

Fasting Urinary Calcium-to-Creatinine and Oxalate-to-Creatinine Ratios in Dogs with Calcium Oxalate Urolithiasis and Breed-Matched Controls

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Background: Hypercalciuria and hyperoxaluria are risk factors for calcium oxalate (CaOx) urolithiasis, but breed-specific reports of urinary metabolites and their relationship with stone status are lacking.

Objective: To compare urinary metabolites (calcium and oxalate) and blood ionized calcium (iCa) concentrations between CaOx stone formers and breed-matched stone-free controls for the Miniature Schnauzer, Bichon Frise, and Shih Tzu breeds.

Animals: Forty-seven Miniature Schnauzers (23 cases and 24 controls), 27 Bichons Frise (14 cases and 13 controls), and 15 Shih Tzus (7 cases and 8 controls).

Methods: Prospective study. Fasting spot urinary calcium-to-creatinine and oxalate-to-creatinine ratios (UCa/Cr and UOx/Cr, respectively) and blood iCa concentrations were measured and compared between cases and controls within and across breeds. Regression models were used to test the effect of patient and environmental factors on these variables.

Results: UCa/Cr was higher in cases than controls for each of the 3 breeds. In addition to stone status, being on a therapeutic food designed to prevent CaOx stone recurrence was associated with higher UCa/Cr. UOx/Cr did not differ between cases and controls for any of the breeds. Blood iCa was higher in cases than controls in the Miniature Schnauzer and Bichon Frise breeds and had a moderate correlation with UCa/Cr.

Conclusions and Clinical Importance: Hypercalciuria is associated with CaOx stone status in the Miniature Schnauzer, Bichon Frise, and Shih Tzu breeds. UOx/Cr did not correlate with stone status in these 3 breeds. These findings may influence breed-specific stone prevention recommendations.

Key words: Hypercalciuria; Lower urinary tract.

Calcium oxalate (CaOx) urolithiasis is a common urinary tract disease in dogs, but the etiology is poorly understood. In people, hypercalciuria (high urinary calcium excretion) is well established as the most common metabolic abnormality underlying CaOx stone formation.¹ Hypercalciuria in the face of normal serum calcium concentrations is termed idiopathic hypercalciuria (IH). As the name implies, the pathophysiology of IH is largely undefined, but it is believed to be influenced by both environmental and genetic factors. High urinary concentrations of oxalate also will promote CaOx supersaturation, but idiopathic hyperoxaluria (IHO) is a less common metabolic disturbance in human CaOx stone formers.²

Over the past 3 decades, several veterinary studies have evaluated urinary calcium and oxalate concentrations in canine CaOx stone formers.^{3–5} The earliest of these studies documented abnormally high urinary

Abbreviations:

ANCOVA	analysis of covariance
CaOx	calcium oxalate
CI	confidence intervals
iCa	ionized calcium
IH	idiopathic hypercalciuria
IHO	idiopathic hyperoxaluria
LSM	least square means
MUC	Minnesota Urolith Center
UCa/Cr	urinary calcium-to-creatinine ratio
UMN VMC	University of Minnesota Veterinary Medical Center
UOx/Cr	urinary oxalate-to-creatinine ratio

calcium concentrations in CaOx stone-forming Miniature Schnauzers compared to healthy Beagles, despite controlled housing, diet, and water intake.³ Both fasted and fed 24-hour urinary calcium concentrations were higher in the stone-forming Miniature Schnauzers compared to Beagle controls. Urinary oxalate excretion was lower in the Miniature Schnauzers, and serum total calcium concentrations were not different between groups. These features support the presence of IH in Miniature Schnauzer dogs, but the use of disparate breeds for case and control groups imparts a crucial limitation on the interpretation of this data. Namely, it does not determine if the trait of IH segregates within the breed and associates with stone risk. It is possible that all purebred Miniature Schnauzers have IH, similar to the situation observed with hyperuricosuria in Dalmatian dogs.⁶

A subsequent study on urinary metabolites in CaOx urolithiasis used a breed-matched approach.⁴ Seventeen CaOx stone-forming dogs from 14 different breeds were breed-, age-, and sex-matched to a control group.

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A portion of this work was presented as an oral abstract at the 2012 Research on Calculus Kinetics annual meeting in Indianapolis, IN and as a research report at the 2014 ACVIM Forum in Nashville, TN. This work was a chapter in Dr Furrow's doctoral dissertation submitted to the Faculty of the Graduate School of the University of Minnesota in partial fulfillment of the requirements for a PhD degree awarded June 2014.

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Submitted July 28, 2014; Revised September 29, 2014; Accepted November 17, 2014.

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DOI: 10.1111/jvim.12527

The stone-former group had both higher 24-hour urinary calcium and oxalate concentrations relative to the control group. The results of this breed-matched study suggest that IH and IHO are traits that vary within breeds and impart stone risk. However, there were too few dogs of each breed to report breed-specific results. To the authors' knowledge, no studies have been published that report individual dog breed urinary metabolite data for CaOx stone formers and controls. This information is important for informing breed-based medical recommendations such as hydrochlorothiazide for IH or vitamin B6 for IHO.⁷

The first aim of this study was to compare fasting spot urinary calcium and oxalate concentrations between CaOx stone formers and breed-matched controls for each of the 3 most common breeds reported to be at increased risk for CaOx urolithiasis: the Miniature Schnauzer, Bichon Frise, and Shih Tzu.⁸ We hypothesized that the stone formers for each breed would have higher urinary calcium concentrations than the respective control dogs, but that urinary oxalate concentrations would not differ. A second aim was to compare blood ionized calcium (iCa) concentrations between the aforementioned stone-former dogs and breed-matched controls. We hypothesized that iCa concentrations would not differ between stone formers and controls for each of the 3 breeds.

Materials and Methods

Study Population

Between February 2011 and March 2014, dogs were recruited from the patient population at the Veterinary Medical Center, University of Minnesota (VMC UMN) and through outreach to primary care veterinary clinics and breed groups in Minnesota and Wisconsin. Purebred dogs of 3 breeds were recruited: Miniature Schnauzers, Bichons Frise, and Shih Tzus. Cases were defined as dogs with a history of uroliths composed of CaOx ($\geq 70\%$ of the central core), as determined by standard stone analysis at the Minnesota Urolith Center (polarizing light microscopy and infrared spectroscopy). Controls had no history of CaOx uroliths or lower urinary tract disease aside from previous culture-positive bacterial urinary tract infections. To minimize the inclusion of latent stone formers, the control dogs were selected to be ≥ 8 of age (the reported mean age of CaOx urolithiasis diagnosis in dogs).⁹ Controls were screened with abdominal radiographs to eliminate radiopaque uroliths and by urinalysis to eliminate CaOx crystalluria.

For both groups, dogs were excluded if they had received glucocorticoids within the past week or another drug with known effects on urinary calcium excretion (eg, furosemide, thiazide diuretics, levothyroxine, theophylline, potassium citrate) within the past 24 hours. Dogs also were excluded if they had a clinical diagnosis of a disease that alters urinary calcium excretion (eg, hyperparathyroidism, hypercalcemia of malignancy, hyperadrenocorticism, diabetes mellitus, osteolytic disease, granulomatous disease). Dogs in both groups were permitted to be on therapeutic foods designed to minimize CaOx recurrence; dietary information was used in the data analysis. Written informed consent was obtained from the owners of each study participant, and the study protocol was approved by the University of Minnesota Institutional Animal Care and Use Committee.

Laboratory Measurements

Owners were instructed to withhold food, but not water, for 12–18 hours before sample collection. All dogs had urinated at least once before sample collection to insure that the experimental urine sample was never the first micturition of the day. Urine was collected by free catch, cystocentesis, or catheterization. Unfiltered 1–3 mL urine aliquots were analyzed immediately for calcium (spectroscopy and the calcium-sensitive dye Arsenazo II) and creatinine (modified Jaffe procedure).^{10,11} A 4-mL urine aliquot was filtered through a 0.22 μm polyethersulfone membrane,^a stored at -80°C , and analyzed for oxalate (ion chromatography on nonacidified urine) within 6 months.¹² Spot urinary calcium-to-creatinine and oxalate-to-creatinine ratios in mg/mg (UCa/Cr and UOx/Cr, respectively) were calculated for each dog. Venous blood was collected in a syringe with dry lithium heparin, and iCa and creatinine concentrations were determined with a blood gas analyzer.^b

Statistical Analysis

The distribution of the data was visually inspected with Q-Q plots to determine if transformations or nonparametric tests were necessary. For skewed measurements (urinary data), Wilcoxon rank sum tests were used to compare UCa/Cr and UOx/Cr between case and control groups for each individual breed and across breeds. Medians were reported for the urinary data. In addition, this data was log-transformed to achieve a more normal distribution, and regression analyses were performed on the log-transformed UCa/Cr and UOx/Cr with the following variables as predictors: stone status (case versus breed-matched control), breed, sex (male versus female), age (years) as a quadratic, and diet (therapeutic CaOx stone prevention diet versus other foods). The significance of each predictor was assessed using Type II tests (analysis of covariance [ANCOVA]). The least square means (LSM) and 95% confidence intervals (CI) were calculated and back-transformed to the original scale for reporting. For the normally distributed data (blood iCa and creatinine concentrations), Student's *t*-tests were used to compare results between the case and control groups for each individual breed and across breeds, and data are reported as mean \pm standard deviation. A regression analysis also was performed for blood iCa concentration, using the predictors described for the urinary analyses. The Pearson correlation coefficient (*r*) was calculated to test the relationship between the log-transformed UCa/Cr and blood iCa concentration. All analyses were performed by the R software for statistical computing,^c and a *P*-value of $< .05$ was considered significant.

Results

Forty-seven dogs were recruited as potential cases for the study. Three dogs were excluded because of ionized hypercalcemia identified at the study appointment and subsequent diagnoses of primary hyperparathyroidism (1 Bichon Frise and 1 Shih Tzu) and hypercalcemia of malignancy secondary to an anal gland adenocarcinoma (1 Miniature Schnauzer). Data from the remaining 44 cases (23 Miniature Schnauzers, 14 Bichons Frise, and 7 Shih Tzus) were included in the analysis. The signalment data for the cases are presented in Table 1. More than half (28/44, 64%) of the cases had experienced recurrent CaOx stones with a median of 2 (range: 1–4) episodes. The mean age at the time of first stone diagnosis was 7.5 ± 2.3 years, and the mean age at the time of study enrollment was 9.5 ± 2.3 years. Eighteen cases

(41%) had known cystoliths at the time of sample collection and had their stones removed later that same day.

Sixty-one dogs were screened as potential controls for the study. Sixteen dogs (26%) were excluded because radiopaque uroliths consistent with a composition of CaOx were detected on screening radiographs. Data from the remaining 45 controls (24 Miniature Schnauzers, 13 Bichons Frise, and 8 Shih Tzus) were included in the analysis. The mean age of the control dogs at the time of study enrollment was 10.5 ± 1.9 years.

Within each breed, age at the time of study enrollment and sex were not significantly different between cases and breed-matched controls (Table 1). However, for across breed comparisons, the age of the entire control group was older than the case group ($P = .025$), and more cases than controls were male ($P = .027$). Fourteen cases and 1 control were fed therapeutic foods designed to prevent CaOx recurrence;^{d,e} the control dog was fed the therapeutic food^e because another household dog had been affected with CaOx stones.

UCa/Cr was significantly higher in cases than controls for each of the 3 breeds (Table 1, Fig 1A) and across breeds ($P < .001$). In the UCa/Cr regression analysis, stone status was a strong predictor of UCa/Cr ($P < .001$, Table 2). Being on a therapeutic food for CaOx stone prevention also had a positive correlation with UCa/Cr ($P = .027$). There was no significant effect of breed, sex, or age on UCa/Cr. UCa/Cr was not different between cases with as compared to without known cystoliths at the time of sample collection ($P = .18$). UOx/Cr was not different between cases and controls for any of the 3 breeds (Table 1, Fig 1B), and none of the predictors in the UOx/Cr regression analysis were significant (Table 2).

Blood iCa concentration was within the laboratory's established reference interval for dogs (5.1–5.9 mg/dL) in all but 1 dog: a Bichon Frise control with a low blood iCa concentration at 4.9 mg/dL. Nine cases and 3 controls did not have blood iCa concentrations determined because of clotting of the sample (1 dog) or lack of collection (11 dogs). All 12 dogs without blood gas analysis had serum biochemistry panels performed (10

at the UMN VMC and 2 at the primary care veterinary clinic), and serum total calcium concentrations were within the respective laboratory reference intervals. For dogs with available measurements, blood iCa concentration was significantly higher in cases than controls for the Miniature Schnauzer and Bichon Frise breeds (Table 1, Fig 1C) and for across breed comparisons between cases and controls ($P < .001$). Stone status was the only significant predictor of blood iCa concentration in the regression model (Table 2). There was a moderate positive correlation between blood iCa concentration and UCa/Cr ($r = 0.31$, $P = .0067$). Blood creatinine concentration did not differ between cases and controls within or across breeds.

Discussion

This study demonstrates that fasting spot UCa/Cr values are higher in dogs with CaOx uroliths than in breed-matched controls for the Miniature Schnauzer, Bichon Frise, and Shih Tzu breeds. These results support our hypothesis that hypercalciuria is an important underlying metabolic abnormality associated with stone formation in these 3 dog breeds. The UOx/Cr did not associate with stone status for any of the breeds studied. An unexpected finding was higher blood iCa concentrations in stone formers than in controls even though no results were above the reference range.

In people, hypercalciuria is the most common driving force behind CaOx supersaturation, occurring in up to 60% of patients with kidney stones.¹ Most hypercalciuric patients have normal blood calcium concentrations, a phenomenon classified as IH.¹³ None of the dogs included in this study had blood iCa concentrations, serum total calcium concentrations, or both above laboratory reference intervals. Thus, the hypercalciuria for the 3 breeds is appropriately referred to as IH. Three disturbances in calcium homeostasis are theorized to contribute to IH in stone formers: intestinal hyperabsorption, excessive bone resorption, and decreased renal resorption of calcium. A previous study on urinary metabolites in Miniature Schnauzers with CaOx urolithiasis proposed intestinal hyperabsorption as the likely

Table 1. Patient characteristics, median fasting spot urinary calcium-to-creatinine and oxalate-to-creatinine ratios (UCa/Cr and UOx/Cr, respectively), and mean blood ionized calcium and creatinine in dogs with a history of calcium oxalate stones (cases) and breed-matched stone-free dogs (controls).

Breed	Age (years)	Sex (M/F)	UCa/Cr (mg/mg)	UOx/Cr (mg/mg)	iCa (mg/dL)	Creatinine (mg/dL)
Miniature Schnauzer						
Cases, 23	9.1 ± 2.4	19/4	0.067***	0.034 (19)	5.5** (20)	0.9 (20)
Controls, 24	10 ± 1.4	15/9	0.022	0.033 (20)	5.3 (23)	0.9 (23)
Bichon Frise						
Cases, 14	10.1 ± 2.3	11/3	0.093**	0.068 (11)	5.5* (10)	0.8 (10)
Controls, 13	10.9 ± 2.4	8/5	0.041	0.076	5.3 (11)	0.8 (11)
Shih Tzu						
Cases, 7	9.1 ± 2.1	5/2	0.12***	0.079	5.6 (5)	0.8 (5)
Controls, 8	11.1 ± 2.2	3/5	0.028	0.038 (7)	5.4	0.8

UCa/Cr and UOx/Cr were obtained by dividing urinary calcium or oxalate, respectively, in mg/dL by urinary creatinine in mg/dL. For measurements that were not available for all dogs, the total number of dogs with the measurement is listed in parentheses. Significantly higher values in cases compared to controls (within-breed comparisons) are denoted with * ($P < .05$), ** ($P < .01$) or *** ($P < .001$).

Table 2. Analysis of covariance (ANCOVA) for the effects of patient and environmental factors on urinary calcium-to-creatinine and oxalate-to-creatinine ratios (UCa/Cr and UOx/Cr, respectively) and blood iCa.

	LSM	95% CI	df	F value	P-value
UCa/Cr					
Stone status					
Case	0.109	0.080–0.148	1	34	<.001
Control	0.037	0.027–0.052			
Breed					
Miniature Schnauzer	0.058	0.042–0.080	2	0.3	.74
Bichon Frise	0.066	0.047–0.093			
Shih Tzu	0.068	0.043–0.105			
Sex					
Male	0.055	0.041–0.073	1	2.7	.10
Female	0.074	0.052–0.105			
Age	NA	NA	2	1.8	.17
Diet					
CaOx prevention diet	0.084	0.054–0.132	1	5.1	.027
Other	0.048	0.038–0.061			
UOx/Cr					
Stone status					
Case	0.039	0.026–0.059	1	0.25	.62
Control	0.045	0.028–0.072			
Breed					
Miniature Schnauzer	0.038	0.024–0.060	2	2.4	.10
Bichon Frise	0.062	0.039–0.100			
Shih Tzu	0.031	0.017–0.057			
Sex					
Male	0.038	0.026–0.058	1	0.39	.54
Female	0.045	0.028–0.073			
Age	NA	NA	2	2.5	.087
Diet					
CaOx prevention diet	0.047	0.025–0.087	1	0.38	.54
Other	0.037	0.027–0.052			
iCa					
Stone status					
Case	5.5	5.4–5.6	1	8.6	.0046
Control	5.3	5.2–5.4			
Breed					
Miniature Schnauzer	5.4	5.3–5.5	2	1.5	.22
Bichon Frise	5.3	5.2–5.4			
Shih Tzu	5.5	5.3–5.6			
Sex					
Male	5.4	5.3–5.5	1	3.5	.065
Female	5.3	5.2–5.4			
Age	NA	NA	2	0.2	.80
Diet					
CaOx prevention diet	5.4	5.3–5.5	1	0.5	.47
Other	5.4	5.2–5.5			

LSM, least squares mean; CI, confidence interval; df, degrees of freedom. P-values in bold denote significance (<0.05).

mechanism behind IH in the breed.³ The authors of that study based their hypothesis on the finding of more pronounced hypercalciuria in fed versus fasted states. The previous study did not detect differences in total serum calcium concentrations between stone formers and controls, but total calcium concentration has a 27% diagnostic discordance for predicting iCa concentration status.¹⁴

In the present study, the stone formers were shown to have significantly higher blood iCa concentrations than the control group. This finding supports either intestinal hyperabsorption or bone resorption as the cause. However, a concurrent defect in renal calcium resorption

cannot be ruled out. Studies in humans have shown that multiple disturbances can be present simultaneously,¹ and research on urinary calcium excretion relative to net calcium absorption and bone mineral loss would be needed to determine the source of IH in dogs. Furthermore, although the previous study on stone-forming Miniature Schnauzers found vitamin D and parathyroid hormone concentrations to be normal,³ these hormones were not measured in this study.

In the previous Miniature Schnauzer study³ and another on urinary metabolites in dogs and cats with CaOx urolithiasis,⁵ urinary calcium concentration was higher, but urinary oxalate concentration was lower in

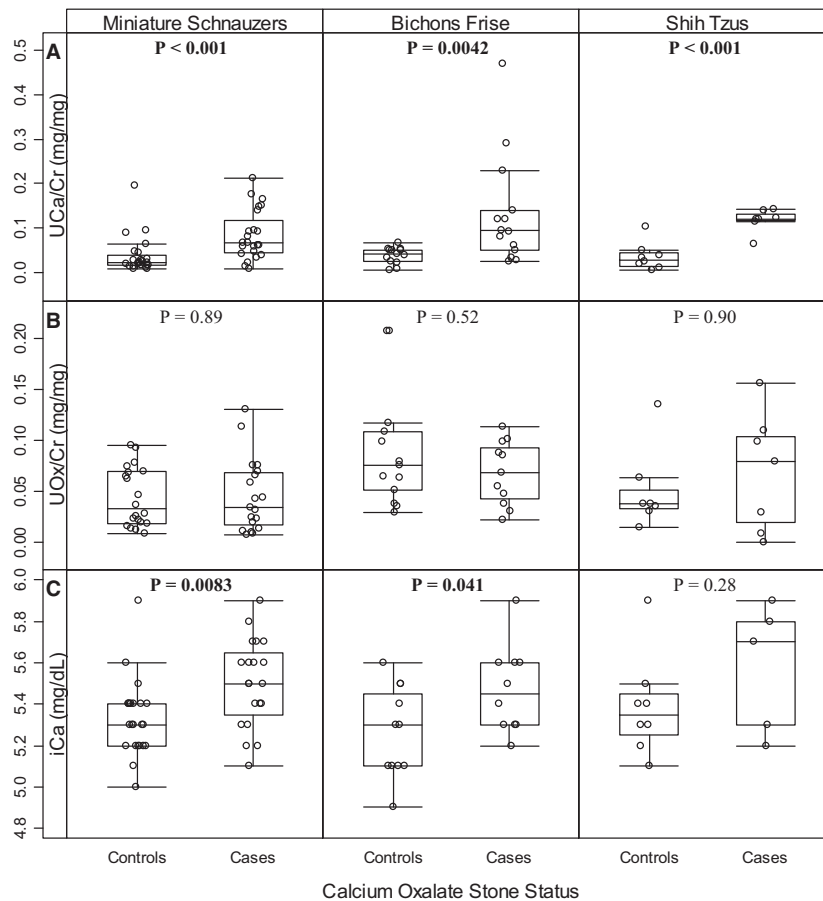


Fig 1. Box and whisker plots of fasting spot urinary (A) calcium-to-creatinine ratio (UCa/Cr, mg/mg), (B) oxalate-to-creatinine ratio (UOx/Cr, mg/mg), and (C) blood iCa (mg/dL) for dogs with a history of calcium oxalate stones (cases) and breed-matched stone-free dogs (controls). The boxes represent the interquartile range (25th–75th percentile), the horizontal line within the boxes represents the median, and the whisker bars extend to 1.5 times the interquartile range. Dots represent individual dog measurements; those that fall above or below the whisker bars are outliers. P-values in bold denote significance (< 0.05).

stone formers compared to controls. In contrast, another report on urinary metabolites in CaOx stone formers found both higher urinary calcium and oxalate concentrations in a group of stone-forming dogs relative to a breed-matched control group.⁴ The present study did not detect differences in UOx/Cr between stone formers and controls for any of the individual dog breeds or when data were analyzed across breeds. The conflicting results between studies may be because of evaluation of different dog breeds. The report that found higher urinary oxalate concentrations included 14 different breeds.⁴ Results for each individual breed were not reported, and ≥ 1 may have been affected by IHO instead of or in addition to IH. Idiopathic hyperoxaluria is reported in approximately 30% of human kidney stone patients.² Hypocitraturia also is associated with stone risk in humans.^{2,15} Urinary citrate concentration was not measured in the present study, but a previous study did not detect any difference in urinary citrate excretion between Miniature Schnauzers with CaOx uroliths and healthy Beagle controls.³

In people, urinary metabolite measurements often are used to guide treatment decisions and monitor response

to preventative measures.⁷ The present study successfully used fasting spot UCa/Cr and UOx/Cr to compare groups of CaOx stone formers to breed-matched controls, but it remains to be determined whether or not these measurements can be used to characterize individual dogs. Although the stone formers had significantly higher spot UCa/Cr than controls, there was considerable variability among dogs, and overlap was present between the case and control groups for all 3 breeds. There are a few possible explanations for this finding. First, 24-hour urine collection is a superior method of screening for hypercalciuria than is a fasting spot UCa/Cr in people. Studies in humans have reported varying correlations ($r = 0.52$ – 0.76) between these 2 techniques, and fasting spot UCa/Cr may systematically underestimate urinary calcium excretion.^{16–19} Therefore, the spot measurements used in this study may have missed mild cases of hypercalciuria. Measurement of 24-hour urine calcium excretion would have been preferable, but this technique was not used because of the expense, owner inconvenience, and technical difficulty of complete urine collection in dogs. Second, even within a breed, there could be multiple risk

factors present for the development of CaOx uroliths. As stated earlier, we did not measure urinary citrate concentrations or molecular inhibitors of stone formation. A third explanation for the overlap between spot UCa/Cr in cases and controls is that some cases may have experienced hypercalciuria at the time of stone formation from a temporary dietary or drug exposure that resolved before the time of study participation. Also, there were high UCa/Cr outliers in the control groups (4 Miniature Schnauzers and 1 Shih Tzu). These control dogs with IH may not have formed stones because of a protective environmental or genetic factor, or they could have had small stones that either passed or were not detected by survey radiography.

An unexpected finding in this study was the strikingly high incidental stone prevalence in the population screened as potential controls. More than a quarter of the dogs recruited as controls were identified to have radiopaque cystoliths, nephroliths, or both on radiographs. The owners of these dogs did not report any clinical signs of lower urinary tract disease, despite some dogs having a large stone burden. The true prevalence of stones in these 3 breeds cannot be determined with this data, but it is likely much higher than the estimated all breed prevalence of 0.3–2%.²⁰

In people, there is a documented relationship between nephrolithiasis and increased risk for chronic kidney disease.²¹ There was no association between stone status and blood creatinine concentration within the individual breeds or across breeds in the present study. The absence of a link could be because of stone type (eg, risk in people may be specific to struvite and urate stones), location (cystoliths versus nephroliths), or the imprecision of using creatinine concentration to estimate renal function.

A limitation of this study is that urinary oxalate and blood iCa and creatinine concentration measurements were not available for a subset of the dogs. This was because of inadequate urine volume in the case of urinary oxalate concentrations and either blood clotting or absence of appropriate sample collection in the case of the blood measurements. Serum total calcium concentration was available for all dogs with missing iCa concentrations, but total calcium concentration is not as accurate for assessing calcium status.¹⁴ Therefore, without iCa concentrations on all dogs, we cannot rule out that some cases may have had hypercalcemia. In addition, although we excluded dogs with a clinical diagnosis of a disease that alters urinary calcium excretion, it was not feasible to screen each case and control dog for all underlying diseases that could influence urinary calcium excretion.

Another limitation is that the case and control dogs were not matched on patient characteristics such as age and sex. In people, urinary calcium excretion peaks in middle age²² and is higher in males than females.²³ Thus, matching of these characteristics would have been ideal but was not possible because of the age limitation required for controls (older dogs were recruited to minimize the risk of enrolling latent cases) and the difficulty in recruiting sufficient numbers of male controls (many

were excluded because of incidental stones detected by screening). Despite these obstacles, age (analyzed as a quadratic to permit a curved relationship) and sex for case and breed-matched control groups were not different within each individual breed. When the breed data were combined, the case group was significantly younger overall and had a higher proportion of males than the control group, but neither age nor sex affected UCa/Cr or UOx/Cr in the regression models.

Diet also was not controlled or matched between cases and controls. A standardized diet would have added additional inconvenience and expense and was not possible for this study. A 12–18-hour fast was required before sample collection to minimize the effects of variation in nutrient intake on urinary metabolites, but this would not be expected to eliminate all effects of diet. Furthermore, 15/89 dogs (14 cases and 1 control) were on therapeutic foods that are specially formulated to decrease the precipitation of CaOx. Being on such a diet was associated with an increase in UCa/Cr in the regression model. This finding does not mean that the therapeutic diets directly increased urinary calcium excretion, especially given published data to the contrary.²⁴ Rather, the difference could be explained by stricter diet recommendations for the more severe stone formers suffering from higher urinary calcium concentrations and more stone recurrences than those dogs permitted to eat an over-the-counter diet. There were insufficient dogs on the therapeutic CaOx stone prevention foods to investigate this theory.

In conclusion, IH is a common metabolic abnormality in Miniature Schnauzer, Bichon Frise, and Shih Tzu dogs with a history of CaOx urolithiasis, and it is not a fixed trait in any of the 3 breeds. Because of overlap between case and control groups and undetermined intraindividual variability, it is unknown if UCa/Cr will be useful in the clinical monitoring of individual dogs. However, in general, stone formers of these breeds may benefit from preventative treatments directed at lowering urinary calcium excretion, such as thiazide diuretics.^{7,24}

Footnotes

^a MillexGP Filter Unit, Merck Millipor Ltd, Cork, IRL

^b i-STAT 1, Abbott Point of Care Inc, East Windsor, NJ

^c R Core Team (2012). R: A language and environment for statistical computing. R Foundation for Statistical Computing, Vienna, Austria. ISBN 3-900051-07-0, URL <http://www.R-project.org/>

^d Prescription Diet canine u/d, Hill's Pet Nutrition Inc, Topeka, KS

^e Royal Canin Veterinary Diet canine urinary SO, Waltham Centre for Pet Nutrition, Leicestershire, UK

Acknowledgments

The authors thank Dr. James R. Mickelson for providing comments on the manuscript, Aaron Rendahl

for statistical support, and the technicians at the Center for Investigative Studies and the Minnesota Urolith Center at the University of Minnesota for their assistance recruiting dogs and collecting samples for the study.

Funding: This research was funded by a Morris Animal Foundation grant (#D12CA-031), and Dr. Furrow was funded by an institutional NIH T32 Comparative Medicine and Pathology Training Grant (University of Minnesota, T32OD10993).

Conflict of Interest: Authors disclose no conflict of interest.

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

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