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Efficacy and safety of radioiodine therapy for 10 hyperthyroid cats: a retrospective case series study in South Korea

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Abstract

Hyperthyroidism, characterized by elevated thyroid hormone levels and thyroid gland hyperplasia or adenoma, is a prevalent endocrinopathy in older cats. Treatment options include antithyroid drugs, surgical thyroidectomy, and radioiodine therapy (RAIT), which is non-invasive treatment option that can achieve complete remission. However, efficacy and safety of RAIT in hyperthyroid cats have not been investigated in South Korea. This study includes 10 hyperthyroid cats with RAIT. Initial assessments comprised history, physical examination, blood analysis, and serum total T4 (tT4) concentration. Thyroid scintigraphy revealed hyperactivity and enlargement of thyroid gland at 24 hours before the RAIT. Radioiodine (RAI) was injected subcutaneously with 2 to 6 mCi, determined by the fixed dose or the scoring system based on severity of clinical signs, tT4 concentration, and thyroid size individually. After RAIT, the concentration of serum tT4 and liver enzymes were significantly decreased at discharge. However, no significant differences were noted in blood urea nitrogen, creatinine, symmetric dimethylarginine, hematocrits, and white blood cell counts pre- and post-treatment. Although 4 cats received RAI twice, clinical signs disappeared and tT4 levels decreased following the RAIT. All 10 cats achieved complete remission after 6 months without critical adverse effect. The safety and the effectiveness of RAIT was confirmed based on protocols reported other countries. Therefore, RAIT could be considered the treatment option and prevent adverse effects from medication or surgery. This preliminary study presents the first evaluation of RAIT for hyperthyroid cats using locally produced RAI in South Korea and provide valuable insight for clinicians and further studies.

Keywords: cats; feline hyperthyroidism; hyperthyroidism; iodine-131; radioiodine therapy; radionuclide imaging; thyroid gland

Introduction

Hyperthyroidism is reported as the most commonly diagnosed endocrinopathy in older cats [1]. The prevalence of hyperthyroidism in older cats was reported between 3.93% and 21.1% in many countries [2–6]. Feline hyperthyroid patients had elevated levels of thyroid hormone accompanied with one or more lobe of thyroid gland hyperplasia or adenoma [7]. Because thyroid hormone involved in various metabolic controls, its excessiveness induces clinical signs such as weight loss, gastrointestinal sign, hyperactivity, and tachycardia [1,7,8]. Because of its pathogene-

sis is unclear, the goal of treatment is controlling excessive thyroid hormone which affect systemic metabolic status [1,7,8].

The treatment options include administration of antithyroid drugs, surgical thyroidectomy, and radioiodine therapy (RAIT) [1,7,8]. Regardless of its disadvantages, such as restriction of facilities or permission of using isotopes, the RAIT is considered as an optimal treatment option for feline hyperthyroid cats [8,9]. To maximize therapeutic effect and avoid adverse effect such as iatrogenic hypothyroidism, several ideal dosing protocols of the RAIT was reported in veterinary field [9–12]. However, RAIT for feline hyperthyroidism has not yet been investigated in South Korea. Therefore, this preliminary study describes the efficacy and the safety of the RAIT using locally produced radioiodine (RAI) in South Korea through demonstrating clinical features of 10 hyperthyroid cats in pre- and post-treatment.

Materials and Methods

Animals

This study includes the client-owned hyperthyroid cats who were treated with the RAI from March 2020 to March 2021. The antithyroid drugs were stopped at least 2 weeks before the application of the RAIT. Prior to the RAIT, renal and cardiac functions were evaluated to assess the risk factor of the RAIT complications, such as cardiopulmonary dysfunction or renal suppression. Cats were pre-medicated with atenolol before the RAIT if they had cardiomyopathy.

RAIT

The history taking, physical exam, and blood analysis (complete blood cell count [CBC], serum biochemistry profile, and serum total T4 [tT4] concentration) were performed in all hyperthyroid cats before the RAIT.

Clinical signs

To assess the disease severity, total 18 clinical signs (weight loss, polyphagia, increased activity/restless, polydipsia/polyuria, vomiting, diarrhea, increased fecal volume, anorexia, polypnea, muscle weakness, muscle tremor, increased nail growth, dyspnea, alopecia, tachycardia, cardiac murmur, congestive heart failure, and ventroflexion of neck) were evaluated through physical examination or history taking from the owner. The score of clinical sign was evaluated based on its severity (score 1, mild, 1 to 6 clinical signs; score 2, moderate, 7 to 12 clinical signs; score 3, severe, 13 to 18 clinical signs) [9].

Thyroid hormone

Initially, the serum tT4 concentration was measured by in-house assay at the local animal hospital, at the time of initial diagnosis. In our clinic, the serum concentration of tT4 was re-evaluated on the admission day for the RAIT and measured by an enzyme immunoassay analyzer (Immulite 2000; Siemens Healthcare Diagnostics, USA) validated for use in cats. The severity of the elevation in the thyroid hormone level was classified as mild (below 10 μg/dL), moderate (10 to 20 μg/dL), and severe (exceed 20 μg/dL) [9].

Scintigraphy

Thyroid scintigraphy was performed to assess the size of each thyroid lobe or find ectopic thyroid, and used as a diagnostic modality for its hyperactivity. Images were obtained with breast-specific gamma camera (Dilon 6800 Gamma Camera; Dilon Technologies, USA) with low energy high-resolution, 15-degree slant parallel-hole collimator. After 111 to 148 MBq of technetium pertechnetate (New Korea Industrial, Korea) was injected intravenously, 3 views of thyroid images (dorsoventral, right and left lateral recumbency) were obtained between 20 to 60 minutes later [13,14]. Each image was acquired for a total of 200,000 counts. Images were integrated and processed using dedicated computer running program (Dilon 6800 software). The thyroid size was classified and scored as 3 groups (score 1, small, $< 1.0 \times 0.5$ cm; score 2, median, 1.0×0.5 to 3.0×1.0 cm; score 3, large, $> 3.0 \times 1.0$ cm) [9].

Injection of the RAI

The dose of the RAI (Thyrokitty; Korea Atomic Energy Research Institute) was calculated for each cat based on the severity of the clinical signs, the level of measured tT4, and the size of the thyroid glands [9]. The score was allocated to each of these parameters. Although the dose of the RAI was determined based on the scoring system [14], fixed low-dose (2 mCi) was applicated to the cat which had serum tT4 below 13 μg/dL or had risk factors of cardiopulmonary problem and renal function decreased after the RAIT [10]. The determined dose of the RAI was administrated subcutaneously. After the RAIT, cats were isolated in the shielding facility and discharged if detected radiation exposure below 5 μSv/hr at 1 m based on the release criterion [15].

Efficacy of RAIT

The 18 clinical signs of hyperthyroidism were re-assessed at 1 month after the RAIT through history taking from the owner. Blood analysis, contains CBC, serum biochemistry, and serum

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tT4, were assessed within 3 days before and at 6 to 9 days after the RAIT. Leukocyte counts and hematocrits were measured with a veterinary hematology analyzer (ProCyte Dx Hematology Analyzer, IDEXX, USA). The serum level of symmetric dimethylarginine (SDMA) (Catalyst One; IDEXX) and the concentration of serum alanine aminotransferase (ALT), alkaline phosphatase (ALP), blood urea nitrogen (BUN), and creatinine (Hitachi 7020; Hitachi High-Technologies Co., Japan) were measured with biochemical analyzers.

Adverse effects

After the RAIT, the clinical signs, which include gastrointestinal, cardiovascular, respiratory, genitourinary, neurologic and general behavioral signs, that may occur due to drug administration were monitored. The occurrence of abnormal clinical signs (nausea, vomiting, anorexia, and swelling of neck, etc.) which could be associated acute risks of the RAI administration was monitored by clinicians throughout the hospitalization period [16]. The complications of the RAIT, such as myelosuppression, renal function depletion, and iatrogenic hypothyroidism, had been evaluated until 6 months after the therapy.

Statistical analysis

Data was analyzed using GraphPad Prism 7 software (GraphPad Software Inc., USA). The Kolmogorov-Smirnov Test was performed to evaluate the normality of study data. The average values of all data were calculated using descriptive statistics and were expressed as mean ± standard deviation for data with normal distribution but as median and interquartile range (IQR) for skewed data. The Wilcoxon test was performed to analyze significant differences of tT4, CBC, and blood chemistry profiles between pre- and post-RAIT. Differences of all data were considered statistically significant at $p < 0.05$.

Results

Animals

During the study period, 164 cats had visited and 14 cats (8.5%) were treated for hyperthyroidism in our clinic. Among 14 hyperthyroid cats, 10 cats were treated with the RAI by the owner's request. Four cats (ID 1, 2, 6, and 8) were retreated due to the low efficacy of the first therapy. The median age of cats treated with the RAI was 13.0 years (IQR, 11.5–13.0 years). This group was consisted with 5 spayed female and 5 castrated male. Four cats were domestic short hair and another 4 cats were Russian blue, and 2 cats were Persian and Scottish fold each. Eight cats had been diagnosed less than one year ago. At the time of diagnosis, the serum concentration of tT4 was under 10 ug/dL for 7 cats, 10 to 15 ug/dL for 2 cats, and lost the result for 1 cat. Eight cats were treated with methimazole initially. The initial information of 10 cats treated with the RAIT is summarized in Table 1.

RAIT

Clinical signs

Total 18 clinical signs were evaluated through history taking and physical examination (Table 2). Weight loss was the most common (n = 10), followed by polyuria/polydipsia (n = 7), tachycardia (n = 6), and vomiting (n = 5). The clinical signs of hyperactivity (n = 4), polypnea (n = 4), diarrhea (n = 2), increased fecal volume (n = 2), and alopecia (n = 2) were less common. Based on their severity of clinical signs, 6 cats and 4 cats were scored as 1 and 2, respectively.

Thyroid hormone

Initially, tT4 of the cats was measured at 14 days after discontinuance of methimazole (Table 2). Before the application of the

Table 1. Clinical information of 10 hyperthyroid cats at the presentation for the application of the radioiodine therapy

ID	Breed	Age (y)	Sex	Initial tT4 (μg/dL)[a]	Duration of illness (mo)	Medication (prescription period, mo)
1	Russian blue	9	Spayed female	8	4	Methimazole (3)
2	Domestic short hair	13	Castrated male	8	5	Methimazole (5)
3	Persian	12	Spayed female	5.9	15	Methimazole (3)
4	Domestic short hair	9	Castrated male	8	34	Methimazole (32)
5	Domestic short hair	13	Spayed female	15	2	NP
6	Russian blue	13	Castrated male	7	3	Methimazole (1)
7	Russian blue	14	Spayed female	6.9	2	NP
8	Scottish fold	13	Castrated male	7.72	3	Methimazole (1)
9	Domestic short hair	16	Spayed female	9.52	6	Methimazole (5)
10	Russian blue	12	Castrated male	14	1	Methimazole (1)

ID, identification number; tT4, total T4; NP, not prescribed.
[a]At the time of diagnosis of hyperthyroidism.

Table 2. The results of scoring and injection doses of the RAI in 10 hyperthyroid cats

ID	Clinical signs (score)	tT4 (μg/dL, score)	Thyroid size (cm × cm, score)	Total score[b]	Dosing method	Injection dose (mCi)
1	Weight loss, polyphagia, tachycardia, polyuria/polydipsia, increased fecal volume (1)	16.3 (2)	L) 4.1 × 2.8 (3)	6	Fixed low-dose	2.0
1[a]		10.4 (2)	L) 3.1 × 1.7 (3)	6	Scoring	3.5
2	Weight loss, tachycardia, cardiac murmur (1)	15.7 (2)	L) 2.8 × 0.9, R) 2.9 × 1.9 (3)	6	Fixed low-dose	2.0
2[a]		11 (2)	L) 2.1 × 0.1, R) 2.8 × 1.4 (3)	6	Scoring	3.0
3	Weight loss, polyphagia, tachycardia (1)	11.6 (2)	L) 2.2 × 1.4 (3)	6	Scoring	3.5
4	Weight loss, polyphagia, hyperactivity, vomiting, increased fecal volume, polypnea, alopecia (2)	14.8 (2)	R) 2.4 × 2.0 (3)	7	Scoring	4.0
5	Weight loss, polyphagia, hyperactivity, tachycardia, polyuria/polydipsia, vomiting, diarrhea, muscle weakness, muscle tremor, dyspnea (2)	14.4 (2)	R) 2.9 × 1.7 (3)	7	Scoring	4.0
6	Weight loss, polyphagia, hyperactivity, tachycardia, polyuria/polydipsia, vomiting, diarrhea (2)	14.3 (2)	L) 1.9 × 1.1, R) 2.9 × 1.5 (3)	7	Scoring	4.0
6[a]		10.2 (2)	L) 1.1 × 1.0, R) 2.8 × 1.1 (3)	7	Scoring	4.4
7	Weight loss, polyuria/polydipsia, vomiting (1)	6.9 (1)	L) 2.1 × 1.2, R) 1.7 × 1.1 (3)	5	Fixed low-dose	2.0
8	Weight loss, polyphagia, polyuria/polydipsia, polypnea (1)	13 (2)	R) 2.6 × 1.9 (3)	6	Fixed low-dose	2.0
8[a]		9.2 (1)	R) 1.9 × 1.5 (2)	4	Fixed low-dose	2.0
9	Weight loss, polyuira/polydipsia, vomiting, anorexia (1)	12.7 (2)	R) 2.7 × 1.8 (3)	6	Scoring	3.5
10	Weight loss, polyphagia, hyperactivity, tachycardia, polyuria/polydipsia, polypnea, alopecia (2)	15.2 (2)	R) 2.7 × 1.8 (3)	7	Scoring	4.4

ID, identification number; L, left; R, right; fixed low-dose: total 2 mCi of the radioiodine (RAI) application if the cat had total T4 (tT4) lower than 13 μg/dL or had risk factors such as cardiopulmonary or urinary problem; scoring, RAI dose determination by scoring system.
[a]The cases were retreated at 3 months after the first radioiodine therapy. [b]Dose determination: total score 3 to 5, low dose (ranged 2.0 to 3.4 mCi); total score 6 and 7, moderate dose (ranged 3.5 to 4.4 mCi); total score 8 and 9, high dose (ranged 4.5 to 6.0 mCi).

first RAIT, 7 cats (ID 2, 3, 4, 5, 6, 9, and 10) were scored 2 as their tT4 was between 10 to 20 μg/dL and 3 cats (ID 1, 7, and 8) were scored 1 based on their tT4 below 10 μg/dL, but the score of 2 cats (ID 1 and 8) were corrected as 2 after the first RAIT based on their re-evaluated serum tT4 concentration. The serum tT4 in 2 cats (ID 1, tT4 = 8 μg/dL and ID 8, tT4 = 7.72 μg/dL) were evaluated primary by in-clinic analyzer at the local animal hospital. However, it was lower than the result (ID 1, tT4 = 16.3 μg/dL and ID 8, tT4 = 13 μg/dL) that measured by enzyme immunoassay in our clinic. After 3 months of the first RAIT, 4 cats had confirmed tT4 elevation and re-scored for the second RAIT (ID 1, 10.4 μg/dL, score 2; ID 2, 11 μg/dL, score 2; ID 6, 10.2 μg/dL, score 2; ID 8, 9.2 μg/dL, score 1).

Scintigraphy

Bilateral hyperactive thyroid lobes were identified in 3 cats (ID 2, 6, and 7) and unilateral in other 7 cats. The ectopic thyroid tissues were identified only one cat (ID 6) (Fig. 1). The length of long axis of thyroid gland were ranged between 2 to 3 cm in 9 cats and over 3 cm in 1 cat. Based on the thyroid size criteria, all cats were scored as 3 (Table 2). The second scintigraphy was performed to re-treatment in 4 cats after 3 months of the first RAIT. All of 4 cats had decreased size of hyperactive thyroid than the first scintigraphy and re-scored based on the second scan (ID 1, score 3; ID 2, score 3; ID 6, score 3; ID 8, score 2) (Table 2).

Injection of RAI

In the first RAIT, total score was 5 in 2 cats (ID 7 and 8), 6 in 4 cats (ID 1, 2, 3, and 9), and 7 in 4 cats (ID 4, 5, 6, and 10) (Table 2). The injection dose of the RAI was determined in 6 cats by these scores, while 4 cats (ID 1, 2, 7, and 8) were treated with fixed low-dose (2 mCi). Four cats (ID 1, 2, 6, and 8) were re-treated with the second RAIT at 3 months after the first treatment. In comparison with the first RAIT, total score was not

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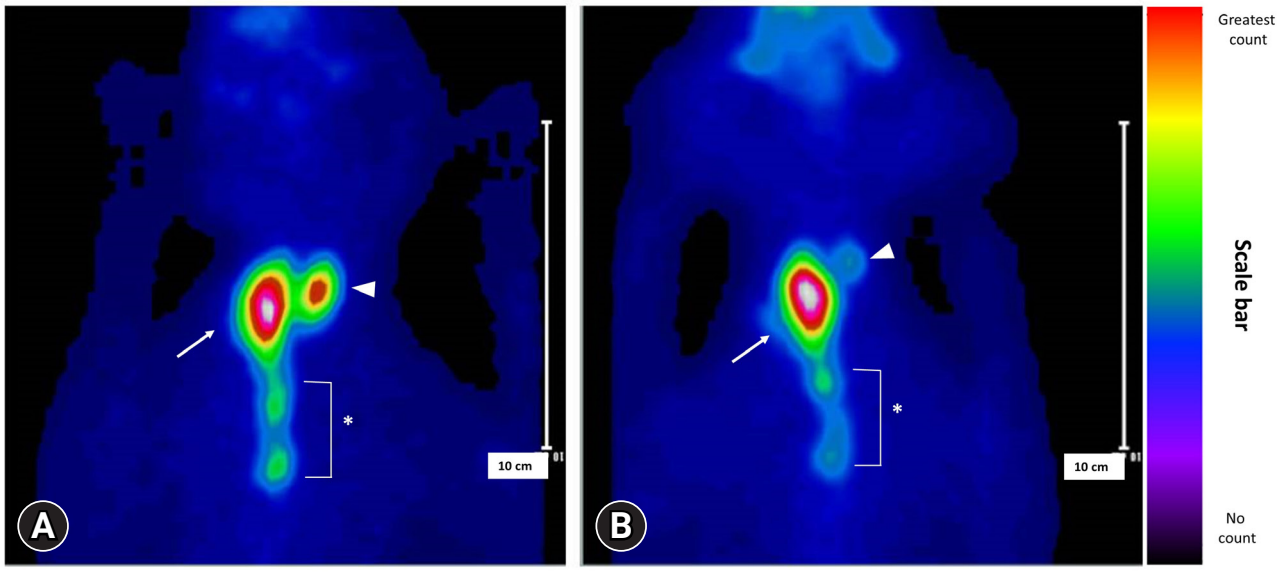

Fig. 1. The image of thyroid scintigraphy in one hyperthyroid cat (ID 6). The color display pattern of rainbow was used in this planar scintigraphic images. The shade of color represents the counts per pixel. Thyroid image was obtained before (A) and 3 months after (B) the radioiodine therapy. Bilateral thyroid lobes were identified with hyperactivity. After the radioiodine therapy, the size of the left lobe (arrowhead) has decreased, but the size of right thyroid lobe (arrow) which was the main hyperactive thyroid gland was unchanged. The ectopic thyroid tissues (asterisk) were detected at the first scintigraphy, and confirmed to decreased size and activity at the second scintigraphy.

different in 3 cats (ID 1, 2, and 6) but decreased in one cat (ID 8). Three cats (ID 1, 2, and 6) were prescribed with 3.5 mCi, 3 mCi, and 4.4 mCi individually, and one (ID 8) cat was injected with 2 mCi. Total dose of administered RAI comprising both the first and second treatments was 5.5 mCi, 5 mCi, 8.4 mCi, and 4 mCi in cats ID 1, 2, 6, and 8, respectively.

Efficacy of the RAIT

All of clinical signs were disappeared at 1 month after treatment in all hyperthyroid cats. When laboratory data of the first and the second RAIT was combined, the serum tT4 was decreased significantly at 6 to 9 days after the treatment (pre-RAIT, 12.5 μg/dL (IQR, 9.5–15.5 μg/dL); post-RAIT, 4.3 μg/dL (IQR, 3.6–11.7 μg/dL); $p = 0.001$) (Table 3). In addition, elevated serum levels of ALP and ALT had been decreased after the RAIT with significant differences (ALP: pre-RAIT, 218.5 U/L (IQR, 176.0–441.0 U/L); post-RAIT, 189.0 U/L (IQR, 90.0–279.0 U/L); $p = 0.002$; ALT: pre-RAIT, 346.8 U/L (IQR, 3.3–690.3 U/L); post-RAIT, 104.0 U/L (IQR, 46.5–197.5 U/L); $p = 0.003$) (Table 3). Other hematologic results, such as BUN, creatinine, SDMA, white blood cell (WBC) count, and hematocrit, were not different significantly ($p > 0.05$) (Table 3).

Adverse effects

After the RAIT, there were no adverse effects on gastrointestinal, cardiovascular, respiratory, genitourinary, neurologic and general behavioral signs were observed after drug administration. Abnormal clinical signs associated with the RAI administration, such as nausia, vomiting, anorexia, and swelling of neck, were not noted in all cats. In addition, the complications of the RAIT, such as myelosuppression and renal dysfunction were not identified at the time of discharge. However, in 1 cat (ID 7), serum creatinine level was increased from 0.9 mg/dL to 2.1 mg/dL at 6 months after the RAIT. Iatrogenic hypothyroidism was not identified when all cats were discharged, but occurred in 1 cat (ID 3) at 1 month after the RAIT. This cat had monitored for 6 months after the RAIT, but any clinical signs of hypothyroidism were not existed.

Discussion

This study evaluated the clinical efficacy of the RAIT in 10 hyperthyroid cats. Disappearance of the clinical signs, significant decrease in serum tT4 and liver enzymes were identified within 9 days after the RAIT. There were no significant differences in serum level of BUN, creatinine, SDMA, hematocrits and WBC counts between pre- and post-treatment. These results present that the RAIT is safe and effective treatment for hyperthyroid cats.

Within the current cases, the clinical findings of the hyper-

Table 3. Changes of total T4, serum chemistry profiles, and blood cell counts following the first and second RAIT in 10 hyperthyroid cats

Items (reference range)	Pre-RAIT[a]	Post-RAIT[b]	*p*-value
total T4 (0.8–4.7) (μg/dL)	12.5 (9.5–15.5)	4.3 (3.6–11.7)	0.001[c]
BUN (18–33) (mg/dL)	27.8 (16.3–39.3)	26.9 (14.7–39.1)	0.91
Creatinine (0.7–1.8) (mg/dL)	1.1 (0.7–1.5)	1.2 (0.8–1.6)	0.36
ALT (20–107) (U/L)	346.8 (3.3–690.3)	104.0 (46.5–197.5)	0.003[c]
ALP (23–107) (U/L)	218.5 (176.0–441.0)	189.0 (90.0–279.0)	0.002[c]
SDMA (0–14) (μg/dL)	9.4 (7.0–11.8)	10.0 (8.3–11.5)	0.20
WBC count (2.87–17.02) ($\times 10^3$/μL)	11.4 (7.4–17.9)	13.5 (4.7–22.3)	0.94
Hematocrit (30.3–52.3) (%)	35.5 (26.7–45.3)	34.8 (24.8–44.8)	0.35

Values are presented as median (interquartile range).
RAIT, radioiodine therapy; BUN, blood urea nitrogen; ALT, alanine aminotransferase; ALP, alkaline phosphatase; SDMA, symmetric dimethylarginine; WBC, white blood cell.
Pre-RAIT: total T4, BUN, creatinine, ALT, SDMA, WBC count, and hematocrit; post-RAIT: BUN, creatinine, ALP, WBC count, and hematocrit) or as the median and interquartile range (pre-RAIT: ALP and WBC count; post-RAIT: total T4, ALT, and SDMA).
[a]Results within 3 days before the first and second RAIT. [b]Results at 6 to 9 days after the first and second RAIT. [c]Significant differences ($p < 0.01$) between pre- and post-RAIT.

thyroid cats had no unexpected features and they were similar with the results of the previous studies [7,17,18]. Feline hyperthyroidism is the most common endocrine disorder in middle to old aged cats and its prevalence is up to 10% with cats older than 10 years [1]. In these cases, hyperthyroid cats were 8.5% of total cats that have visited our clinic and 8 of 10 RAI treated hyperthyroid cats were aged over 10 years. Therefore, the prevalence may increase if they were grouped by the age of cat over than 10 years from the whole population. The most common clinical signs of 10 hyperthyroid cats were weight loss, polyuria/polydipsia, tachycardia, and vomiting; however, tachycardia could be over-estimated because of white-coat effect [19]. Additionally, numerous studies have suggested that purebred cats, such as Siamese and Himalayan, were associated with lower prevalence than domestic short- and long-haired cats [17,20,21]. Similarly, domestic short hair was 40% of 10 hyperthyroid cats, but purebred of Siamese and Himalayan was not identified in this study. Moreover, purebred of Russian blue was 40% of the total, either. In one statistical survey of Korea in 2021, the most common bred cat was domestic short hair (45.2%), followed by Russian blue (19.0%) and Persian (18.7%) [22]. Despite the breeding percentage, Russian blue had a similar prevalence to domestic short hair but a higher prevalence than Persian. This finding suggests that the high prevalence of Russian blue may have different etiology, not because of its population. The etiology for feline hyperthyroidism is still unclear but some studies have reported environmental suspicions such as canned food or phthalates which is goitrogenic compounds [17,20,23]. However, evaluation of the association between environmental factors and hyperthyroidism was difficult in the current study because of its small sample size. For the evaluation of the variable risk factors associated with etiology of feline hyperthyroidism, further studies of larger population are needed.

In a previous study, the response to the RAIT using scoring system had rapid response with 84.7% of cats having tT4 within or below the reference range by the time at hospital discharge and tT4 was within or below the reference range in 98.5% of cats after 6 months [9]. In another study, the cure rate of > 97% with reduced frequency of side effect (e.g. iatrogenic hypothyroidism and azotemia) was reported in low-dose (2 mCi) RAI treatment for mild-to-moderate hyperthyroid cats [10]. All of 10 cats had decreased tT4 after the RAIT, but 4 of 10 cats (ID 1, 2, 6, and 8) were retreated at 3 months after the first RAIT, because the tT4 was maintained above than the normal (serum tT4 ≥ 4 μg/dL). These 2 (ID 1, 8) of 4 retreated cats had fixed low-dose RAIT based on the initial tT4 at the first time, but the therapeutic effect was insufficient because actual concentration of initial tT4 was above 13 μg/dL. Some studies reported the differences of tT4 concentration with measurement methods [24,25]. Initial tT4 concentration of these cats might have been suppressed due to transient non-thyroidal illness or laboratory differences which can influence errors [24–26]. The other cat (ID 2) had fixed low-dose RAI at the first RAIT because of its accompanied cardiomyopathy. The cardiopulmonary dysfunction can be caused by thyroid storm, and it is resulted from a sudden release of thyroid hormones by administered radioiodine that immediately destroys hyperactive thyroid cells [27]. Three months after, the cat was retreated by scoring system that confirmed a lower score than before, and cured completely after the second RAIT. The last cat (ID 6) had insufficient treatment response even though the injected dose was optimized by the scoring system. Because the cat had ectopic thyroid tissues and relatively large thyroid gland, it was suspected as thyroid carci-

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noma but was not differentiated through a histopathology because of the owner's disagreement of thyroid biopsy. Three months after the second RAIT, serum tT4 level was identified as 3.5 μg/dL. By these all cases, various doses of RAI between 2 and 5 mCi were administered in the initial treatment, and the treatment efficacy differed according to disease severity. Furthermore, the superiority of therapeutic effect between the scoring system and fixed low-dose treatment was not identified. Inappropriate RAI application can reduce the therapeutic effect, while administering an overdose of RAI may lead to iatrogenic adverse effects such as hypothyroidism. Therefore, accurate evaluation of disease severity is necessary for determining the appropriate dose, and further study involving statistical analysis of various parameters such dosage, disease severity, and treatment outcomes should be needed.

The aim of the RAIT is to achieve euthyroid through single dose of the RAI application without producing hypothyroidism [9]. The most common adverse effect of the RAIT was iatrogenic hypothyroidism and concurrent chronic kidney disease which is masked due to hyperthyroidism [9,28]. Currently, iatrogenic hypothyroidism of the RAI treated cats was reported 25 % to 50% in most studies of the RAI treatment protocols [10,29,30]. In these case series, one cat (ID 3) was confirmed serum tT4 concentration below 0.9 μg/dL at 1 month after the RAIT, but maintained subclinical state during the monitoring period. Thyroid function can be degraded by the destruction of hyperactive thyroid cells by the RAI, but could be recovered normally as restoration of suppressed normal thyroid cells by thyroid stimulating hormone increasement [9]. Additionally, in one cat (ID 7), the serum creatinine level was increased from 1.9 mg/dL to 2.1 mg/dL at 6 months after the RAIT in accordance with the normalization of thyroid hormone. Thyroid hormone can be reduced gradually during 6 months, and the glomerular filtration rate may also be decreased concurrently [9]. Thus, the serum levels of thyroid hormone and creatinine should be monitored together periodically.

In this study, a significant decrease in ALT and ALP along with serum tT4 level was identified in post-RAIT. Liver functions and enzymes can be affected by several mechanisms, but its etiology is not fully understood yet [31]. First, elevated thyroid hormone can affect increase in liver enzymes because liver is associated with synthesis and metabolism of thyroid hormones [31]. Thyrotoxicosis can increase local and systemic metabolism and oxygen requirement that leads to relative hypoxic damage of hepatocyte [32–34]. Additionally, elevated serum bone ALP isoenzyme which is affected by thyroid hormone may contribute to serum ALP elevation [35,36]. A previous study reported that hyperthyroid cats, even with severely high level of liver enzymes, had a normal liver function and the serum activity of liver-derived enzymes returned to normal at 6 weeks after successful treatment with the RAI [31]. Also, this study supports the finding of previous studies by identifying decreased liver-derived enzyme levels due to decreased serum tT4 concentration in a shorter period than those reported before.

There were some limitations in these case series. First, small number of hyperthyroid cats were enrolled, which might not represent the entire population of cats with the RAIT. Second, comparison of clinical data between pre- and post-treatment was done with short term period, and it may not reflect the long-term outcome. Third, only 2 dosing methods were used in these cases, and it was hard to compare with other novel dosing methods, such as using algorithm or other fixed dose method, that have been reported recently [12,30,37]. Additionally, differences in treatment efficacy based on the underlying cause of hyperthyroidism, such as thyroid malignancy, could not be confirmed because histopathologic diagnosis through thyroid biopsies were unable to be performed on all cats. Therefore, additional studies should be performed to compare the effectiveness of treatment in the various underlying conditions of feline hyperthyroidism.

In conclusion, this preliminary study marks the first investigation of RAIT for feline hyperthyroidism in South Korea, using locally manufactured RAI. The treatment efficacy varies depending on the severity of disease, while the safety of RAI doses ranging from 2 to 5 mCi in the initial treatment was investigated. To ensure the adequate therapeutic effect and avoid iatrogenic adverse effect, it will be necessary to determine the RAI dose based on the severity of the disease. Based on these findings, the RAIT could be considered the treatment option and prevent adverse effects from medication or surgery in hyperthyroid cats.

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