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Comparison of body condition score and urinalysis variables between dogs with and without calcium oxalate uroliths

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Abstract

OBJECTIVE—To compare body condition score (BCS) and urinalysis variables between dogs with and without calcium oxalate (CaOx) uroliths.

DESIGN—Case-control study.

ANIMALS—46 Miniature Schnauzers, 16 Bichons Frises, and 6 Shih Tzus.

PROCEDURES—Medical records were reviewed for Miniature Schnauzers, Bichons Frises, and Shih Tzus that were examined between January 2001 and November 2014 for another urolithiasis study or for a urolith removal procedure. Dogs with CaOx uroliths were classified as cases. Dogs without a history of urinary tract disease and with no evidence of radiopaque uroliths on abdominal radiographs were classified as controls. Each case was matched with 1 control on the basis of age ($\pm$ 2 years), sex, and breed. Body condition score and urinalysis results were compared between cases and controls, and the relationship between BCS and urine pH was analyzed.

RESULTS—Median BCS was significantly greater for cases than controls, although the proportion of overweight dogs did not differ significantly between the 2 groups. Urine pH was negatively associated with age, but was not associated with BCS or the presence of CaOx uroliths. Cases infrequently had acidic urine or CaOx crystalluria but frequently had hematuria and proteinuria.

CONCLUSIONS AND CLINICAL RELEVANCE—Results indicated that dogs with CaOx uroliths had a greater median BCS than control dogs, but the clinical importance of that finding was unclear. Acidic urine and CaOx crystalluria were uncommon and not adequate predictors of CaOx urolith status. Hematuria and proteinuria were commonly observed in dogs with CaOx urolithiasis, but they are not pathognomonic for that condition.

The prevalence of CaOx uroliths has been increasing in both companion animal and human medicine over the last few decades. For example, review of the Minnesota Urolith Center's

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^bRoyal Canin Veterinary Diet Urinary SO Canine, Royal Canine USA Inc, St Charles, Mo.

^cHill's Prescription Diet s/d Canine, Hill's Pet Nutrition Inc, Topeka, Kan.

database revealed that 45% of canine uroliths submitted in 2009 and 2010 were composed of CaOx, whereas only 5% of canine uroliths submitted in 1981 were composed of CaOx.¹ Similarly, most uroliths evaluated from human patients are composed of CaOx, and the global prevalence of CaOx uroliths is increasing.² Obesity is also becoming an epidemic in canine³ and human populations,⁴ and the human medical literature^{5–8} suggests a positive correlation between BMI and the risk of CaOx urolith formation.

Published literature regarding the association between body condition and risk of CaOx urolithiasis in dogs is limited and inconsistent. Results of 1 study⁹ indicate that overweight dogs are twice as likely to develop CaOx uroliths as are dogs with an ideal BCS; however, results of another study¹⁰ do not indicate an association between BCS and CaOx urolithiasis. The dogs with CaOx uroliths in those 2 studies^{9,10} were not matched with the dogs without CaOx uroliths on the basis of age, sex, or breed, and those factors could have confounded the results. Another limitation of those studies^{9,10} was that control dogs were classified as such on the basis of history alone instead of with radiographic screening to verify that they did not have uroliths. Calcium oxalate uroliths are a common incidental finding in dogs of breeds predisposed to those types of uroliths.¹¹ Therefore, it is likely that some of the control dogs in those previous studies^{9,10} had latent CaOx uroliths.

It is believed that obesity contributes to urolithiasis by causing urine acidification. There is an inverse relationship between BMI and urine pH in human patients with urolithiasis.^{7,8} To our knowledge, the relationship between body condition and urine pH has not been evaluated in dogs. Furthermore, although acidic urine is a risk factor for the development of CaOx uroliths in humans, only limited data are available regarding the association between urine pH and CaOx uroliths in dogs. Results of 1 study¹⁰ indicate that the proportion of dogs with acidic urine is greater for dogs with CaOx uroliths than for control dogs without CaOx uroliths; however, the interpretation of this finding is limited by the aforementioned lack of matching between cases and controls on the basis of age, sex, and breed and lack of radiographic screening of control dogs for uroliths.

The primary purpose of the study reported here was to compare BCS and urinalysis variables between dogs with CaOx uroliths and age-, sex-, and breed-matched control dogs that were radiographically confirmed to not have uroliths. Our hypothesis was that dogs with CaOx uroliths were more likely to be overweight and have acidic urine than dogs without CaOx uroliths. An additional aim of the study was to determine the relationship between BCS and urine pH. We hypothesized that there would be an inverse relationship between BCS and urine pH.

Materials and Methods

Animals

The study took place at the University of Minnesota Veterinary Medical Center. Medical records were obtained for Miniature Schnauzers, Bichons Frises, and Shih Tzus that were recruited between January 2009 and November 2014 for a study¹¹ of CaOx urolithiasis. The electronic medical record database was also searched to identify dogs examined between January 2001 and November 2014 that had a charge code for cystotomy, lithotripsy, basket

retrieval, or voiding urohydropulsion. Dogs were classified as cases if they had uroliths composed primarily of CaOx (ie, uroliths with central cores composed of 70% CaOx) as determined by standard polarizing light microscopy and infrared spectroscopy methods¹² performed at the Minnesota Urolith Center. Dogs were classified as controls if they had no history of uroliths or lower urinary tract disease and had no evidence of radiopaque uroliths on survey abdominal radiographs.

Dogs were included in the study if the medical record contained a BCS and results of a urinalysis performed by the Clinical Pathology Laboratory at the University of Minnesota Veterinary Medical Center 30 days prior to diagnosis of CaOx urolithiasis (cases) or radiographic screening of the abdomen (controls). For dogs with multiple episodes of CaOx urolithiasis, the earliest episode with urinalysis results available for review was used in the analysis. Information extracted from the medical record included age, sex, breed, diet, clinical signs, BCS, concurrent diseases, medications administered, and results of urinalysis and bacterial culture of urine samples (when available). Body condition was graded on a 9-point scale where 1 = very thin and 9 = morbidly obese and was rounded to the nearest integer when necessary. For the present study a BCS 3 was considered underweight, 4 or 5 was considered ideal, and 6 was considered overweight. Dogs were excluded from the study if they had a concurrent disease (eg, diabetes mellitus, kidney disease, hyperadrenocorticism, neoplasia, or other systemic disease) or were receiving therapeutic diets (eg, diets formulated to prevent formation of uroliths^{a,d} or manage kidney disease^{e,f}) or medications (eg, diuretics, potassium citrate, corticosteroids, phenobarbital, or thyroxine) that might affect urinalysis results. The study had a case-control design, and each case was matched with 1 control on the basis of age (± 2 years), sex, and breed.

Sample size calculation

A priori sample size calculations were performed to determine the number of dogs necessary in each group to detect a minimum difference of 1 BCS between cases and controls and a difference of 1.0 in urine pH between cases and controls and between dogs with an ideal BCS (BCS, 4 or 5) and overweight dogs (BCS, 6). For all calculations, the estimated SD was 1.0, power was set at 0.8, and α (confidence level or type I error rate) was set at 0.05. All calculations were performed with a freeware program^g as described,¹³ and the resulting sample size was 34 dogs (ie, 17 cases and 17 controls, or 17 dogs with an ideal BCS and 17 overweight dogs).

Urinalysis

All urinalysis results evaluated in the study were for urine samples collected while the dogs were at the University of Minnesota Veterinary Medical Center and analyzed by standard methods at the on-site clinical pathology laboratory. Briefly, the urine samples were stored at

^aHill's Prescription Diet u/d Canine, Hill's Pet Nutrition Inc, Topeka, Kan.

^dHill's Prescription Diet c/d Canine, Hill's Pet Nutrition Inc, Topeka, Kan.

^eHill's Prescription Diet k/d Canine, Hill's Pet Nutrition Inc, Topeka, Kan.

^fPurina Veterinary Diets NF Canine, Nestlé Purina Petcare, St Louis, Mo.

^gPS: Power and Sample Size Calculation Program, version 3.1.2, William D. Dupont and Walton D. Plummer Jr, Department of Biostatistics, Vanderbilt University, Nashville, Tenn. Available at: biostat.mc.vanderbilt.edu/wiki/Main/PowerSampleSize. Accessed Oct 10, 2016.

room temperature (approx 22°C) until analysis, which was generally performed within 6 hours after sample collection. Refractometry was used to determine the USG. Commercially available dipsticks and manual interpretation were used to determine urine pH and semiquantitative protein concentration. Cytologic analysis of urine sediment was used to determine WBC and RBC counts and the presence of bacteriuria, casts, epithelial cells, and crystalluria.

Statistical analysis

The data distribution for all continuous variables was assessed for normality with Q-Q plots. Results were reported as the mean $\pm$ SD for continuous variables that were normally distributed. Results for BCS were summarized as the median (range), and a Wilcoxon rank sum test was used to compare BCS between cases and controls. A χ^2 test was used to determine whether the proportion of overweight (BCS ≥ 6) dogs differed between cases and controls. A Student *t* test was used to compare urine pH between cases and controls and between dogs with an ideal BCS (BCS, 4 or 5) and overweight dogs. A Fisher exact test was used to determine whether the proportion of dogs with CaOx crystalluria differed between cases and controls.

Multivariable linear regression was used to identify factors associated with urine pH. Fixed effects included in that model were urolith status (case or control), sex (male or female), age, breed (Miniature Schnauzer, Bichon Frise, or Shih Tzu), BCS, and whether food had been withheld from the dog for ≥ 12 hours prior to collection of the urine sample (yes or no). Multivariable logistic regression was used to identify factors associated with the classifying of a dog as a case (ie, presence of CaOx uroliths). Fixed effects included in that model were USG, urine pH, leukocyturia (present or absent), hematuria (present or absent), urine protein concentration (recorded on a scale of 0 to 4 with trace protein assigned a value of 0.5), and CaOx crystalluria (present or absent). For both regression models, an ANCOVA was used to assess the significance of the respective associations between the fixed effects and the outcome variable. Additionally, both regression models were assessed with and without all possible 2-way interaction terms, and an ANOVA was used to determine whether the model that included the interaction terms differed significantly from the corresponding model without the interaction terms. No significant interactions were identified for either model, and inclusion of the interaction terms did not significantly alter the results of either model. Therefore, the model that did not include the interaction terms was reported as the final multivariable model for each outcome. All analyses were performed with a statistical software program,^h and values of $P < 0.05$ were considered significant.

Results

Dogs

Ninety-seven dogs (43 cases and 54 controls) met the inclusion criteria for the study, of which 29 (8 cases and 21 controls) were excluded because an appropriately matched case or control could not be identified. The most common reason dogs were excluded was that an

^hR, version 3.2.2, R Foundation for Statistical Computing, Vienna, Austria. Available at: www.r-project.org. Accessed Sep 3, 2015.

appropriate match could not be made on the basis of sex (ie, the case group contained more males than the control group), and 7 males in the case group and 21 females in the control group were excluded for that reason. One female dog in the case group could not be matched to a control on the basis of age and was also excluded from the study.

The final study population consisted of 68 dogs (34 age-, sex-, and breed-matched case-control pairs). The case and control groups each contained 4 females and 30 males and 23 Miniature Schnauzers, 8 Bichons Frises, and 3 Shih Tzus. As expected, the mean $\pm$ SD age of the cases (9.4 ± 2.2 years) did not differ significantly ($P = 0.24$) from that of the controls (9.8 ± 2.0 years). Dogs were fed various commercial diets, and the information available regarding nutritional history was too limited for analysis. Of the 34 cases, 25 (73.5%), 8 (23.5%), and 1 (3%) were evaluated during their first, second, or third documented episode of urolithiasis, respectively. The proportion of dogs from which food was withheld before urine sample collection was significantly ($P = 0.003$) greater for the control group (30/34 [88%]) than for the case group (18/34 [53%]).

BCS and urinalysis variables

Thirty-three of the 68 (49%) study dogs were overweight (BCS, ≥ 6). The median BCS for the cases (6; range, 4 to 7) was significantly ($P = 0.035$) greater than the median BCS for the controls (5; range, 4 to 7). However, the proportion of cases that were overweight (20/34 [59%]) did not differ significantly ($P = 0.15$) from the proportion of controls that were overweight (13/34 [38%]).

The mean $\pm$ SD urine pH did not differ significantly between cases (7.0 ± 0.7) and controls (6.9 ± 0.8 ; $P = 0.65$) or between dogs with an ideal BCS (BCS, 4 or 5; 7.0 ± 0.8) and overweight dogs (6.8 ± 0.8 ; $P = 0.43$). Twenty-one of 34 (62%) cases and 14 of 34 (41%) controls had a neutral urine pH (6.5 to 7.5), and the proportion of dogs with acidic urine (pH, < 6.5) did not differ significantly ($P = 0.17$) between cases (6/34 [18%]) and controls (12/34 [35%]). Results of the multivariable linear regression model for urine pH were summarized (Table 1). Age was the only factor assessed that was significantly ($P = 0.017$) associated with urine pH; when all other factors were held constant, urine pH decreased by 0.13 for every 1-year increase in age.

Results of the multivariable logistic regression model for the probability of CaOx uroliths were also summarized (Table 2). Hematuria (OR, 11; 95% CI, 2.4 to 80; $P = 0.001$) and proteinuria (OR, 1.9; 95% CI, 1.1 to 3.3; $P = 0.021$) were positively associated with the presence of CaOx uroliths, whereas USG (OR, 0.6; 95% CI, 0.3 to 0.9; $P = 0.024$) was negatively associated with the presence CaOx uroliths.

The proportion of cases with CaOx crystalluria (3/34 [9%]) did not differ significantly ($P = 0.24$) from the proportion of controls with CaOx crystalluria (0/34 [0%]). Other types of crystals were observed in the urine of both cases and controls and included struvite crystals in the urine of 3 controls and amorphous phosphate crystals in the urine of 5 cases and 1 control.

Bacteria were observed in the urine of 2 cases and 2 controls. None of those 4 dogs had pyuria, and only 1 had hematuria. A bacterial culture was performed on a urine sample for only 1 of the 4 dogs with bacteriuria, and that culture yielded light growth of a *Pseudomonas* sp. Bacterial cultures were performed on urine samples from 8 additional cases that did not have bacteriuria, and no bacterial growth was observed on any of those cultures. Urine was collected by free catch for 7 of 34 (21%) cases and 21 of 34 (62%) controls and by cystocentesis or catheterization of the urinary bladder for the remaining 27 cases and 13 controls. The proportion of dogs for which the urine sample was collected by free catch was significantly ($P = 0.001$) lower for the case group than for the control group. However, the presence of hematuria ($P = 0.10$) or proteinuria ($P = 0.55$) did not differ significantly between urine samples collected by free catch and those collected by cystocentesis or catheterization of the urinary bladder.

Discussion

Results of the present study indicated that dogs with CaOx uroliths (cases) had a significantly greater median BCS than age-, sex-, and breed-matched controls that did not have uroliths on survey abdominal radiographs. In the human medical literature, results of multiple studies⁵⁻⁸ indicate a positive association between obesity and the risk of nephrolithiasis. In a large prospective study⁵ of 3 cohorts of human patients, obesity and weight gain were associated with a significant increase in the relative risk for nephroliths in each of the cohorts. Although nephrolith composition was not assessed in that study,⁵ results of a subsequent study⁶ suggest that human patients who are obese are at greater risk for the formation of CaOx and uric acid uroliths than are patients with an ideal body weight. Investigation of the association between obesity and CaOx urolithiasis in veterinary patients has yielded conflicting results. Review of patient data for 1,074 canine CaOx uroliths evaluated by the Minnesota Urolith Center revealed that overweight (as reported by the owner) dogs were 2.2 times as likely to have CaOx uroliths, compared with dogs with an ideal body weight.⁹ In another study¹⁰ of 452 dogs with CaOx uroliths that were evaluated at general care veterinary hospitals in the United States, the proportion of patients did not vary significantly among 3 body condition categories (thin, normal, or heavy as determined by the primary care veterinarian). However, the control dogs in those 2 studies,^{9,10} unlike the control dogs of the present study, were not matched with the case dogs (ie, dogs with CaOx uroliths) on the basis of age, sex, or breed, which might have biased the results. In the present study, although the median BCS for the cases was significantly greater than that for the controls, the proportion of dogs that were overweight (BCS 6) did not differ significantly between the case and control groups. It is important to note that none of the dogs of the present study were obese (BCS 8). The risk of CaOx urolith formation for obese dogs may differ from that for dogs that are only mildly overconditioned and needs to be researched further.

The biological link between body condition and CaOx urolithiasis is not fully understood in either human or veterinary medicine. Although proof that excess body condition causes CaOx urolithiasis is lacking, evidence suggests that obesity promotes acidic urine, which creates a favorable environment for the formation of CaOx uroliths. In human medicine, there is a strong inverse correlation between urine pH and body weight or BMI in patients

with nephrolithiasis,^{7,8} and acidic urine is a feature of metabolic syndrome. Urine pH is inversely related with insulin resistance, and insulin resistance is the proposed cause of acidic urine in obese human patients.¹⁴ The results of the present study failed to identify a significant relationship between BCS and urine pH. However, no obese dogs were enrolled in the study, and insulin resistance is likely to be most severe in dogs with a BCS of 8 or 9.¹⁵ Evaluation of dogs with a wider range of BCSs than that for the present study population might reveal a significant association between BCS and urine pH. Alternatively, obesity may not have the same effect on urine pH in dogs as it does in human patients. The apparent positive association between BCS and CaOx uroliths for the dogs of the present study might be related to other systemic effects of increasing adiposity. It is also possible that increasing body condition, or obesity, does not cause CaOx uroliths, and both conditions could be a consequence of a third factor such as an increase in caloric intake, differences in dietary composition or feeding habits, lower activity level, or genetic differences in metabolism. Further studies are necessary to investigate those factors.

In the present study, urine pH was not associated with the presence of CaOx uroliths. This was an unexpected finding. In fact, of the 34 cases, 21 (62%) and 7 (21%) had a neutral (pH, 6.5 to 7.5) or alkaline (pH, > 7.5) urine pH, respectively, and only 6 (18%) had acidic urine (pH, < 6.5). In humans, acidic urine is a risk factor for CaOx crystalluria, and the risk for the development of CaOx crystalluria is greatest when the urine pH is 4.5 to 5.5.¹⁶ In dogs, the physiologically normal urine pH range is 5.0 to 8.0,¹⁷ and the risk of CaOx urolith formation may be less profound within that pH range, compared with the risk at lower pH values. An abnormally increased acid load has multiple consequences that can affect the risk of urolith formation. For example, metabolic acidosis decreases excretion of citrate, an important inhibitor of CaOx crystal formation.¹⁸ Acidosis also promotes mobilization of buffers such as phosphate and carbonate from bone, which is accompanied by a concurrent release of calcium from bone, resulting in hypercalciuria.¹⁹ Additionally, metabolic acidosis decreases calcium resorption in both the proximal and distal renal tubules, which further exacerbates hypercalciuria.¹⁹ Although results of a few studies^{10,20,21} suggest a positive association between acidic urine and the risk of CaOx formation in dogs, each of those studies had design limitations. In 1 study,²⁰ dogs fed dry diets designed to acidify urine were almost 3 times as likely to develop CaOx uroliths as were dogs fed dry diets designed to maintain a neutral or alkaline urine pH. However, the conclusions of that study²⁰ were based on theoretical predictions of nutrient effects on acid load; urine pH was not actually measured. In a parallel study,²¹ the risk of CaOx urolith formation did not differ significantly between dogs fed canned diets designed to acidify urine and dogs fed canned diets designed to maintain a neutral or alkaline urine pH. Neither of those 2 studies^{20,21} used age-, sex-, or breed-matched controls. In another study,¹⁰ results of a multivariable regression model that included age, sex, and breed size suggested that dogs with CaOx uroliths were more likely to have a urine pH < 7.0 than a urine pH > 7.5, compared with dogs without urolithiasis. A limitation of that study¹⁰ was that urine pH could be affected by breed-specific effects that were not adequately controlled by the inclusion of breed size in the model.

Breed affects the urine pH of dogs.^{11,22} Results of 1 study²² indicate that Miniature Schnauzers have a higher urine pH than Labrador Retrievers. In the present study, the majority (46/68 [68%]) of dogs were Miniature Schnauzers, and acidic urine was not

associated with CaOx uroliths in that breed or the other 2 breeds studied, Bichon Frise and Shih Tzu. A subset of the dogs evaluated in the present study was part of another study¹¹ in which idiopathic hypercalciuria was positively associated with CaOx urolithiasis; thus, hypercalciuria may be a greater contributor to the formation of CaOx uroliths than acidic urine in those 3 breeds.

Further research is necessary to elucidate the effect of urine pH on the risk of CaOx urolithiasis in dogs. Results of a study²² involving healthy Labrador Retrievers and Miniature Schnauzers indicate that urine pH can vary throughout the day and is often lowest early in the morning prior to feeding. Evaluation of urine pH over a 24-hour period or at specific times throughout the day might reveal a relationship with CaOx urolithiasis that was not apparent from random spot measurements. The time of day at which urine samples were collected for urinalysis was not evaluated in the present study.

Although urine pH was not significantly associated with the presence of CaOx uroliths in the present study, there was a significant inverse correlation between urine pH and age. A similar inverse correlation between urine pH and age has been identified in humans, including those with urolithiasis.^{23,24} Other urinary lithogenic factors may also change with age. For example, in humans, urinary citrate excretion increases with age, whereas 24-hour urine calcium excretion and supersaturation of urine with CaOx decrease with age.²⁴

Another unexpected finding of the present study was the negative association between USG and the presence of CaOx uroliths. The urine samples evaluated for 9 of 34 (26%) cases were collected during a recurrent bout of CaOx urolithiasis. Although dogs fed diets designed to prevent uroliths were excluded from the study, the owners of some cases might have been instructed to add water to the existing diet or feed a nonprescription canned diet to increase the dog's water intake after the first episode of urolithiasis, which could have affected the USG of urine samples collected during subsequent episodes.

In the present study, hematuria and proteinuria were significantly associated with the presence of CaOx uroliths, which was consistent with the findings of another study.¹⁰ Unfortunately, hematuria and proteinuria are nonspecific abnormalities that cannot be used to differentiate between various lower urinary tract diseases and, in fact, were significantly associated with the presence of struvite uroliths in dogs of another study.²⁵ Nevertheless, dogs with hematuria and proteinuria, particularly in the absence of pyuria and bacteriuria, should be evaluated for the presence of CaOx uroliths.

Calcium oxalate crystalluria was rare in the cases of the present study and thus appeared to be an unreliable indicator of CaOx uroliths. To our knowledge, this study was the first to describe the prevalence of CaOx crystalluria in dogs with CaOx uroliths. In a retrospective study²⁶ of cats with lower urinary tract disease, crystalluria was present in 4 of 13 (31%) cats with urolithiasis, 34 of 59 (58%) cats with idiopathic cystitis, and 6 of 14 (43%) cats with bacterial cystitis. The types of crystals and uroliths identified in the cats of that study²⁶ were not reported, which hinders interpretation of those results. The low proportion of dogs with CaOx crystalluria in the present study could have been a reflection of sample handling. In another study,²⁷ urine samples obtained from 31 dogs and 8 cats were subdivided into

equal aliquots and stored for various times at various temperatures to determine the effect of storage time and temperature on in vitro crystal formation. When urine aliquots were stored at room temperature (20°C) for 6 hours, only 1 of 39 (3%) aliquots formed CaOx crystals. In contrast, 9 of 39 (23%) aliquots formed CaOx crystals when stored at refrigeration temperature (6°C) for 24 hours.²⁷ All the urine samples evaluated in the present study were collected in the hospital, stored at room temperature, and processed by the same laboratory, generally within 6 hours after collection; therefore, in vitro crystal formation associated with urine sample processing should have been minimal.

The present study had limitations. Only 3 breeds (Miniature Schnauzer, Bichon Frise, and Shih Tzu) of dogs that are reportedly predisposed to CaOx urolithiasis²⁸ were evaluated; therefore, the results of this study might not be applicable to other breeds of dogs. Additionally, the proportion of dogs from which food was withheld prior to urine sample collection was significantly greater for the control group, compared with that of the case group. Urine pH peaks approximately 2 to 5 hours after consumption of a meal.²² However, results of the multivariable linear regression analysis indicated that urine pH was not associated with whether food was withheld from a dog prior to urine sample collection, and it is unlikely that withholding food from dogs prior to urine sample collection significantly confounded our results. Urine pH was semiquantitatively measured by use of a urine dipstick. Although urine dipsticks are commonly used to measure urine pH in clinical practice, use of a pH meter would have provided more accurate urine pH measurements.¹⁷ Finally the period during which the cases were recruited (2001 to 2014) was substantially longer than that during which controls were recruited (2009 to 2014). Even though all urine samples were evaluated by the same laboratory the standard urinalysis methods used by that laboratory might have evolved over the study period, which could have confounded our results.

In the present study, the median BCS for dogs with CaOx uroliths was significantly greater than that for age-, sex-, and breed-matched control dogs that did not have uroliths on survey radiographs. The clinical importance of that finding is unclear, and the association between BCS and CaOx uroliths was independent of urine pH. Other effects of obesity or factors that predispose dogs to both obesity and the formation of uroliths should be considered. Acidic urine and CaOx crystalluria were uncommon findings in dogs with CaOx uroliths and should not be used as predictors for the presence of CaOx uroliths. Hematuria and proteinuria were significantly associated with the presence of CaOx uroliths but are commonly observed in dogs with urinary tract disease and are not pathognomonic for CaOx urolithiasis.

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ABBREVIATIONS

BCS	Body condition score
BMI	Body mass index
CaOx	Calcium oxalate
CI	Confidence interval
USG	Urine specific gravity

References

1. Osborne CA, Lulich JP, Kruger JM, et al. Analysis of 451,891 canine uroliths, feline uroliths, and feline urethral plugs from 1981 to 2007: perspectives from the Minnesota Urolith Center. *Vet Clin North Am Small Anim Pract.* 2009; 39:183–197. [PubMed: 19038658]
2. Romero V, Akpinar H, Assimos DG. Kidney stones: a global picture of prevalence, incidence, and associated risk factors. *Rev Urol.* 2010; 12:e86–e96. [PubMed: 20811557]
3. Lund EM, Armstrong PJ, Kirk CA, et al. Prevalence and risk factors for obesity in adult dogs from private US veterinary practices. *Intern J Appl Res Vet Med.* 2006; 4:177–186.
4. Ogden CL, Carroll MD, Curtin LR, et al. Prevalence of overweight and obesity in the United States, 1999–2004. *JAMA.* 2006; 295:1549–1555. [PubMed: 16595758]
5. Taylor EN, Stampfer MJ, Curhan GC. Obesity, weight gain, and the risk of kidney stones. *JAMA.* 2005; 293:455–462. [PubMed: 15671430]
6. Chou YH, Su CM, Li CC, et al. Difference in urinary stone components between obese and non-obese patients. *Urol Res.* 2011; 39:283–287. [PubMed: 21161648]
7. Najeeb Q, Masood I, Bhaskar N, et al. Effect of BMI and urinary pH on urolithiasis and its composition. *Saudi J Kidney Dis Transpl.* 2013; 24:60–66. [PubMed: 23354193]
8. Maalouf NM, Sakhaee K, Parks JH, et al. Association of urinary pH with body weight in nephrolithiasis. *Kidney Int.* 2004; 65:1422–1425. [PubMed: 15086484]
9. Lekcharoensuk C, Lulich JP, Osborne CA, et al. Patient and environmental factors associated with calcium oxalate urolithiasis in dogs. *J Am Vet Med Assoc.* 2000; 217:515–519. [PubMed: 10953715]
10. Okafor CC, Lefebvre SL, Pearl DL, et al. Risk factors associated with calcium oxalate urolithiasis in dogs evaluated at general care veterinary hospitals in the United States. *Prev Vet Med.* 2014; 115:217–228. [PubMed: 24834804]
11. Furrow E, Patterson EE, Armstrong PJ, et al. Fasting urinary calcium-to-creatinine and oxalate-to-creatinine ratios in dogs with calcium oxalate urolithiasis and breed-matched controls. *J Vet Intern Med.* 2015; 29:113–119. [PubMed: 25581880]
12. Ulrich LK, Bird KA, Koehler LA, et al. Urolith analysis. Submission, methods, and interpretation. *Vet Clin North Am Small Anim Pract.* 1996; 26:393–400. [PubMed: 8711873]
13. Dupont WD, Plummer WD Jr. Power and sample size calculations. A review and computer program. *Control Clin Trials.* 1990; 11:116–128. [PubMed: 2161310]
14. Maalouf NM, Cameron MA, Moe OW, et al. Low urine pH: a novel feature of the metabolic syndrome. *Clin J Am Soc Nephrol.* 2007; 2:883–888. [PubMed: 17702734]
15. Verkest KR, Rand JS, Fleeman LM, et al. Spontaneously obese dogs exhibit greater postprandial glucose, triglyceride, and insulin concentrations than lean dogs. *Domest Anim Endocrinol.* 2012; 42:103–112. [PubMed: 22130330]
16. Berg C, Tiselius HG. The effect of pH on the risk of calcium oxalate crystallization in urine. *Eur Urol.* 1986; 12:59–61. [PubMed: 3948899]
17. Johnson KY, Lulich JP, Osborne CA. Evaluation of the reproducibility and accuracy of pH-determining devices used to measure urine pH in dogs. *J Am Vet Med Assoc.* 2007; 230:364–369. [PubMed: 17269867]

18. Wagner CA, Mohebbi N. Urinary pH and stone formation. *J Nephrol.* 2010; 23(suppl 16):S165–S169. [PubMed: 21170875]
19. Moe OW, Huang CL. Hypercalciuria from acid load: renal mechanisms. *J Nephrol.* 2006; 19(suppl 9):S53–S61. [PubMed: 16736442]
20. Lekcharoensuk C, Osborne CA, Lulich JP, et al. Associations between dry dietary factors and canine calcium oxalate uroliths. *Am J Vet Res.* 2002; 63:330–337. [PubMed: 11911566]
21. Lekcharoensuk C, Osborne CA, Lulich JP, et al. Associations between dietary factors in canned food and formation of calcium oxalate uroliths in dogs. *Am J Vet Res.* 2002; 63:163–169. [PubMed: 11843112]
22. Stevenson AE, Markwell PJ. Comparison of urine composition of healthy Labrador Retrievers and Miniature Schnauzers. *Am J Vet Res.* 2001; 62:1782–1786. [PubMed: 11703024]
23. Goldfarb DS, Parks JH, Coe FL. Renal stone disease in older adults. *Clin Geriatr Med.* 1998; 14:367–381. [PubMed: 9536110]
24. Friedlander JI, Moreira DM, Hartman C, et al. Age-related changes in 24-hour urine composition must be considered in the medial management of nephrolithiasis. *J Endourol.* 2014; 28:871–876. [PubMed: 24571654]
25. Okafor CC, Pearl DL, Lefebvre SL, et al. Risk factors associated with struvite urolithiasis in dogs evaluated at general care veterinary hospitals in the United States. *J Am Vet Med Assoc.* 2013; 243:1737–1745. [PubMed: 24299545]
26. Lund HS, Krontveit R, Halvorsen I, et al. Evaluation of urinalyses from untreated adult cats with lower urinary tract disease and healthy control cats: predictive abilities and clinical relevance. *J Feline Med Surg.* 2013; 15:1086–1097. [PubMed: 23783431]
27. Albasan H, Lulich JP, Osborne CA, et al. Effects of storage time and temperature on pH, specific gravity, and crystal formation in urine samples from dogs and cats. *J Am Vet Med Assoc.* 2003; 222:176–179. [PubMed: 12555980]
28. Low WW, Uhl JM, Kass PH, et al. Evaluation of trends in urolith composition and characteristics of dogs with urolithiasis: 25,499 cases (1985–2006). *J Am Vet Med Assoc.* 2010; 236:193–200. [PubMed: 20074011]

Table 1

Results of a multivariable linear regression model to identify factors associated with urine pH in a population of Miniature Schnauzers, Bichons Frises, and Shih Tzus with (cases; n = 34) and without (controls; 34) CaOx uroliths.

Variable	Regression coefficient	SE	P value
CaOx uroliths present	0.10	0.21	0.63
Sex (referent = male)	0.27	0.31	0.40
Age (per 1-y increase)	-0.13	0.05	0.017
Breed (overall)	—	—	0.84
Miniature Schnauzer	-0.14	0.24	0.57
Shih Tzu	-0.14	0.38	0.71
Bichon Frise	Referent	—	—
BCS (per 1-point increase)	-0.17	0.12	0.17
Food withheld before urine sample collection	-0.02	0.23	0.94

All dogs were examined at the University of Minnesota Veterinary Medical Center. Cases consisted of dogs with CaOx uroliths (70% of the central core). Controls consisted of dogs that did not have a history of lower urinary tract disease and did not have evidence of radiopaque uroliths on abdominal radiographs. Each case was matched with 1 control on the basis of age (± 2 years), sex, and breed. Body condition was graded on a 9-point scale where 1 = very thin and 9 = morbidly obese and rounded to the nearest integer when necessary. Values of $P < 0.05$ were considered significant.

— = Not calculated.

Table 2

Results of a multivariable logistic regression model to identify factors associated with the presence of CaOx uroliths in the dogs of Table 1.

Variable	OR (95% CI)	P value
USG (per each 0.01 increase)	0.6 (0.3–0.9)	0.024
Urine pH (per each 1.0 increase)	1.1 (0.5–2.3)	0.86
Leukocyturia present	1.9 (0.1–61.0)	0.68
Hematuria present	11 (2.4–80.0)	0.001
Protein (per 1-score increase)	1.9 (1.1–3.3)	0.021
CaOx crystalluria present	Infinity (—)	0.055

Refractometry was used to determine the USG. Cytologic analysis of urine sediment was used to detect the presence of leukocyturia, hematuria, and CaOx crystalluria. Urine pH and semiquantitative urine protein concentration were determined by use of a urine dipstick; protein results were recorded on a scale of 0 to 4, with trace protein assigned a value of 0.5.

See Table 1 for remainder of key.