Efficacy of nutritional management of struvite uroliths in cats

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Introduction

Successful dietary dissolution of a naturally-occurring struvite urolith in a cat was first reported in 1983.[1] Since that time, three additional case series have been published demonstrating the efficacy of therapeutic foods to dissolve struvite uroliths.[2–4] Despite the unprecedented success associated with dietary dissolution, struvite remains one of the most common uroliths submitted to laboratories for quantitative analysis, an indication that invasive urolith extraction is often selected for many cats in which non-invasive nutritional dissolution would have resolved disease with overwhelming success and little or no risk.

Reasons for rationalizing urolith extraction over nutritional dissolution have not been evaluated; however, the following factors are likely involved in maintaining some misconceptions of the benefits of surgery over nutritional dissolution:

- Surgery averts an impending urethral obstruction
- Surgery averts prolonged discomfort during protracted dissolution
- Surgery resolves the problem immediately.
- Surgery resolves the clinical signs immediately
- Surgery avoids having to predict mineral composition
- Surgery is more appropriate because it is more successful than nutritional dissolution.
- Surgery eliminates worry about diet acceptance by the patient
- Familiarity with surgical techniques makes it easier for the clinician.

The following is a description of our study[5] emphasizing the ease and appropriateness of nutritional dissolution in addition to the reduced costs of effective care for clients.

Study objectives and design

Our study was designed to evaluate efficacy, safety, and speed with which two therapeutic foods dissolve sterile struvite uroliths in cats. To test these hypotheses, cats with naturally-occurring urocystoliths participated in a prospective, multicenter, double-masked, randomized, controlled, clinical trial. These client-owned cats were enrolled following validated client consent. Cats were included if survey abdominal radiography supported a diagnosis of struvite urocystoliths (moderately radiopaque, round or discoid stones with a smooth to slightly irregular contour) and were found to be otherwise healthy based on results of the physical examination, survey abdominal radiography, urinalysis, urine culture, serum biochemical profile and complete blood cell count. Survey radiography was selected over ultrasonography as the method of diagnosis because although ultrasonography is more sensitive at detecting the presence of uroliths, ultrasonography does not provide accurate information about urolith radiopacity or shape which are helpful when predicting urolith composition.[6,7] In addition, results of a recent in-vitro study indicated that uroliths measured by survey radiography more accurately reflected actual urolith size compared to uroliths measured by ultrasonography.[8]

Cats were excluded if they had nephroliths, urethroliths, urethral obstruction, or urinary tract infection at the time of initial evaluation. In addition, cats had to be free of significant diseases of the skin, heart, liver, eyes or kidneys. Cats were excluded if they were receiving medications or diets to manage lower urinary tract diseases except for the administration of medication to reduce pain (ie, buprenorphine).

Cats entering the study were randomly assigned to one of two treatment groups. One group was fed a prevention-dissolution food (ie, Hill's Prescription Diet c/d Multicare Feline) and the other group was fed a dissolution food (ie, Hill's Prescription Diet s/d Feline). In addition to patient randomization, the clinical care team and clients were masked as to which food the cat was assigned to eat. To achieve masking, both foods were identical in appearance, form (dry kibble), and packaging. Treatment foods were distinguished by a color coded square (gray or peach) on the front cover of each sealed package of food; and each was manufactured, analyzed for its nutrient content, and packaged with its appropriate color code prior to shipment to the clinical study centers. Food was dispensed at the end of the first patient appointment. A suggested daily quantity of food to maintain the cat's current body weight was calculated, and owners were advised to feed the assigned food exclusively to maintain body condition. Treatment foods were to start immediately without a gradual transition. To improve feeding compliance, sufficient study food was dispensed to feed all clinically healthy cats in the same household.

This was an eight-week study and the primary

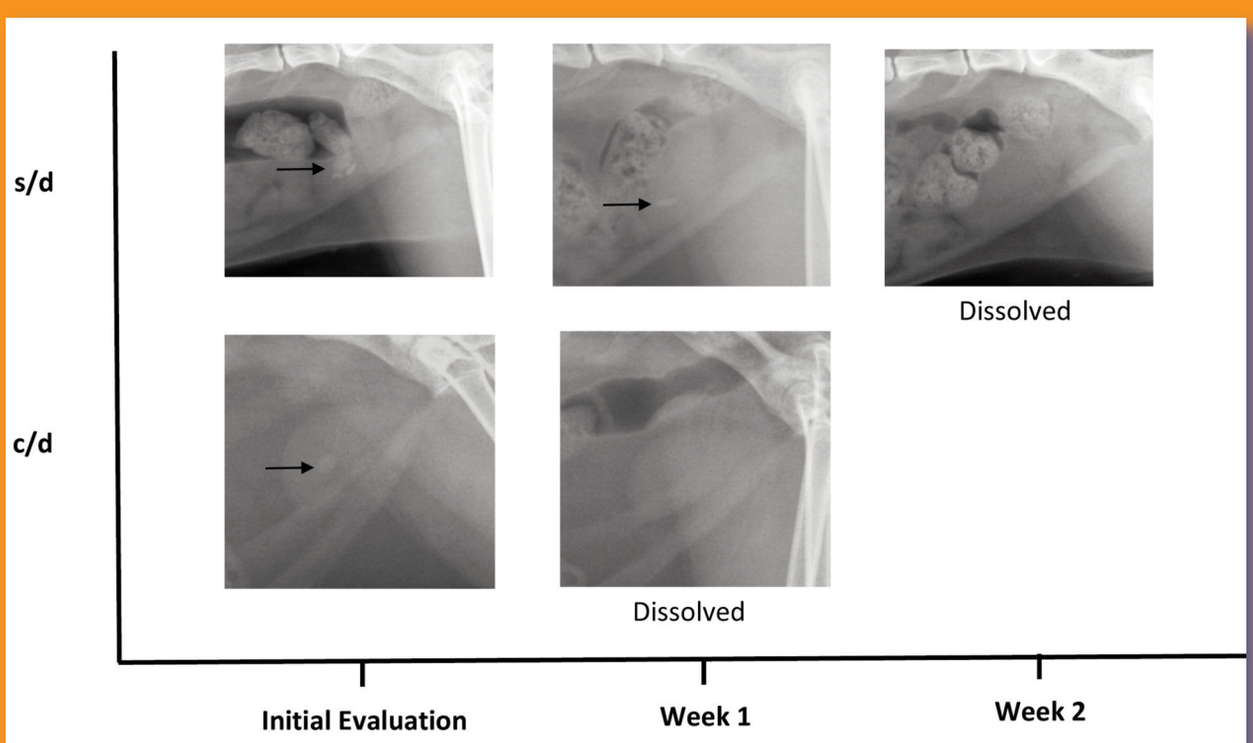


FIGURE 1 Right lateral radiographic images of the caudal aspect of the abdomens of a 5-year-old male domestic shorthair cat (top row) whose uroliths were managed with Hill's Prescription Diet s/d Feline dry (s/d) and a 5-year-old female domestic shorthair cat (lower row) whose uroliths were managed with Hill's Prescription Diet c/d Multicare Feline dry (c/d). Radiographs were obtained during initial examination and each subsequent week until uroliths were no longer radiographically visible

endpoint with respect to treatment (ie, food) efficacy was time to urolith dissolution. To determine dissolution time, cats were evaluated weekly with a physical examination, survey abdominal radiographs, and a complete urinalysis including urine pH determined by meter. Survey abdominal radiographs were digitally acquired. All radiographic images were assessed by board-certified radiologists without their knowledge as to the cat's group assignment. The time for urolith dissolution was the number of days from initial group assignment to the radiologist's assessment that uroliths were no longer radiographically visible. Cats, whose uroliths were unaffected by treatment were withdrawn from the study; their owners were offered urolith removal for no additional cost. Removed uroliths were quantitatively analyzed for their mineral composition. Cats with undissolved uroliths composed of struvite were categorized as treatment failures. Cats with undissolved uroliths not composed of struvite were categorized as diagnostic failures.

Results and discussion

Thirty-seven cats were included in the study; on the basis of laboratory tests, all cats were considered healthy, other than the presence of urocystoliths. In five cats, uroliths did not dissolve. These uroliths were surgically removed and quantitatively analyzed for their mineral composition; no undissolved uroliths were composed of struvite. In four cats persistent uroliths were composed of 100% ammonium urate and in one cat the urolith was 100% calcium oxalate. These five cats were excluded from further evaluation of the foods because they were classified as diagnostic failures.

In the remaining 32 cases; 16 (five male and 11 female) were fed the prevention-dissolution food (Hill's Prescription Diet c/d Multicare Feline) and 16 (two male and 14 female) were fed the dissolution food (Hill's Prescription Diet s/d Feline). Complete urolith dissolution was achieved in all of these 32 cats (Figure 1) with presumed struvite urocystoliths (Figure 2). Mean dissolution times between treatments were significantly different (P = 0.002); the prevention-dissolution food dissolved uroliths in 27.0 ± 2.6 (range = 7 to 52) days and the dissolution food dissolved uroliths in 13.0 ± 2.6 (range = 6 to 28) days. The time for urolith size to decrease by 50% was 1.75 ± 0.27 weeks for the prevention-dissolution food and 0.69 ± 0.1 weeks for the dissolution food. Owners indicated that cats strictly consumed the study food with 99 ± 6% (mode, 100%; range, 55% to 100%) assurance over the total 92 treatment weeks (ie, the cumulative number of surveys completed). At only two rechecks did owners indicate that cats may have eaten less than 95% of the study food. Both of these cats were in the dissolution food group (ie, Hill's Prescription Diet s/d), and uroliths dissolved in less than 14 days. Adverse events were not observed and urethral obstruction did not occur in any cat (there were seven males and 25 females enrolled in the study). Results of serum biochemistry and CBC remained within their normal ranges during treatment and did not change from pretreatment values.

Results of this study indicate that dietary dissolution is an effective, safe and rapid method of eradicating sterile struvite uroliths from the urinary bladders of cats. Only diagnostic failures (ie, uroliths composed of minerals other than struvite, including four urate and one calcium oxalate) were associated with incomplete urolith dissolution. Our results are in agreement with previous studies that also demonstrated successful urolith dissolution.[2–4] Guidelines are available to help predict urolith mineral composition based on results of diagnostic imaging and urinalysis fndings (Table 1).

This study has several unique strengths. It is the first multicenter, double-masked, randomized, controlled, clinical trial evaluating nutritional dissolution of sterile struvite uroliths. This is also the first study measuring urine pH with a pH meter. Sodium levels exceeding 1.1% of the food on a dry matter basis have been recommended to encourage water consumption producing less concentrated urine and reducing urinary saturation for struvite.[4] The foods evaluated in this study contained less than half that sodium recommendation and were as effective. In fact, in our study, the dissolution food had the shortest mean dissolution time compared with any other published studies using foods with higher sodium content.[3,4] This observation is consistent with reports in healthy cats in which diets with 0.4% to 1.2% sodium on a dry matter basis had no effect on relative supersaturation and activity product ratios for urine struvite, even though urine volume significantly increased with the high-sodium food.[9]

In conclusion, both therapeutic foods were 100% successful in dissolving sterile struvite

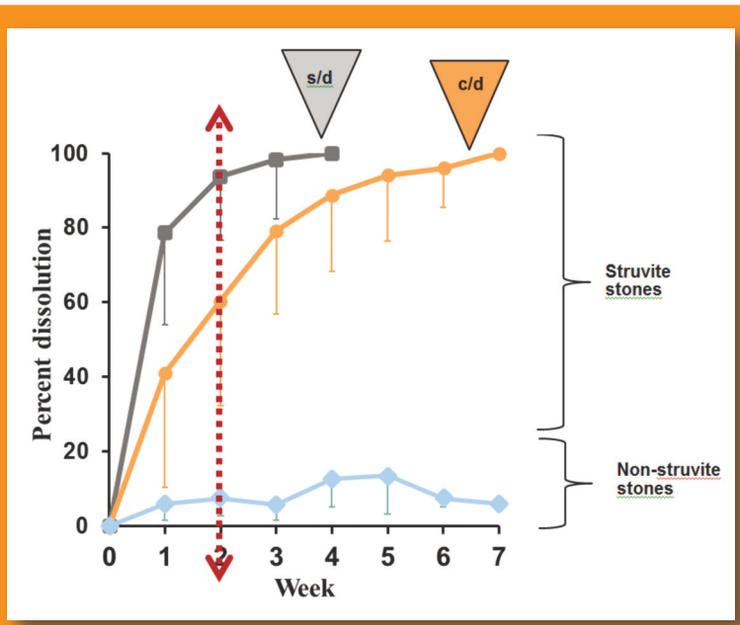
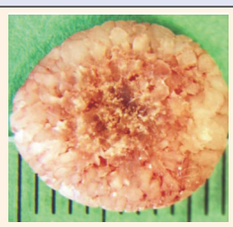
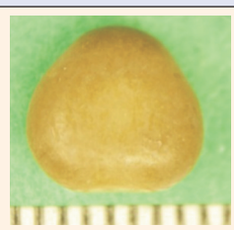
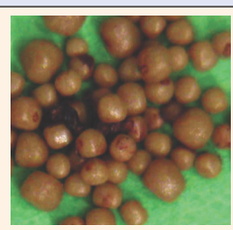
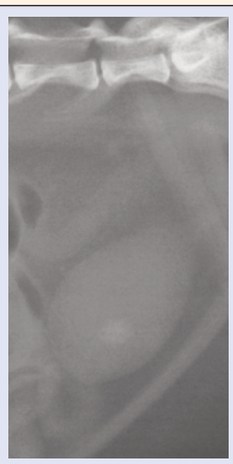
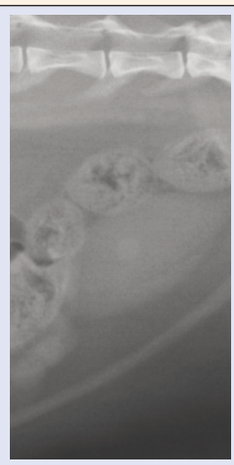
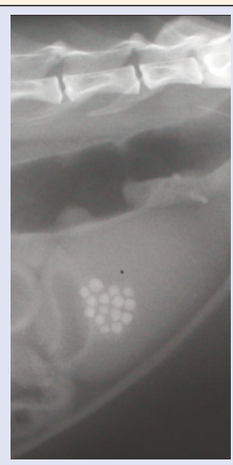
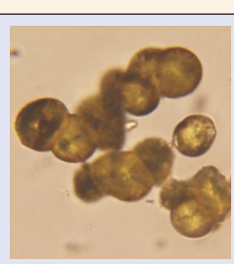
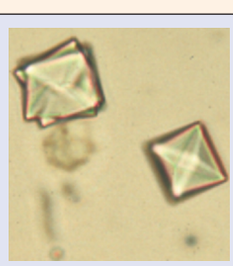


Figure 2 Percentage stone dissolution (mean and SD) by week for cats with struvite uroliths that were treated with either Hill's Prescription Diet s/d Feline (s/d) (n = 16 [squares] or Hill's Prescription Diet c/d Multicare Feline (c/d) (n = 16 [circles]) and five cats fed food either food that had uroliths not composed of struvite (100% ammonium urate (n = 4) or 100% calcium oxalate (n = 1). All cats (n = 32) whose stones were struvite dissolved. Of interest is the observation at two weeks (dashed line); the point at which struvite stones decreased by 35 to 100% irrespective of which treatment diet was feed. Stones that were not struvite had minimal change. Evidence of a marked reduction in stone size at this therapeutic midpoint can be used to support a diagnosis of struvite, and the decision to continue nutritional dissolution therapy

Table 1 Predicting mineral composition of feline uroliths based on radiographic findings and urinalysis

	Struvite	Urate	Calcium oxalate
Prevalence (%)	40 to 50	35 to 45	4 to 6
Physical appearance			
Radiographic appearance			
Radiographic density	Moderately radio-opaque	Usually radiolucent; however, larger uroliths are moderately radio-opaque	Usually very radio-opaque Monohydrate salts have smooth edges; dihydrate salts have irregular sharp edges
Radiographic contour	Smooth to slightly rough edges	Smooth to rough edges	Monohydrate salts have smooth edges; dihydrate salts have irregular sharp edges
Radiographic number	Usually < 3 to 5	Usually <3	Usually > 3 to 5
Microscopic crystalluria			
Description of microscopic crystalluria	Pyramidal to low square	Spherules or amorphous crystals that dissolve in alkaline urine	Double envelope (dipyramidal) of dihyddrate salt, rarely picket fence or dumbbell of monohydrate salt
Urine pH	> 6 to 6.5	< 6 to 6.5	< 6 to 6.5

uroliths in cats. Food selection should be based on individual needs of the patient, management conditions of the household, owners' ability to feed the patient in a multicat household, and the likelihood that owners will remain compliant with diet and follow-up recommendations. Use of a prevention-dissolution food (ie, Hill's Prescription Diet c/d Multicare Feline) eliminates the need to transition cats from a dissolution food to a different long-term maintenance food for prevention, and allows for the convenience of feeding all healthy adult cats in a household a single food. Use of a dissolution food (ie, Hill's Prescription Diet s/d Feline) may be advantageous in situations where a faster rate of dissolution is optimal for patient well-being or when a different food is indicated for

long-term dietary management of other health problems. In the later circumstance, uroliths can be rapidly dissolved with a dissolution food and then the cat transitioned to a food more suitable for treatment of its other health conditions (eg, obesity, inflammatory bowel disease, renal disease, etc). Irrespective of the food selected, we recommend repeating radiographic imaging in two weeks after initiating therapy. At this therapeutic midpoint, our results indicated that when feeding these foods (Hill's Prescription Diet c/d Multicare or s/d), uroliths composed of struvite should be approximately 50% (range = 35% to 100%) smaller (Figure 2). If urolith size has changed minimally, consider the possibility that the owner or patient is not compliant with dietary recommendations, or that uroliths are composed of minerals other than sterile struvite.

Cystotomy remains a common method of urolith removal, and while major complications are rare, minor ones are common.[10,11] Some of these adverse surgical associations can be avoided by selecting nutritional urolith dissolution as your primary method of therapy (Table 2).

Table 2 Benefits of nutritional dissolution compared to surgical urolith extraction

	Nutritional dissolution	Surgical extraction
Efficacy	100%	80%
Cost	Relatively inexpensive	Relatively expensive
Anesthetic risks	None	Potential
Resolution of clinical signs	6–28 days	3–19 days
Potential for suture nidus contributing to recurrence	None	Possible

Key points for applying the study's scientific results to clinical patients in practice

- Medical dissolution of uroliths is safe, effective, cost-effective, rapid and the compassionate choice. Surgical urolith removal may contribute to recurrence by increasing the chance of suture nidus of recurrent stones.
- Use of a prevention-dissolution food (Hill's Prescription Diet c/d Multicare Feline) eliminates the need to transition cats to a long-term prevention food and allows for the convenience of feeding all healthy cats in the same household the same food. In addition to managing struvite related diseases, Hill's Prescription Diet c/d Multicare is a maintenance food for cats.
- Use a dissolution food (Hill's Prescription Diet s/d Feline) when a faster rate of dissolution is optimal for patient well-being (eg, when other types of nutritional therapy are needed; for example, obesity, inflammatory bowel disease, etc). No other food on the market has been shown to dissolve stones faster than Hill's Prescription Diet s/d.
- Urethral obstruction, although possible, was not observed in this or previous studies, and is therefore an unlikely complication of dietary dissolution. Dysuria is a common sign of urethral obstruction in patients with stones. As stones become smaller dysuria is expected to be less, if not existent.
- A gradual transition to therapeutic foods was not needed to ensure patient acceptance. Cats in our study readily accepted an abrupt food change.
- Dry therapeutic foods, which are more commonly preferred by owners and cats, were 100% effective.
- Therapeutic prevention-dissolution foods should be safe and effective for managing other struvite-related disease; for example, minimizing urethral re-obstruction following urethral plug removal, or eliminating struvite crystals in cats with crystal-associated dysuria and inappropriate urination of unknown cause (eg, feline idiopathic cystitis).

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