnosing concomitant disease

The presence of hyperthyroidism can ‘mask’ the presence of CKD because of the effect of the hyperthyroid state on the kidneys and cardiovascular system. Thyroxine increases renal blood flow and GFR via activation of the renin–angiotensin–aldosterone system (RAAS), increased activity of the sympathetic nervous system and decreased peripheral vascular resistance.³⁷ Additionally, as serum creatinine (a product of muscle metabolism) is influenced by muscle mass,³⁸ its utility for diagnosing CKD is limited in a cat with hyperthyroidism because muscle loss commonly occurs in the hyperthyroid state and can persist after restoration of euthyroidism.³⁹ SDMA arises from protein methylation in all nucleated cells and is not affected by muscle mass,³⁸ which has led to investigation of SDMA as a superior biomarker for

☐ Haematology

☐ Biochemistry (including SDMA)

☐ Routine urinalysis (USG, dipstick, sediment analysis, UPC ratio)

☐ Serum TT4 concentration

☐ Systolic blood pressure measurement

Figure 2 Checklist for initial diagnostics. SDMA = symmetric dimethylarginine; USG = urine specific gravity; UPC = urine protein:creatinine; TT4 = total thyroxine

the presence of CKD in hyperthyroid cats. While theoretically this seems likely, studies to date have suggested that, in the presence of hyperthyroidism, SDMA and creatinine,^{40–42} and even SDMA and GFR,⁴³ are not well correlated.

As a general rule, both serum creatinine and SDMA concentrations will be lower when a cat is hyperthyroid than once the cat is treated and becomes euthyroid. However, the exact effect of the hyperthyroidism on these markers varies between individuals and, in some cases, SDMA concentrations decrease following treatment.⁴¹ This therefore means that, at present, it is not possible to determine for certain whether a hyperthyroid cat has concurrent CKD unless it is azotaemic despite high TT4 concentrations or it already had a CKD diagnosis before the hyperthyroidism developed. A recent study found SDMA concentrations prior to radioactive iodine treatment to be 94% specific but only 15% sensitive for the development of azotaemia post-treatment;⁴⁰ therefore, if SDMA is elevated before treatment there is a high probability that the cat will become azotaemic following treatment, but there are also many cats that will be azotaemic after treatment that will have had a normal SDMA concentration while hyperthyroid. Additional studies have found that SDMA and creatinine concentration changes vary between cats pre- and post-treatment with radioactive iodine or bilateral thyroidectomy,^{41–44} making the prediction of which cats will be diagnosed with CKD following treatment difficult for the clinician.

The presence of CKD can also make diagnosis of hyperthyroidism more challenging. Non-thyroidal illness causes a lowering of circulating thyroid hormones.⁴⁵ As a result, CKD can suppress TT4 concentrations to well within the RI despite the cat having hyperthyroidism (also referred to as occult

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hyperthyroidism). In one study of cats with occult hyperthyroidism and CKD, the majority of cats had TT4 concentrations suppressed to within the top half of the RI, but 2/16 had a TT4 concentration <30 nmol/l (RI 19–55).⁴⁶ Furthermore, TT4 concentrations also vary day to day in cats with hyperthyroidism, so it is not recommended to rule out the condition in a cat with compatible clinical signs based on a single normal TT4 measurement.⁴⁷

The logical first step in trying to make a diagnosis of hyperthyroidism in a cat with CKD and a TT4 concentration within the RI is to re-measure TT4 on another day. If TT4 is still within the RI, but hyperthyroidism is strongly suspected, measurement of fT4 concentrations may aid the diagnosis, as fT4 is above the RI in 95% of cats with CKD and occult hyperthyroidism.⁴⁶ Measurement of TSH concentration may also aid diagnosis, with a low concentration being consistent with occult hyperthyroidism; however, the poor sensitivity of available assays for feline TSH results in many healthy euthyroid cats having low TSH concentrations too, limiting the utility of this test. TSH measurement can be more useful for ruling out hyperthyroidism (when TSH is normal or increased) and for detecting iatrogenic hypothyroidism (when TSH is increased).⁴⁸

When to check for hypertension

Systemic hypertension has an incidence risk of 19.5% over 2 years in cats.⁴⁹ Secondary hypertension, which occurs in conjunction with another disease process, is the most common type of hypertension in this species. Studies have reported that 19–61% of cats with CKD^{50,51} and 25–87% of cats with hyperthyroidism^{49,51,52} also have hypertension. Hyperthyroid cats are at increased risk of situational (or ‘white coat’) hypertension. Hyperthyroid cats found to be hypertensive should be checked for evidence of target organ damage (eg, hypertensive retinopathy) and started on treatment immediately if this is present.

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Studies have documented increasing prevalence (approximately two-fold) of hypertension within 6 months of restoration of euthyroidism, although a proportion of these cats also developed azotaemic CKD.^{53,54} Additionally, cats with CKD are at increased risk of developing hypertension over time, even if they do not have it at diagnosis.⁵⁵ It is therefore important to measure blood pressure at diagnosis of CKD or hyperthyroidism. If blood pressure is normal in a hyperthyroid cat, it should be re-measured once euthyroidism is restored. Cats with CKD should have their blood pressure monitored every few months. Monitoring and treatment of feline hypertension is covered in detail in ISFM Consensus Guidelines on the Diagnosis and Management of Hypertension in Cats, published in 2017.⁵⁶

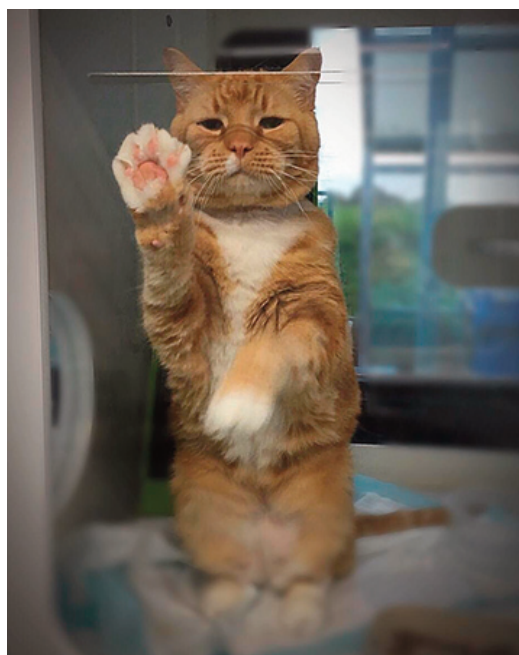


Figure 3 A 9.5-year-old male neutered cat with International Renal Interest Society stage 2 chronic kidney disease (CKD) and concurrent hyperthyroidism, pictured in the radioactive iodine unit of the Royal Veterinary College. Radioactive iodine treatment successfully resolved the hyperthyroidism. The cat's CKD remained stable for 18 months and subsequently progressed to an advanced stage by 24 months after radioactive iodine treatment. Courtesy of Gemma Harvey

Any concurrent diseases, especially CKD, systemic hypertension and cardiac disease, must be taken into account when deciding on the treatment for hyperthyroidism.



be monitored for the development of hypothyroidism at 3 and 6 months post-treatment at a minimum, as hypothyroidism will impact renal function and the function of other vital organs.⁵ Up to 75% of cats will have a low TT4 concentration following treatment, at least transiently. However, fewer than 30% of cats will remain hypothyroid 3 months after I¹³¹ treatment.^{5,48,58} Cats with bilateral thyroid disease on scintigraphy (Figure 4) have been found to be twice as likely to develop hypothyroidism after I¹³¹ than cats with unilateral disease.⁵⁸ The main disadvantages of I¹³¹ treatment include a high short-term cost of treatment and the need for the cat to stay in hospital for a period of time, although the hospitalisation period is not standardised across different hospitals.

❖ **Medical treatment** Pharmacological treatment of feline hyperthyroidism involves the administration of thioureylenes antithyroid drugs (carbimazole and methimazole/thiamazole) either orally or transdermally (Figure 5).^{32,59} Advantages are the efficacy of methimazole/thiamazole or carbimazole (successful response rate of 85%) and that this is a reversible form of treatment, allowing for assessment of the effects that restoration of euthyroidism has on a patient's renal function.^{8,35} Cats receiving oral or transdermal medical treatment require close monitoring of serum TT4 concentrations. Given that most cats regain euthyroid status within 2–3 weeks

Management

Hyperthyroidism

Various treatment options are available for management of feline hyperthyroidism, including: (1) radioactive iodine treatment; (2) oral or transdermal medical treatment; (3) surgical thyroidectomy; and (4) dietary therapy.^{5,8,13,35} Any treatment option has its advantages and disadvantages, and these should be carefully discussed with owners. Furthermore, the decision on any form of treatment for hyperthyroidism must take into account the presence of any concurrent disease, especially CKD, systemic hypertension and cardiac disease.⁸ For example, a short course of medical treatment may be recommended before undergoing radiotherapy or surgery, in order to determine the effect of restoring euthyroidism on renal function.⁸

❖ **Radioactive iodine treatment** Radioactive iodine (I¹³¹) is considered by many to be the treatment of choice for feline hyperthyroidism, including for cases of thyroid carcinoma.^{8,9,57} The technique is simple, non-invasive and is associated with no anaesthetic risk or risk of damage to the parathyroid glands.⁸ Cats usually return to a euthyroid status 2–12 weeks after a single injection of I¹³¹, with a success rate of treatment of over 95% (Figure 3).^{5,58} Cats treated with I¹³¹ should

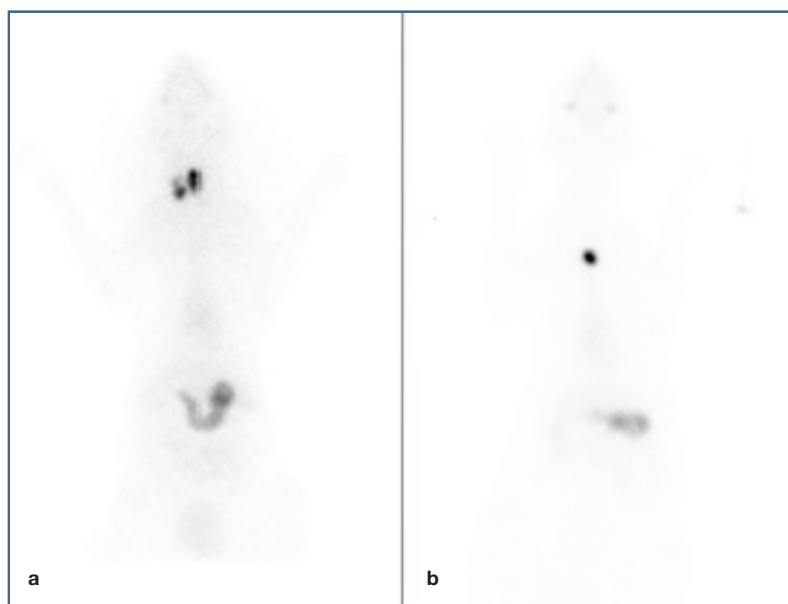


Figure 4 Scintigraphy can help to confirm a diagnosis of hyperthyroidism and indicate where overactive thyroid tissue is anatomically prior to deciding on treatment options. The cat in (a) demonstrates increased uptake of technetium in both cervical thyroid glands, consistent with bilateral thyroid disease; the cat was subsequently treated with radioactive iodine. The cat in (b) demonstrates a single area of increased technetium uptake in the cranial mediastinum, consistent with ectopic thyroid tissue; the cat had subsequent surgery to remove both cervical thyroid glands as well as a 1 cm mass cranial to the thymus, which was confirmed to be a well-differentiated thyroid carcinoma on histopathology



Figure 5 A 16-year-old female neutered domestic shorthair cat diagnosed with concurrent hyperthyroidism, International Renal Interest Society stage 3 chronic kidney disease (CKD; non-proteinuric) and hypertension, with evidence of bullae on retinal examination. Given the more advanced CKD, the hyperthyroidism was managed medically with oral methimazole twice a day, ensuring the total thyroxine concentration was kept within the bottom half of the reference interval. Amlodipine treatment was also administered to control the hypertension and a renal diet was fed. The cat was euthanased approximately 2 years later for progressive anorexia and weight loss

of treatment with antithyroid drugs, it is recommended that serum TT4 concentrations are measured within 3–4 weeks of starting therapy and then every 3–4 weeks until the lowest effective dose is determined.^{32,35,60} Carbimazole or methimazole/thiamazole doses are titrated to effect with the aim of reducing serum TT4 concentrations to the lower half of the RI.³⁵ Once stable, cats can be checked every 4–6 months.³² Over time, adjustments to the dose and frequency of medication may be required as the number and size of the thyroid nodules continue to increase.⁶¹ Disadvantages of medical therapy include the possibility of a lack of client compliance for medication administrations, the possibility of leaving a thyroid carcinoma in situ and the possibility of medication side effects including gastrointestinal upset, facial pruritus or cytopaenias. Although short- to medium-term costs will be lower, in the longer term this option may exceed the cost of definitive treatment.

❖ **Surgical thyroidectomy** Surgery is ideally performed in cats that are already receiving medical treatment and are therefore more cardiovascularly stable, reducing the anaesthetic risk associated with the procedure.^{8,32} Bilateral modified extracapsular thyroidectomy is usually recommended in order to preserve the parathyroid glands in situ and avoid the need for a second surgery (Figure 6). The latter is particularly relevant given that both thyroid glands are affected in two-thirds of cases.^{3,5,8} Thyroidectomy is successful at treating hyperthyroidism in more than 95% of

Should a cat be left mildly hyperthyroid to prevent development of azotaemia?

As tempting as it might be to keep a cat mildly hyperthyroid in an attempt to maintain the serum creatinine concentration within normal limits, this might not be a good idea. By keeping a cat hyperthyroid it is not possible to control the systemic effects of the hypermetabolic state characteristic of this condition, meaning that many body organ systems will continue to suffer, including the kidneys themselves. Furthermore, the renal disease will continue to evolve, even if the patient is not azotaemic due to the effect of thyroxine increasing the GFR.

Cats usually return to a euthyroid status by 12 weeks, and sometimes as early as 2 weeks, after a single injection of I¹³¹.



cases.⁶² Scintigraphy is of great value prior to thyroidectomy as a means to identify unilateral vs bilateral thyroid disease, the presence of ectopic thyroid tissue, which has been reported to occur in 4–20% of cases, or any extension of the cat's goitre into the thoracic inlet and mediastinum.⁸ Because of the short half-life of cats' thyroid hormones, euthyroidism may be achieved 24–48 h post-thyroidectomy.¹³ However, serum TT4 concentrations are usually checked 4–6 weeks after surgery and then, provided the disease is well controlled, every 4–6 months, or earlier if a recurrence of clinical signs is seen.³² The main disadvantages of surgery are the requirement for general anaesthesia, the up-front cost of the treatment, the possibility of hypoparathyroidism and hypocalcaemia developing following bilateral thyroidectomy, and the risk of disease recurrence following unilateral thyroidectomy.

❖ **Dietary therapy** An iodine-restricted diet (Hill's y/d) is marketed as a treatment option for cats with hyperthyroidism.³² However, there are a few factors to consider prior to prescribing this diet: (1) in cats suffering from severe thyrotoxicosis it may take up to 6 months for their hyperthyroidism to be clinically controlled with diet and some cats with particularly severe disease may struggle to achieve euthyroidism; (2) there are no studies looking at the long-term effects of iodine restriction in cats; (3) cats fed Hill's y/d must be indoor-only cats with no access to other food sources; and (4) some medications contain iodine and so may not be compatible with dietary management of hyperthyroidism.⁵

Iatrogenic hypothyroidism is a well-recognised complication of all treatment options for hyperthyroidism (see box on page 647).

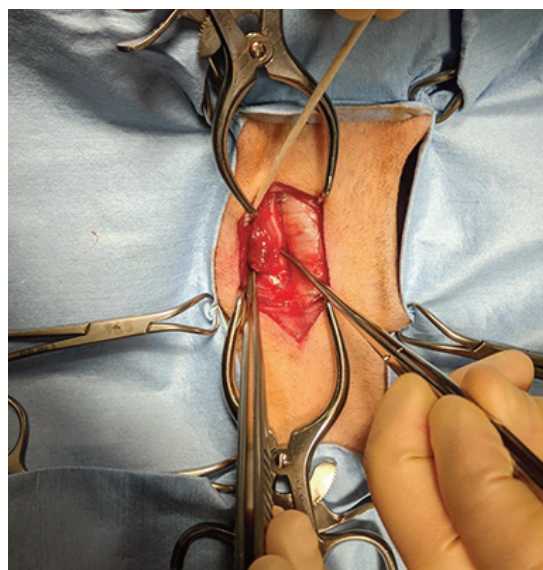


Figure 6 Surgical approach for thyroidectomy. The left thyroid gland is exposed prior to removal. Note the recurrent laryngeal nerve seen here between the thyroid and the trachea. Courtesy of Lynda Rutherford

Iatrogenic hypothyroidism

In one study, 28/75 cats (37%) were hypothyroid 6 months after treatment with antithyroid medication alone or in combination with thyroidectomy.⁴⁸ Clinical signs of iatrogenic feline hypothyroidism may include lethargy, weight gain, inappetence, seborrhoea sicca and a dull, dry, unkempt haircoat that may be associated with alopecia of the pinnae. However, some hypothyroid cats show no overt clinical signs.⁶³

Therapy with levothyroxine (75–100 µg/cat PO q12h) is usually recommended for cats that are hypothyroid (TT4 <10–15 nmol/l

and TSH above the RI) and azotaemic >3 months after ¹³¹I or surgical treatment. Cats diagnosed with iatrogenic hypothyroidism have a greater incidence of azotaemia.⁴⁸ Should no azotaemia or other clinical signs be present 3 months post-¹³¹I treatment or surgery, there is no need to start levothyroxine supplementation, unless the cat remains hypothyroid at 6 months. Once therapy has been initiated, serum TT4 concentration can be monitored every 6–12 months. A blood sample should be taken 4–6 h after the morning dose of levothyroxine.³²

Chronic kidney disease

Once present, CKD cannot be reversed, and management is focused on trying to slow progression of the disease. The mainstay of treatment is to transition the cat onto a protein- and phosphate-restricted clinical renal diet, as this has been shown to reduce the signs of uraemia, slow progression of CKD

and improve survival time in IRIS stage 2–4 azotaemic cases.^{64–66} At present, data supporting the use of protein- and phosphate-restricted diets in non-azotaemic CKD patients are lacking. Cats should be treated for proteinuria if they are persistently proteinuric (UPC >0.4) and for systemic hypertension if present. Additional treatments should be considered

Case notes 1

Sooty, a 10-year-old male neutered domestic shorthair cat, was presented with weight loss, polyphagia, polydipsia and vomiting of approximately 4 weeks' duration.

Initial case work-up Physical examination revealed a mobile goitre on the right-hand side and a thyroid blip on the left, a body condition score of 4/9 and moderate muscle wastage. Sooty was tachycardic at 220 beats per minute (bpm) and weighed 3.4 kg – 400 g less than at vaccination and routine examination 8 months previously. Hyperthyroidism was suspected, and routine biochemistry and haematology revealed a moderate elevation in ALT activity (377.5 U/l; RI 5–60), and mild elevations in alkaline phosphatase activity (87 U/l; RI 0–60) and serum urea concentration (10.0 mmol/l; RI 2.5–9.9). Serum creatinine concentration was within normal limits (77 µmol/l; RI 20–177) and USG was >1.050. TT4 was elevated (175 nmol/l; RI 19–65), confirming a diagnosis of hyperthyroidism. Systolic blood pressure was 145 mmHg.



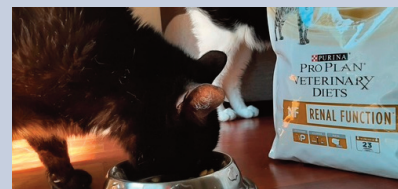
Hyperthyroidism treatment A treatment trial with methimazole was initiated at 2.5 mg PO q12h and re-examination 4 weeks later revealed a body weight of 3.6 kg and heart rate of 190 bpm. Serum TT4 concentration had decreased (50 nmol/l) and serum creatinine concentration was stable (80 µmol/l). After discussing longer-term treatment options, the owner elected for referral for ¹³¹I treatment. Methimazole was discontinued 2 weeks prior to referral, as requested. At discharge, post-¹³¹I treatment, serum TT4 concentration was low (<5.1 nmol/l), liver enzyme activities were within the RI, and serum urea and creatinine were also within normal limits (urea 9.7 mmol/l and creatinine 89 µmol/l), with a USG of 1.045. Systolic blood pressure was 150 mmHg. No specific treatment was prescribed.

Follow-up, and further diagnoses and treatment By 6 months post-¹³¹I treatment, Sooty had gained further weight to 4.0 kg, and was more lethargic, with a heart rate of 140 bpm on examination. Serum TT4 concentration had increased but was still low (11 nmol/l). Mild renal azotaemia was present, with mildly elevated serum creatinine (187 µmol/l) and urea (11.2 mmol/l), and a USG of 1.022. TSH concentration was increased (2.23 ng/ml; >0.3 ng/ml indicative of hypothyroidism in combination with a low TT4). Treatment with levothyroxine was initiated at 100 µg PO q12h to prevent the progressive deterioration in renal function associated with iatrogenic hypothyroidism. One month later, serum TT4 concentration at 4 h post-levothyroxine treatment was well controlled (22 nmol/l), and serum creatinine had returned to normal limits (147 µmol/l). Sooty was maintained on this dose of levothyroxine long term, and was staged as non-azotaemic IRIS stage 2, non-proteinuric and normotensive. No further treatment for CKD was therefore initiated at this time.

✦ **What this case demonstrates:** Iatrogenic hypothyroidism following treatment for hyperthyroidism may be persistent and survival time is shortened if the cat becomes azotaemic while hypothyroid. If hypothyroidism (low TT4 concentration and high TSH concentration) is documented and the cat is also azotaemic, treatment should be instigated to return the patient's TT4 concentration to within the RI (preferably the bottom half of the RI). This may be achieved by altering the dose of hyperthyroidism medication for medically treated cats, or by starting levothyroxine supplementation for cats that have had thyroidectomy or radioactive iodine treatment.

Case notes 2

Roger, a 17.5-year-old male neutered domestic shorthair cat, was presented for investigation of excessive urination, small bowel diarrhoea and weight loss, despite a good appetite.



Initial case work-up and treatment On presentation, Roger was bright, alert and responsive, although it was a little difficult to examine him. His mucous membranes were pink but tacky, with a capillary refill time of less than 2 s. Rectal temperature was 38.4°C, heart rate was 190 bpm and respiratory rate was 24 breaths per minute. Pulses were adequate and synchronous. Thoracic auscultation revealed no abnormalities. Abdominal palpation revealed that both kidneys were small in size, but no other abnormalities were detected. Peripheral lymph nodes were within normal limits, but a left-sided goitre was noted. Roger weighed 2.6 kg and had a body condition score of 3/9. Systolic blood pressure was 160 mmHg and retinal examination was within normal limits. Blood work, including routine haematology, biochemistry and serum TT4 concentration, and routine urinalysis revealed the presence of a mild non-regenerative anaemia (haematocrit 27%; RI 28–40), moderately raised serum creatinine concentration (200 µmol/l; RI 20–177), moderately raised serum alkaline phosphatase activity (334 U/l; RI 0–60), markedly raised serum TT4 concentration (256 nmol/l; RI 19–65) and a USG of 1.007, confirming a diagnosis of hyperthyroidism and azotaemic CKD. To reduce the risk of a sudden deterioration in kidney function, Roger was started on treatment with the lowest recommended dose of thiamazole (2.5 mg PO q12h).

Follow-up and treatment adjustment At re-examination 3 weeks later, Roger's serum TT4 concentration had dropped (70 nmol/l) while his serum creatinine concentration had risen (270 µmol/l), with a USG of 1.010 and blood pressure within normal limits. He was doing better clinically, had put on weight and was more relaxed at home.

Although too early to perform IRIS staging due to Roger still having mild hyperthyroidism, a renal diet was introduced and a mild increase in thiamazole dose was recommended (3 mg PO q12h). This reduced the serum TT4 concentration (25 nmol/l) and there was no change in his serum creatinine concentration (260 µmol/l). Roger was therefore confirmed to have IRIS stage 3 CKD. It was recommended that he continue the same therapy for the hyperthyroidism and return for re-examination in 8 weeks, at which point Roger's thyroid and renal function were unaltered.

❖ **What this case demonstrates:** Patients suffering from hyperthyroidism and concomitant azotaemic CKD should be treated medically for their hyperthyroidism and this should be initiated with the lowest recommended dose. Meantime, their renal function and general wellbeing should be monitored and addressed should they suddenly deteriorate as their GFR drops.

on a case-by-case basis, including potassium supplementation for hypokalaemia, subcutaneous fluids for recurrent episodes of dehydration and use of erythropoietin analogues for anaemia. Further information on CKD management by IRIS stage can be found at iris-kidney.com.

Management of CKD for a cat with concurrent hyperthyroidism should be no different from management of CKD in a euthyroid cat. Feeding a clinical renal diet to a cat with both conditions that is azotaemic should take precedence over the use of an iodine-free diet to treat hyperthyroidism.

KEY POINTS

- ❖ Hyperthyroidism and CKD are very common conditions in older cats that frequently present concurrently.
- ❖ Clinical signs and findings of feline hyperthyroidism may mimic those of CKD and therefore it is important to consider the possibility of the presence of both diseases.
- ❖ The presence of CKD may lead to mild to moderate suppression of thyroid hormone synthesis, masking the presence of hyperthyroidism.
- ❖ Hyperthyroidism may increase a cat's GFR and thereby decrease serum creatinine concentration, masking the presence of CKD.
- ❖ It is important to measure systolic blood pressure at diagnosis of CKD and/or hyperthyroidism. In hyperthyroid cats, if blood pressure is normal, it is recommended that it is remeasured once euthyroidism is restored. Cats with CKD should have their blood pressure monitored every few months.
- ❖ Patients diagnosed simultaneously with hyperthyroidism and azotaemic CKD should be treated medically for their hyperthyroidism with the lowest recommended dose initially, while monitoring their kidney function and general wellbeing.
- ❖ Iatrogenic hypothyroidism is a recognised complication of all of the treatment options for hyperthyroidism. Patients should be monitored and treated if they become azotaemic.



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