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Abdominal Ultrasound Examination Findings in 534 Hyperthyroid Cats Referred for Radioiodine Treatment Between 2007–2010

L.K. Nussbaum, T.D. Scavelli, D.M. Scavelli, J. Pintar, A.K.Henderson, J.A. DeMarco, S. Worwag, R.P. Bastian, and H.S. Kittner

Background: The prevalence of concurrent disease in hyperthyroid cats is unknown.

Objectives: To identify the prevalence of concurrent intra-abdominal disease using abdominal ultrasound examination (AUS) in hyperthyroid cats referred for radioactive iodine treatment (RIT) and to determine whether the requirement for pre-treatment AUS is justified.

Animals: Five hundred and thirty-four client-owned cats diagnosed with hyperthyroidism and referred for RIT.

Methods: Retrospective study. Age, breed, sex, body weight, clinical signs, total serum T4 concentration, blood urea nitrogen (BUN) concentration, serum creatinine concentration, urine specific gravity (USG), AUS results, and biopsy or cytology results, or both (if obtained) were collected from the medical records.

Results: The prevalence of concurrent disease identified using AUS in hyperthyroid cats referred for RIT was 36.1%; 22.8% of the cats in the study had renal disease and 2.4% had confirmed neoplasia. Significant differences in median USG (*P* value 0.032) and median BUN (*P* value 0.028) were found between cats that had abnormal kidneys on AUS compared to those with normal-appearing kidneys. Only 2.2% of the cats were not treated with RIT as a result of changes identified on AUS and subsequently obtained cytology or biopsy results.

Conclusions and Clinical Importance: The results indicate that pretreatment AUS in hyperthyroid cats referred for RIT is unnecessary in most patients.

Key words: Endocrinology; Feline; Radiology and Diagnostic Imaging; Abdominal Ultrasonography.

Hyperthyroidism typically affects middle-aged to older cats and is the most commonly identified endocrine disorder in this species.[1] The clinical presentation has been well described, with the most common clinical signs reported including weight loss, polyuria with polydipsia, and polyphagia.[1–4] The disease can be diagnosed using blood chemistry testing. In some cases however additional diagnostic testing may be warranted to rule out concurrent disease.

Although much has been published regarding the clinical presentation and various treatment options for feline hyperthyroidism, there is little information about the prevalence of concurrent disease in hyperthyroid cats. In one retrospective study of hyperthyroid cats, 14% had renal disease and 54% had cardiac disease at the time of initial diagnosis.[5] Diabetes mellitus has been reported to occur in up to 5.8% of hyperthyroid cats,[6–9] and another study reported that the prevalence of urinary tract infections was 12% in hyperthyroid cats.[10]

Abbreviations:

RIT	radioactive iodine treatment
AUS	abdominal ultrasound examination
T4	total serum thyroxine
fT4	free serum thyroxine
USG	urine specific gravity
BUN	blood urea nitrogen
FNA	fine needle aspirate
ALT	alanine animo transferase

Complications associated with untreated hyper-thyroidism include renal disease, heart disease and hypertension.[1] The reported median life expectancy of treated hyperthyroid cats is 2 years[11,12] and is dependent on the presence of concurrent disease, which may or may not be secondary to hyperthyroidism itself.[1,11] The ability to identify concurrent diseases in hyperthyroid cats is important when considering a patient's treatment options and long-term prognosis.

At our institution as well as others, cats treated with radioactive iodine treatment (RIT) for hyperthyroidism are routinely screened first by abdominal ultrasound examination (AUS). The purpose of AUS is to rule out concurrent diseases that may limit the lifespan of a treated cat, and to identify concurrent diseases in cats with clinical signs that overlap with those of hyperthyroidism. The objective of this study was to determine the prevalence of abnormal AUS findings in cats referred for treatment of hyperthyroidism with RIT, and to determine whether such pretreatment screening is warranted.

Materials and Methods

Cats

Between 2007 and 2010, all cats referred to Garden State Veterinary Specialists in Tinton Falls, New Jersey for RIT were first

From the Garden State Veterinary Specialists, Tinton Falls, NJ (Nussbaum, Scavelli, Pintar, Henderson, DeMarco, Worwag); Cornell University, Ithaca, NY (Scavelli); and the Monmouth University, West Long Branch, NJ (Bastian, Kittner).

The study was based on referred patients and their clinical evaluation at Garden State Veterinary Specialists in Tinton Falls, NJ.

Corresponding author: L. Nussbaum, 1 Pine Street, Tinton Falls, NJ 07753; e-mail: lindsay.nussbaum@gmail.com.

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screened by AUS as part of their pretreatment evaluation. The AUS request log from these years was searched for cats referred for RIT that had AUS, and the medical records and imaging findings of these hyperthyroid cats were reviewed retrospectively. Inclusion criteria for this included referral for RIT as treatment for hyperthyroidism, increased serum total thyroxine (T4) or free thyroxine (fT4) concentrations above the reference ranges provided by the laboratories performing the test, and a complete medical record with an AUS report. In addition, before referral it was recommended, but not required, that each cat had either a urine specific gravity (USG) of >1.030 or had undergone a successful methimazole trial and achieved euthyroidism without subsequent development of azotemia for a minimum of 4 weeks. Information including patient age, breed, sex, body weight, clinical signs, total serum T4 concentration, blood urea nitrogen (BUN) concentration, serum creatinine concentration, USG, AUS results, and biopsy or cytology results, or both (if obtained) were collected from the medical records.

Imaging Studies

All imaging studies were performed by one of four board-certified diplomates of the American College of Veterinary Internal Medicine. An AUS was performed on each cat, and reports were written for each study, describing each organ system as normal or abnormal and any abnormalities that were observed.

Statistical Analysis

Quantitative descriptive data for metric variables are presented as medians and range because the data were not normally distributed. Qualitative data presented as a yes/no column were coded as 0/1 for the purposes of analysis. Tests of association between categorical variables and metric variables used tests of two medians (nonparametric). For all analyses, a value of $P < 0.05$ was considered significant. All data was analyzed using SPSS-PASW, version 19.[a]

Results

Signalment and History

Five hundred and thirty-four cats met the inclusion criteria for this study. The median age of all cats in the study was 12.0 years (range, 5.0–19.0). A total of 292 (55%) of the cats were spayed females, and 242 (45%) were neutered males. Of the 529 cats for which breed was reported, 440 (83%) were Domestic Short Hairs and 43 (8%) were Domestic Long Hairs. Other represented breeds included 10 Siamese, eight Maine Coons, eight American Long Hairs, six Norwegian Forest Cats, two Bombays, two Devon Rexes, two Himalayans, two Persians, two Ragdolls, one Burmese, one Manx, one Russian Blue, and one Tonkinese. The median weight of the cats was 4.3 kg (range, 1.7–8.8).

Five-hundred and twenty-six (98.5%) of the cats in the study had clinical signs related to hyperthyroidism (Table 1). Weight loss was most common and was reported in 513 cats (96%); other clinical signs included polyphagia in 124 cats (23.2%), vomiting in 45 cats (8.4%), polydipsia and polyuria in 20 cats (3.4%), diarrhea in four cats (0.7%) and anorexia or hyporexia in four cats (0.7%). Eight cats (1.5%) had no clinical signs and were diagnosed on the basis of screening blood test results. Three-hundred and fifty-five cats (66.5%) had one clinical sign, whereas 158 cats (29.6%) had two clinical signs and 13 cats (2.4%) had ≥3 clinical signs.

The median total T4 concentration of all cats in the study at the time of diagnosis was 8.4 μg/dL (range, 2.5–35.7). All cats with a T4 concentration <4.0 μg/dL ($n = 43$) had a documented fT4 concentration >55 pmol/L. Median USG, BUN and serum creatinine concentrations of all cats in the study were 1.040 (range, 1.007–1.060 or higher), 26 mg/dL (range, 7–59 mg/dL) and 1.1 mg/dL (range, 0.3–2.8 mg/dL), respectively.

Ultrasound Examination Findings, Cytology Results and Biopsy Results

A total of 193 cats (36.1%) had abnormal AUS findings. Twenty-seven cats (5.1%) had hepatic lesions identified. Of these cats, 1 (0.2%) had a diffusely hyperechoic liver. Nodules, defined as lesions measuring ≤2 cm in diameter, were described in 20 cats (3.7%). The nodules were anechoic in 16 cats (2.9%), hyperechoic in three cats (0.6%) and isoechoic in one cat (0.2%). Of the 20 cats with liver nodules, 10 underwent fine needle aspiration (FNA); all 10 (1.8%) of these cats had cytologic changes consistent with cystadenoma. Hepatic masses, defined as lesions measuring >2 cm in diameter, were described in six cats (1.1%). The masses were hyperechoic in four cats (0.7%) and anechoic in two cats (0.4%). All six cats with hepatic masses underwent FNA; three of these cats were diagnosed with benign lesions including lipid vacuolization, hyperplasia, and cystadenoma. Of the remaining cats with hepatic masses, one was diagnosed with presumptive metastatic neoplasia based on exploratory surgery (this cat had a liver mass as well as a jejunal mass), one was diagnosed with hepatocellular carcinoma on the basis of FNA and also had concurrent ascites, and one had cytologic changes consistent with mixed inflammation. This latter cat also had enlarged mesenteric lymph nodes on AUS and was diagnosed with lymphoblastic lymphoma on the basis of FNA.

Lesions consistent with kidney disease were identified in 122 cats (22.8%). Of these cats, 55 (10.3%) had bilaterally decreased corticomedullary definition, 11 (2.0%) had bilateral renal mineralization, and 11 (2.0%) had both. Of the cats that had bilaterally

Table 1. Reported clinical signs at the time of diagnosis of hyperthyroidism in 534 cats referred for radioiodine treatment.

Clinical sign reported	*n*
Weight loss	513
Polyphagia	124
Vomiting	45
Polydipsia/polyuria	20
Diarrhea	4
Anorexia/hyporexia	4
None	8
One sign	355
2 signs	158
≥3 signs	13

decreased corticomedullary definition, 4 (0.7%) had unilateral renal atrophy (<3.8 cm), 2 (0.4%) had bilateral renal atrophy, and 1 (0.2%) had unilateral mineralization. Sixteen cats (2.9%) had unilaterally decreased corticomedullary definition; 6 (1.1%) of these cats had concurrent atrophy of the abnormal kidney. Seven cats (1.3%) had unilateral mineralization; 2 (0.4%) of these cats had concurrent atrophy of the affected kidney. Two cats (0.4%) had unilateral decreased corticomedullary definition and mineralization.

Ten cats (1.8%) had unilateral renal atrophy, 3 (0.6%) of which had increased size of the contralateral kidney. Five cats (0.9%) had bilateral renal atrophy. One cat (0.2%) had bilateral renal cysts, and 1 (0.2%) cat had bilateral nephroliths. Three cats (0.6%) were found to have unilateral hydronephrosis secondary to ureteroliths in two cats (0.4%) and to a nephrolith in one cat (0.2%).

Fourteen cats (2.6%) had gastrointestinal abnormalities. Six (1.1%) of these cats had diffuse small intestinal thickening (wall thickness of > 3 mm). Of these cats, 1 (0.2%) was diagnosed with lymphocytic lymphoma on the basis of endoscopic biopsy. Biopsy was not performed in the other five cats. Eight cats (1.5%) had focal small intestinal masses. Of these cats, four underwent exploratory surgery; three were diagnosed with lymphoblastic lymphoma based on biopsy results, and one was diagnosed with presumptive metastatic neoplasia based on gross disease found on abdominal exploration; this cat was euthanized during surgery and biopsies were not obtained. This latter cat was previously described as also having a hepatic mass. The remaining four cats with small intestinal masses underwent FNA; two were diagnosed with lymphoblastic lymphoma, one was diagnosed with a mast cell tumor and one was diagnosed with adenocarcinoma.

Six cats (1.1%) were found to have lymphadenopathy, and five underwent FNA for further evaluation. Three of these cats (0.6%) had cytology results consistent with lymphoid hyperplasia; 1 (0.2%) had concurrent splenomegaly and FNA results consistent with lymphoid hyperplasia, 1 (0.2%) was diagnosed with mast cell tumor, and 1 (0.1%) had cytology results equivocal for lymphoma. Two additional cats (0.4%) had splenomegaly alone, consistent with lymphoid hyperplasia on the basis of FNA in both. One cat (0.2%) had hypoechoic splenic nodules that were not biopsied, and one cat (0.2%) had a splenic mass that was consistent ultrasonographically with myelolipoma.

Abnormalities of the pancreas were described in four cats (0.7%); two cats (0.4%) had cystic lesions, one cat (0.2%) had thickening suggestive of chronic pancreatitis or hyperplasia, and one cat (0.2%) had a mass that that was diagnosed on the basis of FNA as pancreatic carcinoma. Choleliths were identified in one cat (0.2%), and one cat (0.2%) had a hyperechoic gallbladder wall. One cat (0.2%) was diagnosed with chylous abdominal effusion secondary to cardiac disease. One cat (0.1%) was diagnosed with a unilateral adrenal mass and did not undergo further evaluation. Abnormalities of the lower urinary tract were identified in 35 cats (6.6%). Of these cats, 33 (6.2%) had urinary sediment, one (0.2%) had cystic calculi, and one (0.2%) had focal urinary bladder wall thickening.

Kidney Disease

Of the 122 cats (22.8%) with ultrasonographic evidence of kidney disease, 103 (96.4%) were IRIS Stage 1, 18 (3.4%) were IRIS Stage 2 and 1 (0.2%) was IRIS Stage 3 as classified by the International Renal Interest Society (IRIS).[13] Thirty-eight cats (7.1%) had USG <1.035. Of the 19 cats with azotemia, 11 of these had a USG of <1.035. Median USG, BUN concentration and serum creatinine concentration of the 122 cats with renal abnormalities identified on AUS were 1.039 (range, 1.012–1.060 or greater), 28 mg/dL (range, 14–58 mg/dL) and 1.2 mg/dL (range, 0.3–2.8 mg/dL), respectively. The median USG, BUN concentration and serum creatinine concentration of the 412 cats with no renal abnormalities identified on AUS were 1.040 (range, 1.007–1.060 or greater), 26 mg/dL (range, 7–59 mg/dL) and 1.1 mg/dL (range, 0.3–2.7 mg/dL), respectively. There was a significant difference in median USG ($P = 0.032$) and median BUN ($P = 0.028$) between the cats that had ultrasonographic evidence of kidney disease and those that did not. There was no significant difference in median serum creatinine concentration ($P = 0.206$) between these groups of cats.

Clinical Outcome

Of the 534 cats in the study, 12 (2.2%) were not treated with RIT as a result of abnormalities identified on AUS and cytology or biopsy results. Ten (1.9%) of these cats were confirmed to have malignant disease on the basis of FNA or surgical biopsy. The other two untreated cats included one cat with hydronephrosis secondary to ureterolithiasis the owner of which elected euthanasia, and the cat with focal urinary bladder wall thickening the owner of which declined RIT. Malignant disease also was definitively identified in three cats the owners of which elected to treat for hyperthyroidism; one of these cats was diagnosed with mast cell tumor in a lymph node on the basis of FNA, one had intestinal thickening and was diagnosed with lymphocytic lymphoma on the basis of endoscopic biopsy, and one had a small bowel mass and was diagnosed with lymphocytic lymphoma on the basis of FNA. The latter cat was treated with chemotherapy before RIT. One cat with mesenteric lymphadenopathy had cytologic changes suggestive of lymphoma and was treated with RIT despite this finding.

Discussion

Our results show that the prevalence of concurrent intra-abdominal disease in the population of hyperthyroid cats referred for RIT based on AUS was 36.1%. Most of the ultrasonographic abnormalities seen in this population were not considered to be deterrents for RIT treatment (e.g., subclinical kidney disease, benign

liver lesions). Only 13 of 534 (2.4%) cats were confirmed to have malignant disease, and three of these were treated despite this diagnosis.

An objective of this study was to determine whether the use of AUS as a prescreening tool for RIT of hyperthyroid cats is justified in all potential patients. The results of the study indicate that AUS identified clinically relevant concurrent disease, which precluded RIT treatment or required further treatment, in a very small number of cats. In cases in which neoplasia was identified, many owners elected to euthanize their cats. A small number of cats were diagnosed with cancer and their owners elected to pursue RIT and subsequent chemotherapy. The low prevalence of abnormal AUS findings in the referred hyperthyroid population lends support to the decision to not screen all hyperthyroid cats with AUS before RIT, but it also highlights the challenge in identifying those cats that do have serious concurrent disease based on clinical presentation alone.

The most common clinical signs reported in the referred hyperthyroid cat population of this study included weight loss and polyphagia, correlating with previously published reports.[1–4] Changes consistent with chronic kidney disease were the most commonly identified ultrasonographic abnormalities in the population of hyperthyroid cats referred for RIT. This finding is not surprising because renal disease is common in older cats, and azotemia previously has been reported in up to 26% of hyperthyroid cats.[1] Although 22.8% of the cats in this study had renal pathology on AUS, only 19 (3.6%) had azotemia and 38 (7.1%) had decreased urine concentrating ability. The low prevalence of clinical renal disease in the population of cats in this study is likely a reflection of the recommendations for referral which presumably selected for cats without kidney disease.

In a prior study of liver function in hyperthyroid cats before and after RIT, there was no significant difference between hyperthyroid and control cats despite the presence of increased liver enzyme activity in the affected group.[14] On AUS of the 19 hyperthyroid cats in the aforementioned study, 15 of which had increased serum liver enzyme activity, no abnormalities were observed either before or after treatment.[14] This finding suggests that increased in serum liver enzyme activity alone in hyperthyroid cats may not warrant further evaluation by AUS. In this, only 27 of 534 cats had liver abnormalities identified on AUS, and of these only three were confirmed to be associated with malignancy.

Of the 13 cats with confirmed malignancy, nine (69.2%) had intestinal disease. Despite this finding, gastrointestinal clinical signs such as vomiting and diarrhea were only reported in two of the cats with confirmed intestinal malignancy. Both of these cats were found to have small intestinal adenocarcinoma. The low prevalence of vomiting and diarrhea in cats with intestinal malignancy reported in this contrasts with other published reports, which describe up to 82% of cats with alimentary lymphoma having vomiting or diarrhea.[15] Weight loss was present in all cats with confirmed malignancy in our study.

Lymphoma was the most commonly identified malignant disease of the cats in our study. Three cats were definitively diagnosed with lymphoblastic lymphoma on the basis of surgical biopsy. Of the four other cats diagnosed with lymphoma, three were diagnosed on the basis of cytology only and one was diagnosed on the basis of endoscopic biopsy results. The cat that underwent endoscopic biopsy was found to have diffuse small bowel thickening on AUS. All of the other cats in the study that had diffuse small bowel thickening ($n = 5$) did not have biopsies, and conditions such as inflammatory bowel disease, lymphoma, or other enteropathies cannot be eliminated. Three other cats with lymphadenopathy had cytologic findings consistent with lymphoid hyperplasia. Cytology alone, however, may be unreliable for distinguishing between lymphoid hyperplasia and lymphoma,[16] and therefore neoplasia cannot be definitively eliminated in these three cats.

Based on the retrospective nature of our study, it could not be determined if all patient samples were analyzed at the same laboratory or what normal ranges were utilized by the different laboratories. This limitation presented a challenge when comparing the measured serum T4 and fT4 concentrations of each patient. For the purposes of our study, we defined hyperthyroidism on the basis of a T4 concentration > 4.0 μg/dL, a fT4 concentration of > 55 pmol/L or both. Forty-three cats in the study had normal serum T4 concentrations with increased fT4 concentrations. Of these cats, 41 had no evidence of coexistent disease identified either before or after referral, and clinical signs in these cats were compatible with a diagnosis of hyperthyroidism. The remaining two cats were found to have neoplasia and were not treated with RIT, which is consistent with prior studies showing that increased fT4 concentrations have been observed in euthyroid cats with non-thyroidal illness.[9] Another limitation of this study is the potential for variability among ultrasonographers. The retrospective nature of the study precluded analysis of the proportion of cats scanned by each imager or further evaluation of the distribution of major findings among them. The fact that board-certified internists and not radiologists performed and interpreted the examinations also is a limitation. However, this is approach is common in many private referral practices that do not employ radiologists. Unfortunately, video or still images were not available for all of these patients to be reviewed by a radiologist.

When the RIT program initially was started at our institution in 2001, suggestions for referral were determined based on personal clinical experience and were designed to exclude cats with severe renal disease. Shortly thereafter, it was shown that data collected before RIT treatment could not reliably predict kidney function after treatment.[17] Similarly, a previous study indicated that USG was not a reliable predictor of azotemia after RIT.[18] Since these reports have been published, the suggestions for referral to our institution have changed and now do not include specifications regarding USG.

A possible reason for the relatively low prevalence of feline hyperthyroidism and concurrent disease in this

study is population bias, because our study only included cats that had been previously diagnosed with hyperthyroidism and referred to a specialty hospital for RIT. Our study does not consider those cats that are excluded from referral for RIT, such as cats with severe renal disease, or cats that are found to have clinically relevant concurrent disease by their primary veterinarians. The prevalence of concurrent disease in hyperthyroid cats may be higher in the population of cats for which RIT is not considered. Without additional research, the prevalence reported in this study should not be considered reflective of the hyperthyroid feline population as a whole. Concurrent disease should be considered as a differential diagnosis in the diagnostic evaluation of these cats, and the recommendation for AUS should be made in those cats in which there is clinical suspicion for neoplasia or other diseases that would preclude RIT.

In summary, the findings of our study support the exclusion of AUS from the required pretreatment screening of hyperthyroid cats being evaluated for RIT. Our current recommendation is to reserve the recommendation of an AUS for those cases in which clinical suspicion for clinically relevant disease is high.

Footnote

[a] SPSS: An IBM Company, Somers, NY.

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Off-label Antimicrobial Declaration: Authors declare no off-label use of antimicrobials.

Conflict of Interest Declaration: Authors disclose no conflict of interest.

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