Outcomes for dogs with primary hyperparathyroidism following treatment with percutaneous ultrasound-guided ethanol ablation of presumed functional parathyroid nodules: 27 cases (2008–2011)

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Objective—To describe outcomes for dogs with primary hyperparathyroidism following treatment with percutaneous ultrasound-guided ethanol ablation of presumed functional parathyroid nodules.

Design—Retrospective case series.

Animals—24 dogs with primary hyperparathyroidism that underwent 27 ultrasound-guided ethanol ablation procedures of presumed functional parathyroid nodules identified by cervical ultrasonography.

Procedures—Dogs were anesthetized for each procedure. For each nodule, 95% ethanol was injected into the center with ultrasound guidance (volume injected calculated on the basis of ultrasonographic measurements). The interval from treatment to resolution of hypercalcemia, complications, and follow-up clinicopathologic data were recorded.

Results—5 procedures involved simultaneous treatment of 2 nodules. Three dogs underwent a second treatment because of initial treatment failure or development of another nodule. Hypercalcemia resolved after 23 of 27 (85%) procedures. In those 23 treatments, 22 (96%) had resolution of hypercalcemia within 72 hours after treatment. Hypocalcemia was detected in 6 different dogs at 2 (1 dog), 7 (3 dogs), 14 (1 dog), and 21 (1 dog) days after treatment; 5 of these dogs had mild transient hypocalcemia and 1 developed clinical signs requiring calcium supplementation. Although there were no periprocedural adverse effects, 2 dogs had delayed adverse effects; the overall rate of complications (including delayed adverse events and clinical hypocalcemia) was 11.1%. Long-term follow-up data indicated sustained normocalcemia in 17 of 19 dogs.

Conclusions and Clinical Relevance—Results suggested that percutaneous ultrasound-guided ethanol ablation of functional parathyroid nodules may be an effective treatment for primary hyperparathyroidism of dogs, with short duration of anesthesia, minimal complications, and low risk for hypocalcemia. (*J Am Vet Med Assoc* 2015;247:771–777)

Hypercalcemia may be caused by PHPT, malignancy, hypoadrenocorticism, chronic kidney disease, vitamin D toxicosis, granulomatous disease, and skeletal lesions.[1–3] The degree of hypercalcemia is not associated with cause.[3] Primary hyperparathyroidism may be a result of development of parathyroid adenoma, parathyroid carcinoma, or parathyroid hyperplasia. Regardless of etiopathogenesis, PHPT results in excess PTH secretion by chief cells in the parathyroid gland, which causes an increase in serum calcium concentration by mobilizing calcium from bone, increasing calcium resorption from the distal convoluted tubule, and increasing phosphorus excretion into urine.[2] The most common clinical signs of hypercalcemia are polyuria, polydipsia, dysuria, lethargy, gastrointestinal signs, and anorexia.[4,5] Urolithiasis is present in 24% to 29% of dogs with PHPT.[4,5] Unlike the condition of dogs with hypercalcemia due to chronic kidney disease or malignancy, dogs are usually healthy at the time PHPT is diagnosed.[5,6] In 1 study,[6] hypercalcemia was an incidental finding in 42 of 110 dogs.

Abbreviations

PHPT	Primary hyperparathyroidism
PTH	Parathyroid hormone
PTHrP	Parathyroid hormone-related peptide

The diagnosis of PHPT is made on the basis of persistent ionized hypercalcemia with an inappropriately normal or high serum PTH concentration, a serum PTHrP concentration of 0 pmol/L, serum phosphorus concentration within or less than the reference interval, ultrasonographic identification of a nodule on a parathyroid or thyroid gland, and exclusion of other causes of hypercalcemia, with no evidence of renal disease.[4] Ultrasonography can detect nodules ≥ 2.1 mm.[7] It has been reported[5] that 85% of canine cases of PHPT are caused by

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parathyroid adenomas, 12.4% by parathyroid hyperplasia, and 5.4% by parathyroid carcinomas. The size of an affected parathyroid gland cannot be used to differentiate an adenoma from a carcinoma.[5] Results of another study[8] of 19 dogs with parathyroid carcinomas suggest that dogs with carcinomas more commonly have weakness, whereas dogs with parathyroid adenomas or hyperplasia typically develop polyuria and polydipsia.

Surgical parathyroidectomy is the current treatment of choice for PHPT.[6,9,10] Parathyroidectomy can lead to hypocalcemia in up to 40% of dogs.[5] Some dogs develop hypocalcemia despite presurgical calcium and vitamin D supplementation.[5,11] Preoperative serum ionized calcium concentrations are not predictive for postoperative hypocalcemia.[11] With regard to surgical parathyroidectomy, hypercalcemia resolved within 6 days after surgery in 44 of 47 treated dogs.[6] In other studies,[10,12] PHPT recurred months to years after surgery in 2 of 29 (7%) to 2 of 12 (17%) dogs.

Prior studies of ethanol ablation of parathyroid nodules for treatment of PHPT had success rates of 8 of 9 procedures (8/8 dogs),[9] 0 of 5 dogs,[12] and 13 of 18 procedures (13/15 dogs).[6] Ethanol ablation for the treatment of hyperthyroidism due to unilateral hyperplastic nodules in 4 cats has also been reported.[13] In the 1 report[12] of treatment failure for all study dogs, the diagnostic criterion for PHPT was high serum PTH concentration only; therefore, those dogs may have been hypercalcemic due to causes other than PHPT (6/29 [20%] dogs in that study[12] had concurrent diseases identified, including acute kidney disease, pathological fracture, and thyroid gland carcinoma). The effect of operator experience was briefly described in those 3 reports.[6,9,12] In 1 study[6] comparing complication rates of surgical parathyroidectomy, heat ablation, and ethanol ablation in dogs, no significant difference among complication rates was found. Reported adverse effects of ethanol ablation of parathyroid nodules include transient bark change in 2 of 9 procedures, coughing in 2 of 18 procedures, and bark change in 1 of 18 procedures.[6,9] Humans undergoing ethanol ablation procedures describe a transient, tolerable pain at the injection site.[14]

The purpose of the study reported here was to describe outcomes for dogs with primary hyperparathyroidism following treatment with percutaneous ultrasound-guided ethanol ablation of presumed functional parathyroid nodules. We hypothesized that by assessing a larger sample size than those used in previous studies, we would be able to determine efficacy, risk of adverse effects (eg, hypocalcemia), and long-term outcome of this treatment process in dogs.

Materials and Methods

Case selection—Medical records were reviewed retrospectively for dogs with suspected PHPT treated by ethanol ablation of parathyroid nodules at the Veterinary Specialty Center of Delaware, New Castle, Del, and VCA Smoketown Animal Hospital, Smoketown, Pa, from 2008 to 2011. The diagnosis of PHPT was based on the following criteria: repeatable high serum ionized calcium concentration with serum phosphorus concentration within or less than the reference interval, serum PTH concentration within or greater than the reference interval, serum PTHrP concentration of 0 pmol/L, and the presence of at least 1 nodule in the region of the thyroid gland detected via ultrasonography. Dogs were excluded from the study if another cause of hypercalcemia was found on the basis of results of a CBC, serum biochemical analysis, urinalysis, thoracic radiography, or abdominal ultrasonography. Twenty-one dogs satisfied the inclusion criteria. Three additional dogs were suspected to have PHPT, had parathyroid nodules, and underwent ethanol ablation but did not have PTH concentration data available. These 3 dogs were included in the study (total, 24 dogs). A dog undergoing an ethanol ablation procedure was defined as a case; if a dog underwent 2 procedures at different times, those data were considered as 2 cases.

Medical record review—Data obtained from medical records included signalment; clinical signs; physical examination findings; clinicopathologic data; previous treatments; serum ionized calcium, PTH, and PTHrP concentrations at the time of diagnosis; results of diagnostic imaging; treatment description; and outcome. Routine methods were used to perform CBCs, serum biochemical analyses, and urinalyses. Serum ionized calcium concentration was determined by fluorescence with an in-house analyzer[a] or at the Michigan State University Endocrine Laboratory. Serum PTH and PTHrP concentration determinations were performed at the Michigan State University Endocrine Laboratory. Cervical ultrasonography was performed by a board-certified radiologist (VWK) with a 7.5- to 12-MHz linear, phased-array transducer and a standard ultrasonography machine.

Ethanol ablation procedure—Ethanol ablation of presumed functional parathyroid nodules was performed by 1 radiologist (VWK). The procedure was performed as described by Long et al.[9] Each dog was anesthetized according to an individualized anesthetic protocol. All procedures were performed by the radiologist by positioning the point of a 27-gauge, 1.5-inch needle into the center of the nodule with ultrasonographic guidance, and under ultrasonographic visualization, the radiologist injected a premeasured volume of 95% ethanol solution.[b] The volume of the parathyroid mass was calculated as the product of its maximum length, height, and width. Subsequently, a volume of ethanol equivalent to that of the mass was used for each injection, as described by Long et al.[9] The ultrasonographic appearance of the gland during and after the procedure was recorded. Complications during or after treatment were recorded in the medical record. Other treatments were chosen by the primary clinician.

Follow-up examinations of the dogs were conducted by the primary clinician at the referral hospital or the local veterinarian. Follow-up examinations and repeated serum ionized calcium concentration determinations were performed at 1, 2, 3, 7, 14, and 30 days after ethanol ablation. Other follow-up examination findings, serum ionized calcium concentrations, and any other biochemical data in the medical records were reviewed.

Results

Twenty-four dogs with suspected PHPT treated by ethanol ablation of parathyroid nodules were included

in the study. These 24 dogs underwent a total of 27 ablation procedures. Among the dogs, there were 10 females and 14 males, all of which were neutered. Their ages ranged from 8 to 15 years, with a median age of 10 years. Breeds represented included mixed breed (n = 7), Golden Retriever (2), Rhodesian Ridgeback (2), Shih Tzu (2), Weimaraner (2), and Bassett Hound, Dachshund, Fila Brasileiro, German Shepherd Dog, Jack Russell Terrier, Labrador Retriever, American Pit Bull Terrier, Siberian Husky, and West Highland White Terrier (1 each).

The most common clinical signs prior to the 27 procedures were polyuria and polydipsia, seen in 14 of 27 (51.8%) cases, followed by dysuria in 3 (11.1%), decreased appetite in 3 (11.1%), generalized weakness in 3 (11.1%), lethargy in 2 (7.4%), coughing in 1 (3.7%), and muscle tremors in 1 (3.7%). Duration of these clinical signs ranged from 2 weeks to 2 years (mean, 5.27 months). Five of the 24 (21%) dogs had no clinical signs, with hypercalcemia being an incidental finding of routine senior wellness blood assessments or preanesthetic blood assessments in these dogs. Three dogs had received prior treatment for hypercalcemia with furosemide alone (2 dogs) or prednisone and furosemide (1 dog).

Each dog had a CBC and serum biochemical analysis performed prior to the procedure. For all of the dogs, abnormalities revealed by preablation CBCs and serum biochemical analyses performed before the first or only ethanol ablation procedure were summarized (**Table 1**). All dogs had high serum total calcium concentrations prior to the first or only procedure. Considering the first or only procedures for the 24 dogs, median preablation serum ionized calcium concentration was 1.73 mmol/L (range, 1.55 to 2.32 mmol/L [reference interval, 1.25 to 1.45 mmol/L]). Serum PTH concentration was measured in 21 dogs (prior to 21 procedures). Nine of the 21 dogs had serum PTH concentrations greater than the reference interval, and 12 of the 21 dogs had serum PTH concentrations within the reference interval. Serum phosphorus concentrations were less than the reference interval in 4 dogs and within the reference interval in 20 dogs. Sixteen dogs had urinalysis results available, of which 8 dogs had a urine specific gravity ≤ 1.016. For 12 dogs, urine sediment analysis results were available; 4 of those dogs had calcium oxalate crystalluria.

Seventeen dogs underwent abdominal ultrasonography prior to their first or only procedure; cystic calculi were detected in 7 of those dogs. Two other dogs underwent abdominal radiography; cystic calculi were detected in 1 of those dogs. For 12 dogs, thoracic radiographic views were available for assessment; none of those dogs had radiographic evidence of primary or metastatic neoplasia.

All dogs underwent cervical ultrasonography prior to each of the 27 procedures. Median length of the detected parathyroid nodules was 6 mm (range, 2.6 to 21 mm; **Table 2**). Five dogs had > 1 nodule identified near or on a thyroid gland. Of these 5 dogs, 4 had bilateral nodules and 1 dog had 2 ipsilateral nodules. In dogs that had multiple nodules identified by means of ultrasonography, each nodule was injected during the same ablation procedure.

Time from initial diagnosis of hypercalcemia to the treatment date ranged from 15 days to 2.5 years. Three dogs were treated with prednisone or furosemide prior to ethanol ablation. One dog was being treated with prednisone at a low dosage for chronic lower airway disease prior to the onset of hypercalcemia, and it remained on this treatment regimen after the hypercalcemia resolved with ethanol ablation.

Among the 27 procedures, the total volume of ethanol used for injection ranged from 0.02 to 2.0 mL, as calculated by the previously described formula. Duration of anesthesia was defined as the interval from induction of anesthesia to extubation and was recorded in increments of 15 minutes (eg, if the duration of anesthesia was between 0 and 15 minutes, it was recorded as 15 minutes). Median total duration of anesthesia was 30 minutes (range, 15 to 45 minutes). During the 27 procedures, no adverse events were noted.

Serum ionized calcium concentrations measured 1 day after treatment were recorded for 24 of the 27 procedures (21 dogs). Of these 24 cases, 4 (16.7%) were

Table 1—Serum biochemical data for 24 dogs obtained prior to ethanol ablation of presumed functional parathyroid nodules for PHPT (first or only procedure).

Variable	Reference interval	No. of dogs for which data were available	No. of dogs with abnormal findings (greater or less than reference interval)	Mean	Median	Range
Alkaline phosphatase (U/L)	10–150	24	16; greater	667.4	391.5	56–4,562
Alanine aminotransferase (U/L)	5–107	24	7; greater	77.5	63	16–180
γ-Glutamyltransferase (U/L)	0–14	17	5; greater	11.4	10	4–31
Albumin (g/dL)	2.5–4.0	24	3; greater	3.78	3.9	3.0–4.3
BUN (mg/dL)	7–27	24	4; greater	20.4	18	9–43
Creatinine (mg/dL)	0.4–1.8	24	1; greater	1.1	1.0	0.6–2.3
Cholesterol (mg/dL)	112–328	24	7; greater	316.5	295.5	234–544
Triglycerides (mg/dL)	20–150	11	5; greater	405	244	138–1,480
Total calcium (mg/dL)	8.2–12.4	24	23; greater	13.5	13.4	11.6–15.6
Ionized calcium (mmol/L)	1.25–1.45	24	24; greater	1.76	1.73	1.55–2.32
Phosphorus (mg/dL)	2.1–6.3	24	4; greater	3.0	2.85	1.5–5.0
PTH (pmol/L)*	3.0–17.0	12	7; greater	34.5	22.85	13.6–88
	0.5–5.8	9	2; greater	11.5	2.5	1.4–46.8
PTHrP (pmol/L)	0–1.0	13	0	0.0	0.0	0.0

*Two different reference ranges for serum PTH concentration in dogs were used during the study time period; thus, data are reported separately.

Table 2—Results of cervical ultrasonography with regard to number of parathyroid nodules, affected parathyroid gland, and nodule size for the 24 dogs in Table 1 before each ethanol ablation procedure.

Dog	Procedure	No. of nodules treated per procedure	Affected parathyroid gland	Size (mm)
1	1	1	Left	8.8 × 6.8 × 5.4
2	1	2*	Left, right	Left 7.8 × 2.3; right 9.2 × 9.2
3	2†	1	Right	6.6 × 7.3
		1	Right	9.8 × 7.1
4	1	1	Right	4.1 × 5.1 × 4.3
5	2‡	1	Left	4.8 × 5.4
		1	Left	5.3 × 6.9 × 6.3
6	1	1	Right	4.6 × 6.6
7	1	2*	Left, right	Left 2.2 × 3.0; right 2.6 × 2.6
8	1	1	Right	4.9 × 3.2 × 3.8
9	1	1	Left	4.0 × 4.0 × 3.0
10	1	2*	Right (cranial), right (caudal)	Cranial 12.0 × 8.8 × 8.8; caudal 7.0 × 6.0 × 5.0
11	1	1	Right	5.0 × 5.0 × 6.0
12	1	1	Right	5.0 × 5.0 × 6.0
13	1	2*	Left, right	Left 3.6 × 5.4; right 7.4 × 8.0
14	1	1	Left	16.0 × 10.0 × 21.0
15	1	1	Left	4.4 × 4.3 × 5.2
16	1	1	Right	5.0 × 6.1 × 7.4
17	1	1	Left	6.0 × 3.3 × 4.3
18	1	1	Left	3.8 × 4.4 × 4.8
19	1	1	Left	6.0 × 2.8 × 3.2
20	1	1	Right	5.2 × 8.3 × 5.6
21	1	1	Left	Not recorded
22	1	1	Right	3.5 × 2.5 × 3.0
23	1	1	Left	Not recorded
24	2†	1	Right	3.0 × 4.0 × 5.0
		2*	Left, right	Left 2.0 × 3.0 × 5.0; right 4.0 × 4.0 × 5.0

*Nodules were detected during the same examination and were treated during the same procedure. †Initial treatment failure followed by a second procedure, which took place 1 month after the initial procedure in dog 24, and 3.5 months after the initial procedure in dog 3. ‡Initial treatment success followed by development of a new functional nodule 2 years after the initial treatment, followed by a second procedure, in dog 5.

associated with resolution of hypercalcemia within 12 hours and 11 (62.5%) additional cases were associated with resolution of hypercalcemia within 24 hours. None of the dogs became hypocalcemic within the first 24 hours after treatment. Serum ionized calcium concentrations measured 2 days after treatment were available for 26 of the 27 procedures (23 dogs). Serum ionized calcium concentrations were within the reference interval for 20 (76.9%) cases, greater than the reference interval for 5 (19.2%) cases, and less than the reference interval for 1 (3.8%) case. The single dog with hypocalcemia at this time point had a serum ionized calcium concentration that was 0.04 mmol/L below the lower limit of the reference interval and had mild weakness. This dog received oral supplementation with calcium carbonate, and clinical signs resolved. Calcium supplementation was weaned and discontinued after 5 months, with maintenance of normocalcemia. At 7 days after the procedure, 21 dogs (23 procedures) had serum ionized calcium concentration measured; serum ionized calcium concentration was within the reference interval for 16 cases (69.6%), greater than the reference interval for 4 (17.4%) cases, and less than the reference interval for 3 (13.0%) cases. Two of the 3 dogs with hypocalcemia at 7 days after the procedure had a serum ionized calcium concentration of 0.01 and 0.02 mmol/L below the lower limit of the reference interval, and the third dog had a serum ionized calcium concentration of 0.11 mmol/L below the lower limit of the reference interval. None of these dogs had clinical signs of hypocalcemia. Fourteen days after the procedure, serum ionized calcium concentrations for 14 dogs (15 procedures) were available; serum ionized calcium concentration was less than the reference interval for 1 dog and within the reference interval for 13 dogs. The dog with hypocalcemia at this time point had a serum ionized calcium concentration that was 0.02 mmol/L below the lower limit of the reference interval and did not have clinical signs of hypocalcemia.

Hypercalcemia resolved after 23 of 27 (85%) procedures (22 dogs). The interval from treatment to resolution of hypercalcemia ranged from 12 hours to 3 weeks. In 20 of the 23 (87%) successful treatments, hypercalcemia resolved within 2 days after treatment; hypercalcemia resolved in 2 other cases by day 3 and in 1 additional case 3 weeks after the procedure. The latter dog had not had its serum ionized calcium concentration measured prior to the 3-week posttreatment time point owing to lack of owner compliance. With the exception of this dog, all treatment successes occurred within 3 days after the procedure.

Hypercalcemia persisted in 3 dogs after the initial procedure. Two of these dogs had ethanol ablation procedures repeated; 1 dog failed a second treatment, and 1 dog had a successful second treatment, with maintenance of normocalcemia at the last recorded serum ionized calcium concentration measurement at 8 months after the second procedure. The third dog with persistent hypercalcemia after the initial treatment had a serum ionized calcium concentration that was only 0.03 mmol/L greater than the upper limit of the reference interval on day 3 after the procedure, and the

owner declined further blood analyses owing to complete resolution of the dog's clinical signs (polyuria and polydipsia). This dog did not receive further treatment.

Mild hypocalcemia was detected after 6 of 27 (22.2%; 6 dogs) procedures, with only 1 (3.7%) dog exhibiting signs of hypocalcemia (weakness). This dog responded quickly to oral calcium supplementation, which was gradually eliminated by 5 months after treatment. The other 5 dogs were not treated, and hypocalcemia resolved within 14 days to 4 months after the procedure.

There were no periprocedural or immediately postprocedural adverse effects. Delayed adverse effects related to serum ionized calcium concentration were noted: 1 dog required treatment for clinical hypocalcemia (weakness), and 3 dogs required a second ethanol ablation procedure. Of those 3 dogs, 2 had treatment failures of the initial ethanol ablation, and the interval between procedures was 29 days and 3.5 months; the other dog developed a new nodule and underwent the repeated procedure 2 years after the first. Other reported delayed adverse effects included possible transient dysphagia and hypersalivation (reported by owner) for 2 days after the procedure in one dog and a cyst on the neck in another dog. Three months later, the primary veterinarian lanced and drained this cyst, and the dog was treated with a 2-week course of antimicrobials; the cyst did not recur. It is unknown whether the cyst was associated with the ethanol ablation procedure, but an association cannot be definitively ruled out.

Follow-up information was available 1 month or more (range, 1 month to 3 years) after the procedure for 19 of the 23 treatment successes (19 dogs). Five dogs had died or were euthanized (1 dog each had hemangiosarcoma, osteosarcoma, adrenal gland tumor, neurologic and cardiac disease, and progressive lower airway disease). None of the deaths were attributable to the ethanol ablation procedure.

Follow-up serum ionized calcium concentrations indicated that 17 of 19 dogs for which clinicopathologic data were available had sustained normocalcemia. Postprocedural serum ionized calcium concentration was measured at 1 to 2 months for 5 dogs, 3 months for 4 dogs, 4 months for 4 dogs, 5 months for 3 dogs, 8 months for 1 dog, and > 1 year for 2 dogs. Follow-up information regarding clinical signs and physical examination findings for > 1 year (range, 1 to 3 years) was available for 6 dogs; clinical signs of hypercalcemia were not noted in the medical records, but serum ionized calcium concentration was documented for only 2 dogs. Those 2 dogs with recurrence of hypercalcemia underwent confirmatory testing for PHPT and had consistently high serum ionized calcium concentration, high serum PTH concentration, PTHrP concentration of 0 pmol/L, and cervical ultrasonographic findings consistent with PHPT. Both dogs had new nodules identified by means of ultrasonography, contralateral to the originally treated parathyroid gland. One dog's recurrence of hypercalcemia was detected 4 months after treatment, and the other dog's recurrence of hypercalcemia was detected 1.5 years after treatment. The former dog did not undergo a second ethanol ablation procedure because there were no clinical signs related to hypercalcemia. The latter dog underwent a second successful ethanol ablation procedure.

Overall, 27 procedures were performed on 24 dogs, with success in treating hypercalcemia in 23 (85%) of those procedures. One dog underwent 2 ethanol ablation procedures, both successful, 2 years apart. Three dogs remained hypercalcemic after their initial treatment, and 2 of those dogs underwent a second ethanol ablation procedure. One of the 2 repeated procedures was successful, and the other was not. The dog that did not undergo a second treatment had resolution of clinical signs with a marginally high serum ionized calcium concentration.

Discussion

Similar to findings of previous studies,[4,5] the most common clinical signs of PHPT in the dogs of the present study were polyuria and polydipsia, dysuria, weakness, lethargy, and decreased appetite. Hypercalcemia was an incidental finding on wellness or preanesthetic screening in 5 of 24 (21%) dogs. Before the first or only ethanol ablation procedure, high serum liver enzyme activities were a common finding among the 24 dogs, with mildly to markedly high serum alkaline phosphatase activity in 16 (66%) dogs and mildly high serum alanine aminotransferase activity in 7 (29%) dogs. These abnormalities have not previously been reported for dogs with PHPT. One possible explanation may be that dogs with PHPT tend to be older dogs, and concurrent metabolic disease or hepatic nodular hyperplasia is more common in older dogs. Other explanations include the effect of endogenous cortisol release associated with illness, exogenous prednisone administration, or an effect of the small sample size in the present study.

Urolithiasis has been detected in 24% to 29% of dogs with PHPT.[4,5] In the present study, 8 of 19 (42%) dogs that underwent either abdominal radiography or ultrasonography had evidence of urolithiasis. This greater proportion of affected dogs may be attributable to increasing awareness of calcium oxalate urolithiasis in dogs with PHPT (and therefore increased frequency of screening) or may be due to the effects of sample size on results.

Compared with other published reports,[6,9,12] the present study had a larger number of dogs and procedures, and the success rate was 85%. This success rate was similar to or higher than rates in previous studies of ethanol ablation for PHPT (success rates of 0% [0/5 dogs],[12] 72% [13/18 procedures],[6] and 89% [8/9 procedures][9]). Successful treatments maintained normocalcemia for 17 of 19 dogs for which long-term follow-up information was available. Two dogs had recurrence of PHPT 4 months and 1.5 years after their initial treatment, with new parathyroid nodules identified via ultrasonography.

With regard to ethanol ablation of suspected functional parathyroid nodules, treatment failures may be due to misidentification of parathyroid nodules, injection failure, or injection of nodules that are not actively secreting PTH. In 1 study,[7] 5 of 35 structures identified ultrasonographically as parathyroid nodules were thyroid tissue, as revealed by histologic evaluation of

nodule samples. Also, 4 of those 35 structures identified ultrasonographically as parathyroid nodules could not be found grossly.[7]

In the present study, 1 dog for which treatment failed was mildly hypercalcemic (serum ionized calcium concentration, 0.03 mmol/L greater than the upper limit of the reference interval) but had resolution of clinical signs. This dog's owner declined further biochemical analyses after day 3 because the clinical signs (polyuria and polydipsia) had resolved after treatment. Resolution of clinical signs despite measurable hypercalcemia may be considered a treatment success. Additionally, if this dog's serum ionized calcium concentration had been measured after 3 days, it may have been found that resolution of hypercalcemia had indeed occurred.

Of the 27 procedures, 23 resulted in treatment success in the present study. Hypercalcemia resolved within 72 hours after the procedure in 22 of those 23 (95.6%) successful procedures. This interval to resolution of hypercalcemia was faster than the typical time of response to surgical treatment (6 days) reported by Rasor et al.[6] Possible reasons for the faster resolution of hypercalcemia following ethanol ablation of parathyroid nodules include small sample size of the present study or previous studies or the release of PTH as a result of surgical manipulation prior to removal of the gland.

Surgical parathyroidectomy for treatment of PHPT in dogs has a reported rate of postoperative hypocalcemia up to 40%, with clinical hypocalcemia in 10% of patients.[6] In the present study, the rate of postablation hypocalcemia was 22.2% (6/27 procedures), with only 3.7% (1/27 procedures) having clinical hypocalcemia requiring treatment. Complication rates reported for the previous studies[6,9] of ethanol ablation of parathyroid nodules in dogs are 25% and 16.7%. The complication rate for the present study was 3 of 27 (11.1%) procedures. These complications included clinical hypocalcemia, owner-reported transient dysphagia and hypersalivation, and possible cyst associated with the procedure each in 1 dog. No laryngeal dysfunction complications were noted. Prospective, controlled studies comparing parathyroidectomy and ethanol ablation of parathyroid nodules are warranted.

The recurrence rate of PHPT in the present study was 8.3% (2/24 dogs). Recurrence of a functional parathyroid nodule or development of a new nodule after surgery for treatment of PHPT has been reported for 7% to 17% of dogs.[10,12]

To our knowledge, we were the first to report the time from original diagnosis to treatment of PHPT in dogs, which ranged from 15 days to 2 years. Additionally, many cases (21%) were identified incidentally on the basis of results of routine serum biochemical analysis, and the dogs had no clinical signs. This raises the question of when to treat PHPT and whether to treat subclinically affected dogs. None of the chronic hypercalcemic dogs in this study had or developed chronic kidney failure. It may be that patients with hypercalcemia as a result of PHPT do not develop the same type of renal damage that occurs in patients with hypercalcemia secondary to other diseases. However, dogs with PHPT and hypercalcemia need to be screened and monitored closely for crystalluria and urolithiasis, the presence of which may be an indication for treatment of PHPT. These questions indicate a need for further research.

To our knowledge, this was also the first report of treatment of multiple parathyroid nodules with ethanol ablation during a single procedure in dogs. Five dogs in the present study had multiple nodules; 1 dog had 2 nodules in the same parathyroid gland, and 4 dogs had a nodule in each of the 2 parathyroid glands. Of these 5 dogs, 3 underwent successful treatments and 2 did not. One of the successfully treated dogs had mild subclinical hypocalcemia at 3 days after the procedure, which resolved with no additional treatment by day 14. The owner of another successfully treated dog reported possible transient dysphagia and hypersalivation. Of the 2 dogs in which treatment failed, 1 was the previously described dog that had a 72-hour postprocedural serum ionized calcium concentration that was 0.03 mmol/L greater than the upper limit of the reference interval and the owner declined further laboratory testing or treatment owing to resolution of the dog's clinical signs. These findings have indicated that dogs with > 1 parathyroid nodule may be at an increased risk for adverse events, compared with dogs with 1 nodule, and may benefit from staging of the treatments. Dogs with > 1 nodule may also be more at risk for treatment failure, considering that 2 of the 4 treatment failures were in dogs with multiple nodules. Larger studies are needed to assess these risks in dogs with multiple parathyroid nodules.

One main argument against ethanol ablation for the treatment of PHPT is the inability to perform histologic evaluation of the nodule. However, histologic differentiation between parathyroid carcinomas and parathyroid adenomas is difficult.[15] In a study[8] of 19 dogs with parathyroid carcinomas treated with parathyroidectomy, 9 had postsurgical hypocalcemia; 1 of those 9 dogs was euthanized owing to intractable clinical signs. Even with marginal excision, there was no local recurrence, metastatic disease, or recurrence of hypercalcemia, suggesting that parathyroid carcinomas may be amenable to other treatment methods such as heat or ethanol ablation.[8] A lower risk of hypocalcemia associated with ethanol ablation may in fact be an indication of this treatment for parathyroid carcinomas. Prospective studies with a control group are indicated to further evaluate this question.

The cost, low level of invasiveness, and short duration of anesthesia associated with the ethanol ablation procedure may make it the preferred treatment option for some patients. Financial considerations are a part of every treatment decision for veterinary patients. At the private referral hospital where these procedures were performed, the cost estimate given to owners of dogs with parathyroid nodules for the ethanol ablation procedure, including anesthesia and overnight hospitalization, was approximately one-third of the cost estimate given to owners for surgical parathyroidectomy, which included 2 nights of hospitalization. The low level of invasiveness of this procedure, compared with surgical parathyroidectomy, may be a factor for consideration by owners, especially in relation to dogs with likely delayed healing, such as patients with hyperadrenocorticism or patients receiv-

ing corticosteroid treatment. Additionally, the short duration of anesthesia may be a reason why ethanol ablation is chosen for some dogs. Median duration of anesthesia was 30 minutes (range, 15 to 45 minutes) in the present study. Given that dogs with PHPT tend to be older and may have comorbidities such as heart disease and hyperadrenocorticism, ethanol ablation may be the preferred treatment option.

One main limitation of the present study was its retrospective nature, and records were incomplete for some cases. For most cases, preprocedural and postprocedural care was provided by a single primary clinician (JSD), but some cases were managed at the primary care hospital, with follow-up serum ionized calcium concentrations measured by means of different analyzers. Three dogs did not have PTH concentrations noted in their medical records. These dogs were treated with ethanol ablation on the basis of history, clinical signs, persistently high serum ionized calcium concentration, and ultrasonographic identification of a parathyroid nodule. Hypercalcemia resolved in all 3 dogs after ethanol ablation, confirming the diagnosis of PHPT. Given that it is not possible to obtain histologic evidence that the ultrasonographically identified nodule is functional for dogs that undergo ethanol ablation, diagnosis is largely based on response to treatment.

Results of the present study indicated that ethanol ablation of parathyroid nodules for the treatment of PHPT in dogs was associated with only rare mild adverse effects. Risk of posttreatment hypocalcemia was low. This study had a larger sample size than other reported studies[6,9,12] of ethanol ablation, and success and complication rates were better. Ethanol ablation of parathyroid nodules requires a short duration of anesthesia, which may be beneficial for a subgroup of dogs with systemic or cardiac disease or other comorbidities.

a. Vetstat Electrolyte and Blood Gas Analyzer, IDEXX Laboratories Inc, Westbrook, Me.
b. Henry Schein Animal Health, Fort Worth, Tex.

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