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Prevalence of iatrogenic hypothyroidism in hyperthyroid cats treated with radioiodine using an individualised scoring system

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Abstract

Objectives The aim of this study was to report the prevalence of iatrogenic hypothyroidism, with or without azotaemia, based on the measurement of serum total thyroxine (T4), thyroid-stimulating hormone (TSH) and creatinine concentrations, in hyperthyroid cats undergoing radioiodine (^{131}I) treatment where the ^{131}I dose was calculated using a previously described scoring system. A secondary aim of the study was to determine the positive and negative predictive values of serum T4 and TSH concentrations obtained 19 days after treatment in order to predict the development of iatrogenic hypothyroidism 6–9 months after ^{131}I treatment.

Methods Serum T4, TSH and creatinine concentrations were measured 19 days and 6–9 months after ^{131}I treatment. The prevalence of iatrogenic hypothyroidism was assessed with the results obtained 6–9 months after ^{131}I treatment.

Results The prevalence of overt and subclinical hypothyroidism 6–9 months after ^{131}I treatment was 40.0% (22/55 cats) and 12.7% (7/55 cats). Overt hypothyroidism with azotaemia was diagnosed in 8/55 (14.5%) cats. The positive and negative predictive values for the prediction of the development of iatrogenic hypothyroidism 6–9 months after ^{131}I treatment were 72.2% and 80.0%, respectively, for a low serum T4 concentration, and 75.0% and 44.6%, respectively, for an increased serum TSH concentration.

Conclusions and relevance The use of an individualised scoring system is effective in determining the ^{131}I dose for the treatment of hyperthyroid cats. However, the prevalence of overt hypothyroidism was higher in comparison with other studies using different dosing protocols. Further studies comparing the efficacy of individualised scoring systems and different fixed doses to determine which method is superior are warranted.

Keywords: Iodine isotopes; hyperthyroidism; hypothyroidism; thyroid gland; azotaemia

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Introduction

Hyperthyroidism is the most common endocrinopathy seen in geriatric cats and is most commonly caused by adenomas or adenomatous hyperplasia of the thyroid gland.[1] Treatment options include medical management with oral or transdermal antithyroid drugs (methimazole or carbimazole), an iodine-restricted diet, thyroidectomy or radioiodine treatment.[2–5]

Radioiodine (^{131}I) therapy is generally considered the treatment of choice for feline hyperthyroidism, whenever significant comorbidities are absent, given its simplicity, safety and efficacy.[1,5–8] As with any other treatment options, there are a few disadvantages to the use of ^{131}I in hyperthyroid cats, including cost of treatment, a limited number of centres offering this treatment modality, the need for a protracted period of hospitalisation following treatment and the risk of causing iatrogenic hypothyroidism.[8]

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Iatrogenic hypothyroidism is a well-recognised complication of ^{131}I treatment, which has been reported in up to 79% of hyperthyroid cats following ^{131}I therapy.[9] Cats that develop iatrogenic hypothyroidism are more likely to develop azotaemia than euthyroid cats.[10] Moreover, cats that become hypothyroid and also develop azotaemia have shorter survival times than non-azotaemic cats.[10] Therefore, the optimal ^{131}I dose should ideally restore euthyroidism without inducing hypothyroidism. Different methods have been used to try to determine the optimal ^{131}I dose including different fixed ^{131}I dosages or individualised ^{131}I dosing protocols using tracer kinetic studies or scoring systems.[7,8] However, the optimal method to calculate the ^{131}I dose remains controversial.[8]

In 1995, Peterson and Becker described a scoring system used to calculate the ^{131}I dose based on serum total thyroxine (T4) concentration, severity of the clinical signs and size of the palpable thyroid gland, and concluded that it was safe and effective to treat feline hyperthyroidism.[5] In this study, only 1.5% of cats were persistently hyperthyroid 6 months after ^{131}I treatment and only 2.1% cats developed clinical features of hypothyroidism with a decreased T4 concentration, despite 11.4% cats having a low serum T4.[5]

At the time of this study, a thyroid-stimulating hormone (TSH) assay was not available, thereby limiting the ability to diagnose and confirm hypothyroidism in these cats. Moreover, many cats with iatrogenic hypothyroidism do not develop overt clinical signs and other cats may only display subtle and non-specific clinical signs such as lethargy, unspecific dermatological changes, decreased appetite or weight gain, some of which could be attributed to the resolution of hyperthyroidism rather than hypothyroidism.[11,12] In addition, the use of subnormal T4 or free T4 concentration alone to diagnose iatrogenic hypothyroidism can also be misleading because non-thyroidal illness can decrease serum T4 and free T4 concentrations.[13–16] Instead, the measurement of serum TSH concentration appears to be more sensitive and specific than T4 and free T4 alone for the diagnosis of iatrogenic hypothyroidism and to differentiate between cats with iatrogenic hypothyroidism and those with non-thyroidal illnesses.[16]

We have routinely been using the scoring system described by Peterson and Becker to determine ^{131}I dosing for several years.[5] Therefore, the aim of this study was to report the prevalence of iatrogenic hypothyroidism, with and without azotaemia, based on the measurement of serum T4, TSH and creatinine concentrations, in hyperthyroid cats undergoing ^{131}I treatment where the ^{131}I dose was calculated using this scoring system. Another objective of the study was to determine the positive and negative predictive values (PPV and NPV, respectively) of serum T4 and TSH concentrations obtained prior to hospital discharge to predict the development of iatrogenic hypothyroidism 6–9 months after ^{131}I treatment.

Material and methods

Cats

Hyperthyroid cats referred for radioiodine treatment at the Centre for Small Animal Studies (Animal Health Trust, Newmarket, UK) between October 2013 and December 2015 were eligible for this prospective study. The diagnosis of hyperthyroidism was based on compatible clinical signs and an increased serum T4 concentration above the reference interval (RI) for the reference laboratory used.[1] Different reference laboratories with different methodologies were used, but none of the cats were diagnosed with hyperthyroidism using an in-house point-of-care analyser. The study was approved by the Animal Health Trust's ethics committee and enrolment of the cats in the study was subject to informed owner consent.

During the study period, 70 cats were prospectively enrolled, receiving 71 ^{131}I treatments, and 55 cats completed the study at 6–9 months after ^{131}I treatment. Eleven cats were lost to follow-up and four cats died due to non-thyroidal illnesses (Figure 1). Most hyperthyroid cats (40/55) that completed the study had a pretreatment assessment performed at our hospital, during a different appointment, which included a review of the history, physical examination, systolic blood pressure measurement, laboratory testing (full haematology, comprehensive serum biochemistry, serum T4 concentration for hyperthyroidism monitoring and urinalysis) if these were not performed within 1 month prior to assessment by the referring veterinarian, along with thoracic and abdominal radiographs and abdominal ultrasound. Further investigations (eg, echocardiography, fine-needle aspirates, etc) were carried out in some cats depending on the findings during the assessment.[17] The remainder of the cats (15/55) had the above investigations performed at the referring veterinarian.

The authors reviewed the clinical history (including the investigations performed and treatments prescribed) of all these cats, and performed a consultation with the owners and a thorough physical examination the day of hospital admission prior to ^{131}I treatment. Treatment with antithyroid drugs or the use of a veterinary prescription iodine-restricted diet were discontinued for 2 weeks prior to ^{131}I treatment.

Procedures

The dose of ^{131}I was determined for each hyperthyroid cat by various internal medicine specialists and based on a scoring system that included severity of clinical signs, serum T4 concentration and palpable thyroid gland size, as previously described.[5] Every variable had a score from 1–3. Five cats without a palpable goitre received a score of 1 for this variable. Cats with a total score of 3–5 received a low ^{131}I dose (74–130 MBq; 2.0–3.4 mCi), cats with a total score of 6 or 7 received a moderate ^{131}I dose (130–167 MBq; 3.5–4.4 mCi) and cats with a total score of 8 or 9

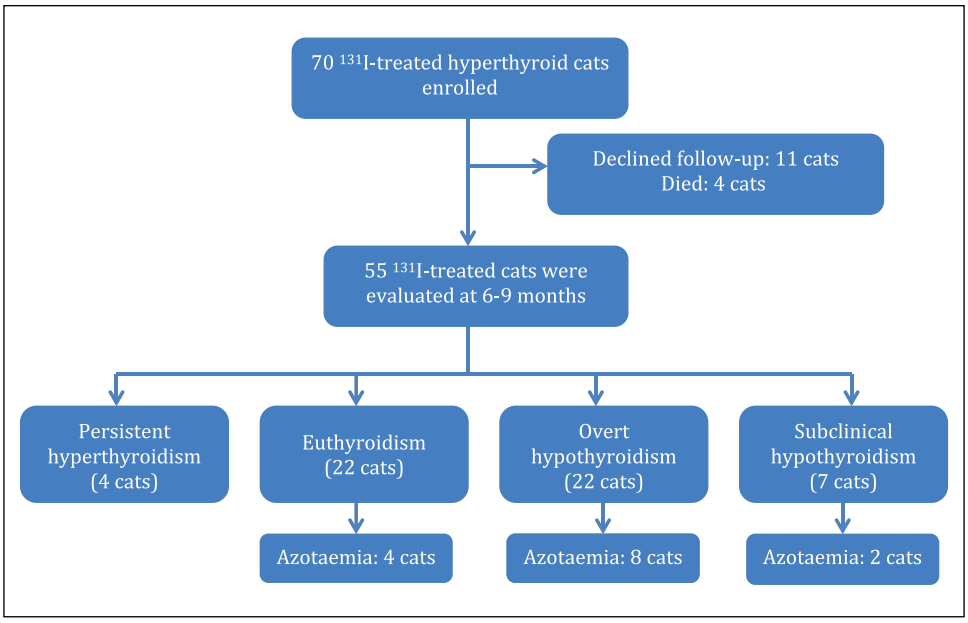

Figure 1 Flowchart for the enrolment of hyperthyroid cats, separated into thyroid status and presence of azotaemia at the end of the study

received a high ^{131}I dose (167–222 MBq; 4.5–6.0 mCi).[5] After ^{131}I treatment, all cats were hospitalised in individual cages in a designated radiation isolation area for 3 weeks and then discharged.

Serum T4, TSH and creatinine concentrations were measured by the same reference veterinary diagnostic laboratory (Powell Torrance Diagnostic Services, UK) 19 days (prior to hospital discharge) and 6–9 months after ^{131}I treatment. Serum T4 concentration was measured by a chemiluminescent immunoassay (Immulite Total T4; Siemens Healthcare Diagnostics Products); serum TSH was measured similarly using a canine assay (Immulite Canine TSH; Siemens Healthcare Diagnostics Products), both validated in cats.[10,18] The T4 and canine TSH assays were also validated for use in cats at the same laboratory (see Appendix A in the supplementary material). Serum creatinine was measured by a modified Jaffe picrate reaction (Werfen-Instrumentation Laboratory, Italy). In order to maintain enrolment compliance, the owners of treated cats could have the follow-ups performed by their local veterinarians, who could submit the blood samples directly to the designated reference veterinary diagnostic laboratory.

Data analysis

SPSS Statistics for Macintosh version 22.0 (IBM) was used for statistical analysis. Continuous data were assessed for normality using the Shapiro–Wilk test. Only serum creatinine was normally distributed and therefore all analyses were performed using non-parametric tests. Continuous data were expressed as median and interquartile ranges (IQR; 25th–75th percentile). Categorical variables were compared between groups by the Pearson's χ^2 test. For all analyses P values <0.05 were considered to be statistically significant.

The thyroid status of treated hyperthyroid cats was classified based on the laboratory RIs, as persistently hyperthyroid (T4: >50.0 nmol/l; TSH: <0.03 ng/ml), euthyroid (T4: <50.0 nmol/l; TSH: ⩽0.20 ng/ml), overtly hypothyroid (T4: <15.0 nmol/l; TSH: >0.20 ng/ml) and subclinically hypothyroid (T4: 15.0–50.0 nmol/l; TSH: >0.20 ng/ml), as previously defined.[7] See Appendix A in the supplementary material for details on how the RIs for serum T4 and TSH concentrations were determined. The lower limits of quantification of the T4 and TSH assays were 12.9 nmol/l and 0.03 ng/ml, respectively. Therefore, for data analysis, all undetectable serum T4 and TSH concentrations were given an arbitrary concentration of 10 nmol/l and 0.02 ng/ml, respectively.[19] The ultimate thyroid status of each cat was assessed with the results obtained 6–9 months after ^{131}I treatment. Azotaemia was defined as a creatinine above the laboratory RI (creatinine: >180 µmol/l).

Results

Study population

Cat breeds that completed the study included domestic shorthair (n = 47), domestic longhair (n = 6), British Shorthair (n = 1) and Birman (n = 1). The median age of these cats was 12 years (IQR 11–14 years). There were 31 male and 24 female cats, all of which were neutered. Prior to radioiodine treatment, 38 cats had been treated with oral anti-thyroid drugs (methimazole [17 cats] or carbimazole [21 cats]), eight cats with transdermal

methimazole, three cats with the use of an iodine-restricted diet and six cats were not receiving any treatment due to antithyroid drug side effects (five cats) or inability to medicate the cat (one cat). None of the cats were azotaemic at diagnosis. Euthyroidism had been achieved in 44 cats prior to ^{131}I treatment, with 42 cats remaining non-azotaemic (median 110 µmol/l; IQR 91–124 µmol/l) and two cats developing a mild azotaemia (184 µmol/l and 189 µmol/l, respectively). None of the 11 cats that remained hyperthyroid prior to ^{131}I treatment were azotaemic (median 76 µmol/l; IQR 60–94 µmol/l).

An immediate pretreatment serum T4 concentration, measured at a single laboratory (Dick White Referrals, Diagnostic Pathology, UK), and performed at least 2 weeks after discontinuing antithyroid treatment, was available in 46/55 cats. A serum T4 concentration, in cats not receiving any antithyroid treatment for at least 2 weeks, was available at a median of 3 months (IQR 2.5–4.0 months) prior to the remaining 9/55 ^{131}I treatments. The median pretreatment serum T4 concentration was 163 nmol/l (IQR 119–229 nmol/l). Based on the scoring system, 17/55 cats (30.9%) received a low ^{131}I dose (median 100 MBq [2.7 mCi]; IQR 80–110 MBq [2.2–3.0 mCi]), 30/55 cats (54.5%) received a moderate ^{131}I dose (median and IQR 130 MBq, 3.5 mCi) and 8/55 (14.5%) cats received a high ^{131}I dose (median 167 MBq [4.5 mCi]; IQR 167–200 MBq [4.5–5.4 mCi]). The median ^{131}I dose administered to all cats was 130 MBq (3.5 mCi) (IQR 110–130 MBq [2.7–3.5 mCi]).

Thyroid and renal parameters after ^{131}I treatment

The modal serum T4 concentration 19 days after ^{131}I treatment for the 55 cats completing the study was 10.0 nmol/l (IQR 10.0–13.6 nmol/l). Serum T4 concentration was within the RI in 14/55 (25.5%) cats and decreased in 35/55 (63.6%) cats, most of which (33/35 cats) had a serum T4 concentration below the detection limit of the assay. Six of the 55 cats (10.9%) had an increased serum T4 concentration (range 53.5–354.0 nmol/l).

The modal serum TSH concentration 19 days after ^{131}I treatment was 0.02 ng/ml (IQR 0.02–0.09 ng/ml). Serum TSH concentration was within the RI in 12/55 (21.8%) cats and below the detection limit of the assay in 39/55 (70.9%) cats, including all cats with increased serum T4 concentration. Serum TSH concentration was increased in 4/55 (7.3%) cats (range 0.24–0.60 ng/ml) and the serum T4 concentration was below the detection limit of the assay in these four cats.

The median serum creatinine concentration was 130 µmol/l (IQR 107–158 µmol/l). Five of the 55 cats (9.1%) had an increased creatinine concentration (range 186–198 µmol/l) and all these cats had a decreased serum T4 concentration, four had a decreased serum TSH concentration and one cat had a normal (0.10 ng/ml) serum TSH concentration. Four cats with decreased serum T4 and increased serum TSH concentrations had a serum creatinine concentration that ranged from 110–179 µmol/l. The serum creatinine concentration in two cats that developed azotaemia after achieving a euthyroid state prior to ^{131}I treatment remained stable (≤16% variation) at 19 days after ^{131}I treatment.[20]

Fifty-five cats completed the study at the 6–9 month re-check (median 206 days; IQR 198–238 days) after ^{131}I treatment. Of the six cats with an increased serum T4 concentration at 19 days, prior to hospital discharge, four cats remained persistently hyperthyroid, giving a treatment failure rate of 5.6% (4/71 ^{131}I treatments). Three of these four cats had received a moderate ^{131}I dose and one cat a low ^{131}I dose. One of these four cats received a successful second ^{131}I treatment and the other three cats were managed with antithyroid drugs because the owners declined a second ^{131}I treatment.

Median serum T4 concentration at the 6–9 month follow-up, excluding the persistently hyperthyroid cats as three of them were already receiving antithyroid drugs, was 13.0 nmol/l (IQR 10.0–21.5 nmol/l) (Figure 2). The serum T4 concentration was within the RI in 22/51 (43.1%) cats and decreased in 29/51 (56.9%) cats. The serum T4 concentration was below the detection limit of the assay in 25/29 of these cats. Median serum TSH concentration 6–9 months after ^{131}I treatment was 0.30 ng/ml (IQR 0.10–1.63 ng/ml). Serum TSH concentration was within the RI in 14/51 (27.4%) cats, below the detection limit of the assay in 8/51 (15.7%) cats and increased in 29/51 (56.9%) cats. The serum creatinine concentration was within the RI in 37/51 (72.5%) cats (median 144 µmol/l; IQR 130–160 µmol/l) and increased in 14/51 (27.5%) cats (median 204 µmol/l; IQR 192–221 µmol/l).

Two cats that were azotaemic after achieving euthyroidism prior to ^{131}I treatment were euthyroid and

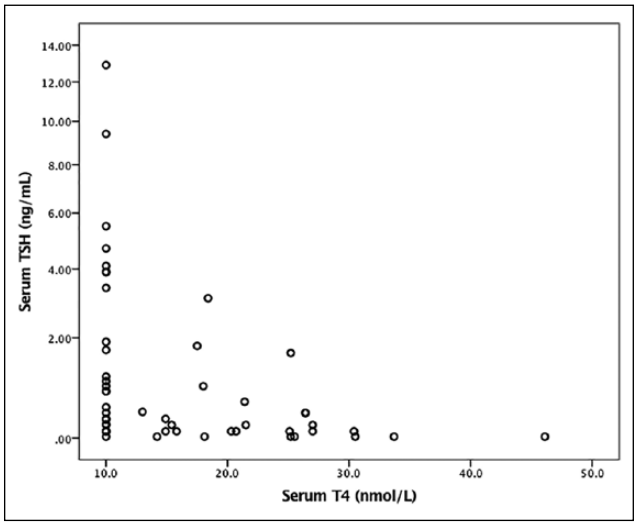

Figure 2 Scatter plots comparing serum thyroid-stimulating hormone (TSH) and total thyroxine (T4) concentrations in 51 cats after radioiodine treatment

subclinically hypothyroid 6–9 months after ^{131}I treatment, but in both cases the serum creatinine concentrations remained stable throughout the study (<4% variation between samples taken at 19 days and 6–9 months).

Thyroid status and development of azotaemia after ^{131}I treatment

The prevalence of euthyroidism, overt hypothyroidism and subclinical hypothyroidism 6–9 months after ^{131}I treatment was 40.0% (22/55 cats), 40.0% (22/55 cats) and 12.7 % (7/55 cats), respectively. There was no statistically significant association between remaining persistently hyperthyroid or the development of either overt or subclinical hypothyroidism and the ^{131}I dose given (low, moderate or high). Fifteen of 22 euthyroid cats had serum T4 concentrations within the RI, with normal or below the detection limit of the assay serum TSH concentrations in nine and six cats, respectively. Seven of 22 euthyroid cats had serum T4 concentrations below the RI, with normal or below the detection limit of the assay serum TSH concentrations in five and two cats, respectively. Both cats with decreased serum T4 and TSH concentrations were suspected to have non-thyroidal illness.

Azotaemia developed in 4/22 (18.2%) euthyroid cats, 8/22 (36.4%) overtly hypothyroid cats and in 2/7 (28.6%) subclinically hypothyroid cats. There was no significant difference in the development of azotaemia between euthyroid cats or cats with either overt or subclinical hypothyroidism.

The PPV and NPV for the prediction of the development of iatrogenic hypothyroidism 6–9 months after ^{131}I treatment were 72.2% and 80.0%, respectively, for a low serum T4 concentration; and 75.0% and 44.6%, respectively, for an increased serum TSH concentration, obtained at 19 days after ^{131}I treatment (prior to hospital discharge).

Discussion

In this study, 40% of cats treated with ^{131}I, where the dose was calculated based on an individualised scoring system, were overtly hypothyroid 6–9 months after treatment. Although the prevalence of iatrogenic hypothyroidism defined as cats with a decreased T4 concentration ⩾3 months after ^{131}I treatment has been reported to be as high as 79%, most studies report a prevalence of ⩽20%, which is significantly lower than that reported in this study.[7,8,21–23] Persistent hyperthyroidism was diagnosed in 5.6% of treated cats, which is comparable to previous studies where the prevalence is usually ⩽5%.[5,7,16,21–23]

Successful treatment of hyperthyroidism in cats results in a decrease in glomerular filtration rate, which can lead to the development of azotaemia if underlying chronic kidney disease is present. In cats with iatrogenic hypothyroidism the glomerular filtration rate may decrease even further leading to an additional decline in renal function.[24] One study identified that cats that developed iatrogenic hypothyroidism were more likely to develop azotaemia in comparison to cats that remained euthyroid, and those cats with iatrogenic hypothyroidism that also developed azotaemia had a shorter survival.[10]

As iatrogenic hypothyroidism appears to contribute to the progression of renal dysfunction, treatment of hyperthyroid cats with ^{131}I should be aimed at restoring euthyroidism without inducing iatrogenic hypothyroidism. However, the optimal method to calculate the ^{131}I dose to achieve this aim remains controversial.[8] The dose employed to treat feline hyperthyroidism in veterinary medicine is determined by either individualised protocols or the use of a fixed ^{131}I dose, with a trend towards the use of fixed ^{131}I doses.[5–7,21,22] However, no method has been demonstrated to be superior. In a previous and larger study evaluating the efficacy of the scoring system used in this study, <2% of treated cats were persistently hyperthyroid and 11% of treated cats had a low serum T4 concentration 6–12 months after ^{131}I treatment.[5] The median ^{131}I dose used was lower than in the current study (110 MBq [3.0 mCi] vs 130 MBq [3.5 mCi]) and almost twice as many cats in the former study received a low ^{131}I dose (59.2% vs 29.6%), which possibly accounts for the lower prevalence of iatrogenic hypothyroidism.[5]

One recent retrospective study using a fixed dose of 124 MBq (3.35 mCi), identified a prevalence of persistent hyperthyroidism and iatrogenic hypothyroidism of 2%.[22] Cats were classified as hypothyroid if they had a subnormal serum T4 concentration and clinical signs consistent with the disease. However, serum TSH concentrations were not measured and cats with iatrogenic hypothyroidism uncommonly develop overt clinical signs.[11,12]

Moreover, the use of low serum T4 concentration without TSH to diagnose iatrogenic hypothyroidism is suboptimal as non-thyroidal illness can lower T4 concentration.[16,25] Therefore, it is possible that the study underestimated the prevalence of iatrogenic hypothyroidism.[12]

While the use of lower ^{131}I doses could decrease the prevalence of iatrogenic hypothyroidism in our cohort of cats, the prevalence of persistent hyperthyroidism could increase above the commonly reported prevalence of ⩽5%.[5,7,16,21–23] Additionally, only one of the four persistent hyperthyroidism cats underwent a second ^{131}I, highlighting that many owners decline a second ^{131}I treatment for various reasons.[26] In the light of this, and as ^{131}I therapy is generally considered superior to other treatment options, many clinicians may try to use higher dosages of ^{131}I to minimise the risk of treatment failure.[6] However, a recent study comparing the efficacy of a lower (74 MBq [2.0 mCi]) or higher ^{131}I dose (148 MBq [4.0 mCi]) for the treatment of cats with mild-to-moderate hyperthyroidism identified a lower incidence of overt and subclinical hypothyroidism in the former group without a significant difference in the rate of persistent hyperthyroidism between both groups.[7] Therefore, an increase in the

incidence of treatment failure may not occur, even when lower ^{131}I dosages are given.

Interestingly, the prevalence of overt hypothyroidism in those cats treated with a higher ^{131}I dose (148 MBq [4.0 mCi]) in the abovementioned study was less than half than in our study (18.0% vs 40.0%), where only 14.5% of cats were treated with a ^{131}I dose of ⩾148 MBq (4.0 mCi), although the prevalence of subclinical hypothyroidism was significantly lower in our study (46% vs 12.7%).[7] The reason for the higher prevalence of overt hypothyroidism in our study is unclear. Possible causes for these results, given that there was no association between the development of iatrogenic hypothyroidism and the ^{131}I dose given, include random variability due to the low number of cases included in both studies, patients' variables (eg, individual variability in ^{131}I uptake by the different thyroid follicles, population differences between American and European hyperthyroid cats), analytical variables (eg, a higher lower limit of the RI for serum T4 concentration was used in this study) and/or human errors such as injecting a higher ^{131}I dose than the calculated or overestimation of the ^{131}I dose (eg, assigning a cat with mild clinical signs a moderate category or overestimation of goitre size) given the degree of subjectivity of the scoring system.[5]

A serum T4 concentration was not available immediately prior to 9/55 ^{131}I treatments and in these cases the most recent T4 concentration, when the cat was not receiving any antithyroid treatment, was used to calculate the ^{131}I dose. It is unknown whether the prevalence of iatrogenic hypothyroidism would change if the ^{131}I dose calculation included a serum T4 concentration obtained just prior to treatment in all cats. However, as T4 concentration increases over time, some cats could have received higher ^{131}I doses, which could have increased and decreased the prevalence of iatrogenic hypothyroidism and persistent hyperthyroidism, respectively.[27]

Seven of 55 (12.7%) cats were classified as subclinically hypothyroid at 6–9 months after ^{131}I treatment. Subclinical hypothyroidism has been used to describe, in human medicine and more recently in veterinary medicine, the finding of a normal (usually low–normal) T4 concentration and an increased serum TSH concentration.[7,12,16,23,28] Subclinical hypothyroidism appears to be a common consequence after ^{131}I treatment in human patients with Graves' disease or toxic nodular goitre, and has been correlated with a relative increase in all-cause mortality when compared with euthyroid controls.[28,29] The clinical significance of subclinical hypothyroidism in cats is not completely understood and it can be self-limiting in about a third of cats with a mild TSH elevation.[12,16,30] However, in a recent study cats with (overt or subclinical) iatrogenic hypothyroidism not given levothyroxine supplementation had a shorter median survival than hypothyroid cats receiving supplementation, suggesting a beneficial effect of thyroid hormone replacement on survival.[16] Overt hypothyroidism and azotaemia were identified in 8/55 (14.5%) cats, 6–9 months after ^{131}I treatment, which has been associated with a shorter survival and therefore could also benefit from levothyroxine supplementation.[10]

The PPV and NPV of decreased serum T4 concentration obtained prior to hospital discharge to predict the development of iatrogenic hypothyroidism 6–9 months after ^{131}I treatment were 72.2% and 80.0%, respectively. In other words, while 72.2% of cats with a decreased serum T4 concentration prior to hospital discharge were subsequently confirmed to have developed either overt or subclinical hypothyroidism, only 20.0% of cats with a normal serum T4 concentration became overtly or subclinically hypothyroid, suggesting the need for a closer monitoring of cats with a low serum T4 concentration prior to hospital discharge given the higher probability of them developing iatrogenic hypothyroidism.

An increased serum TSH concentration obtained prior to hospital discharge had a PPV of 75.0% to predict the development of iatrogenic hypothyroidism 6–9 months after ^{131}I treatment. However, this value was based on only four cats with an increased TSH at 19 days and a larger number of cases would be needed to validate this finding. The NPV of an increased TSH at 19 days after treatment was low (44.6%) as most cats had an undetectable serum TSH concentration. Therefore, three-quarters of cats with increased serum TSH concentration prior to hospital discharge developed iatrogenic hypothyroidism 6–9 months after ^{131}I treatment. However, the presence of a normal or undetectable TSH was not useful to discriminate between which cats would become hypothyroid and which cats would become euthyroid 6–9 months after ^{131}I therapy.

Two cats in the present study had decreased serum T4 and TSH concentrations 6–9 months after ^{131}I treatment. These cats were reported to be clinically well by the referring veterinarian and had not become azotaemic, although the creatinine was in the upper limit of the RI in both cases. This finding was attributed to non-thyroidal illness. However, in contrast to T4, TSH concentrations in cats with non-thyroidal illnesses has been reported to decrease only in severe illness.[25] Additionally, the RI for serum T4 concentration was calculated based on 30 cats, not age-matched (see Appendix A in the supplementary material). Therefore, the lower serum T4 concentration in these two cats may have been normal if more clinically healthy, age-matched cats were initially included and a lower RI for serum T4 concentration was obtained. Unfortunately,

the owners of these cats declined further investigations and the cats were lost to follow-up.

Up to 49% of hyperthyroid cats develop azotaemia within 6 months of treatment of hyperthyroidism and three recent studies have shown that cats that develop iatrogenic hypothyroidism are more likely to become azotaemic than those cats that remain euthyroid.[10,16,23] Although in our study the percentage of azotaemia in overtly hypothyroid cats was double (36.4% vs 18.2%) that of euthyroid cats, the difference was not statistically significant. Given the current literature this likely represents a type II error due to a low number of cases. As the majority of follow-ups were performed by referring veterinarians, the body weight and muscle condition scores of treated cats was not usually available, and repeated serum creatinine or urine specific gravity measurements that could have helped to differentiate cats with pre-renal instead of renal azotaemia, or identify cats with non-azotaemic chronic kidney disease (eg, IRIS stage 1 or early stage 2), were not consistently performed.

Conclusions

This study reaffirms that the use of an individualised scoring system previously described by Peterson and Becker in 1995 is effective to determine the dose of ^{131}I for the treatment of hyperthyroid cats, with rates of treatment failure comparable with other described methods.[5] However, the prevalence of iatrogenic hypothyroidism was higher in comparison with other studies using different dosing protocols. Further studies comparing the efficacy of an individualised scoring system and different dosing regimens are warranted to determine which method is superior to induce euthyroidism while minimising the prevalence of persistent hyperthyroidism and iatrogenic hypothyroidism.

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Supplementary material The following file is available online: Appendix A: Hormone validation information and determination of reference intervals.

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