Clinical Theriogenology 2021; 13: 360

A retrospective review of canine benign prostatic hyperplasia with and without prostatitis

Hannah Ruetten,[a]* Marlyse Wehber,[a]* Mary Murphy,[a]* Clara Cole,[a]* Simran Sandhu,[a] Steven Oakes,[a] Dale Bjorling,[b] Kenneth Waller III,[b] Katrina Viviano,[c] Chad Vezina[a]
*Authors contributed equally
[a]Department of Comparative Biosciences; [b]Department of Surgical Sciences; [c]Department of Medical Sciences
School of Veterinary Medicine, University of Wisconsin-Madison, Madison, WI

Abstract

Benign prostatic hyperplasia (BPH) is the most common prostatic disorder in older intact male dogs, but despite its prevalence, there are inconsistencies in clinical diagnosis and treatment. Although prostate size was historically considered the hallmark feature of BPH in men, currently, there is only a weak correlation between prostate size and clinical severity. We performed a retrospective cohort study with the primary objective of assessing clinical signs, ultrasonographic findings, treatments, and outcomes in dogs diagnosed with BPH, with and without concurrent prostatitis. We reviewed medical records and obtained data on presenting signs, prostatic imaging, and prevalence of concurrent bacteriuria. Prostate size was determined by ultrasonography and compared to the calculated expected size based on patient age and weight. Treatment and outcome were described for the cases with a minimum 2 months follow-up. Median age of dogs diagnosed with BPH was 8 years. Clinical signs were present in 16/25 dogs and scored as mild to moderate (median Zambelli's Symptom Index for BPH score 12). The median prostatic volume to body mass ratio was 1.60 mm^3/kg. Prostate size did not correlate with the symptom severity. Concurrent bacteriuria was confirmed in 4/25 cases via bacterial culture and/or cytology. Treatments pursued and responses were only available in a subpopulation of dogs (n = 9) and were highly variable. Studies are needed to determine if current treatment options for BPH in dogs resolve associated clinical signs in addition to reducing prostate size.

Keywords: Dogs, benign prostatic hyperplasia, prostate size, urinalysis, clinical signs

Introduction

Common prostatic diseases of dogs include benign prostatic hyperplasia (BPH), prostatitis, prostatic cysts, prostatic abscesses, and less commonly neoplasia such as squamous metaplasia.[1,2] The most prevalent prostatic disease is BPH[3] and it is diagnosed in almost every intact male dog.[3,4] Prevalence of BPH is 80% in dogs > 6 years and 95% in dogs > 9 years old.[4]

The etiology and factors that increase severity of clinical signs are still not fully understood in dogs with BPH. Previous studies have retrospectively examined histologic features of canine prostatic disease and characterized affected populations.[3,5] However, many studies focus solely on prostate size as an end point and contrary to previous belief, there may be weak correlation between prostate size and severity of clinical signs.[6,7]

BPH in dogs consists of diffuse, symmetrical prostatic enlargement growing outward, away from the urethra, due to both hyperplastic and hypertrophic processes.[8] Symmetrical growth away from the urethra is a feature unique to canine BPH. In men, BPH growth occurs in a nodular fashion and can be both outward and inward toward the urethra. It is this variation in prostatic growth (suggestive of differences in the pathogenesis of prostatic hyperplasia in people and dogs) that lead some scientists and veterinarians to the false conclusion that dogs do not develop clinical signs in response to BPH like their human counterparts. Available literature reports that clinical signs of BPH are limited to prostatic enlargement and that most dogs do not manifest additional signs.[9] However, some veterinarians have noted, anecdotally, that the ability of older intact male dogs to urinate improves dramatically after castration.

Diagnosis of BPH in dogs is usually presumptive, based on physical examination, patient history, ultrasonographic findings, clinical signs, fine needle aspirate, prostatic wash, or monitored response to therapy.[2] A diagnostic procedure often performed by veterinarians offering reproductive services is collection of prostatic fluid by manual stimulation into a sterile tube, providing a large sample for analysis. Definitive diagnosis is based on prostatic biopsy that is invasive and therefore uncommon.[2] However, prostatic enlargement is listed as a criterion of all canine prostatic diseases, making additional diagnostics beyond digital rectal examination (DRE) critical for an accurate diagnosis.[1,2,8]

Treatment for canine BPH often exclusively focuses on reducing the size of the prostate gland. Castration is currently the most effective way to reduce prostate size in canines.[10] However, in breeding animals or dogs with preexisting prostatic bacterial infection, other modalities may be considered. Medical management includes the 5α-reductase type II inhibitor, finasteride, that prevents conversion of testosterone (T) to the more potent androgen dihydrotestosterone (DHT).[11] Finasteride reduced prostate size in humans and dogs.[12] Finasteride is given for the remainder of life, but does not impair fertility,[11,13] making it an option for breeding animals. However, limited information is available on the efficacy of finasteride in reducing clinical signs associated with BPH (other than prostatic enlargement).

The purpose of this retrospective medical record review was to describe canine BPH in a clinical population of client-owned dogs. The study's primary objectives were to report the clinical signs, prostatic ultrasonographic findings and prevalence of concurrent bacteriuria in dogs diagnosed with BPH, as well as assess if ultrasonographic prostatic size correlated with severity of clinical signs. A secondary objective was to describe the treatments and outcomes of dogs diagnosed with BPH including clinical signs. We hypothesized that BPH is often asymptomatic in intact male dogs, prostatic size does not correlate with clinical signs, and concurrent bacteriuria is an uncommon clinical complication of BPH.

Materials and methods

Animals

A computerized medical record search was performed for discharge reports containing the search term 'benign prostatic hyperplasia' from January 1, 2014 through December 31, 2018 at the University of Wisconsin Veterinary Care. All discharge reports from intact male dogs were reviewed. Client-owned intact male dogs clinically diagnosed with BPH and that underwent ultrasonographic prostatic imaging were considered for study inclusion. Included dogs also needed to have prostatic sampling for evaluation of prostate/urinary tract bacterial colonization (urine or prostatic fluid bacterial culture performed and/or prostatic fine needle aspirate for cytologic evaluation). Dogs did not need to have a complete urinalysis performed to be included, but it was recorded when available. Dogs diagnosed with prostatic abscesses or neoplasia, protein losing nephropathy, chronic kidney disease, bladder neoplasia, penile neoplasia, ureteral obstruction, or newly diagnosed systemic comorbidities were excluded.

Study design

A retrospective cohort design was used. The medical records were read in detail and age, sex, weight, breed, presence of preexisting medical conditions, and whether BPH was the main differential diagnosis or an incidental finding were recorded. Using the information within the medical record including clinical signs, BPH severity was scored according to the published Zambelli's Symptom Index for BPH (ZSI-BPH) score, 11 categories scored from 1 to 4 based on severity, for a total minimum of 11 and maximum of 44.[14] The criteria not specifically defined for ZSI-BPH scoring, weight loss and total score binning, were defined in this study as follows. Weight loss categories were scored as none (no change in body weight in kg), light (< 1 kg), moderate (1 - 5 kg), and severe (> 5 kg). ZSI-BPH total scores were binned into 4 categories: asymptomatic (11), mild (12 - 22), moderate (23 - 33), and severe (34 - 44). This scoring paradigm was selected because it takes an unbiased approach and rates each clinical sign equally for evaluating severity. Additionally, the ultrasonographic prostatic changes were recorded that included the tissue's echotexture and any additional changes noted (e.g. cysts or mineralization). Diagnostic laboratory tests performed were recorded that included cytologic findings, microbiology results, including specimen cultured, and bacterial species isolated. Finally, details of treatment performed, if any, were recorded.

Prostate size was estimated both by expected size using body weight (in kg, BW) and age (in years, A) as previously reported[15] and calculated size (P-CS) based on prostatic ultrasonography. Briefly, expected prostatic length ((0.055 x BW) + (0.143 x A) + 3.3), width (0.047 x BW) + (0.089 x A) + 3.45), height (sagittal (0.046 x BW) + (0.069 x A) + 2.68 and transverse (0.044 x BW) + (0.083 x A) + 2.25), and volume ((0.867 x BW) + (1.885 x A) + 15.88).[15] Using prostatic ultrasonographic images, each dog's prostatic size was calculated. Electronic calipers were used to measure length, width, and height along a sagittal and, when available, transverse plane in ultrasonographic still images (Figure 1). Ultrasonographic measurements were used to calculate prostate volume (length x width x (height sagittal + height transverse)/2) x 0.523).[15] In the absence of transverse views, the sagittal height was used in calculations in place of both the width and the mean of the sagittal and transverse heights. Prostate volume expressed as volume per kg body weight was calculated as P-CS/ BW.

Data analyses

All numerical data is reported as a median and range. A Spearman correlation was used to determine correlations between the calculated ultrasonographic prostatic size and clinical severity scoring (ZSI-BPH). Statistical analyses were performed using GraphPad Prism (Version 8.4.0 for Windows, GraphPad Software, San Diego, CA, www.graphpad.com). Differences were considered significant when $p < 0.05$.

Results

Two hundred and seventy-five discharge reports were examined and after duplicates (n = 90) were removed, a total of 185 canine cases were screened. Twenty-five intact male dogs met the study's inclusion criteria. Cases were excluded for following reasons: neutered males (n = 52), 'puppy discharges' describing the benefits of neutering (n = 3), no imaging pursued (n = 29), no prostatic sampling performed (n = 69), documented concurrent lower urinary tract disease (n=6), and concurrent comorbidities (n = 1).

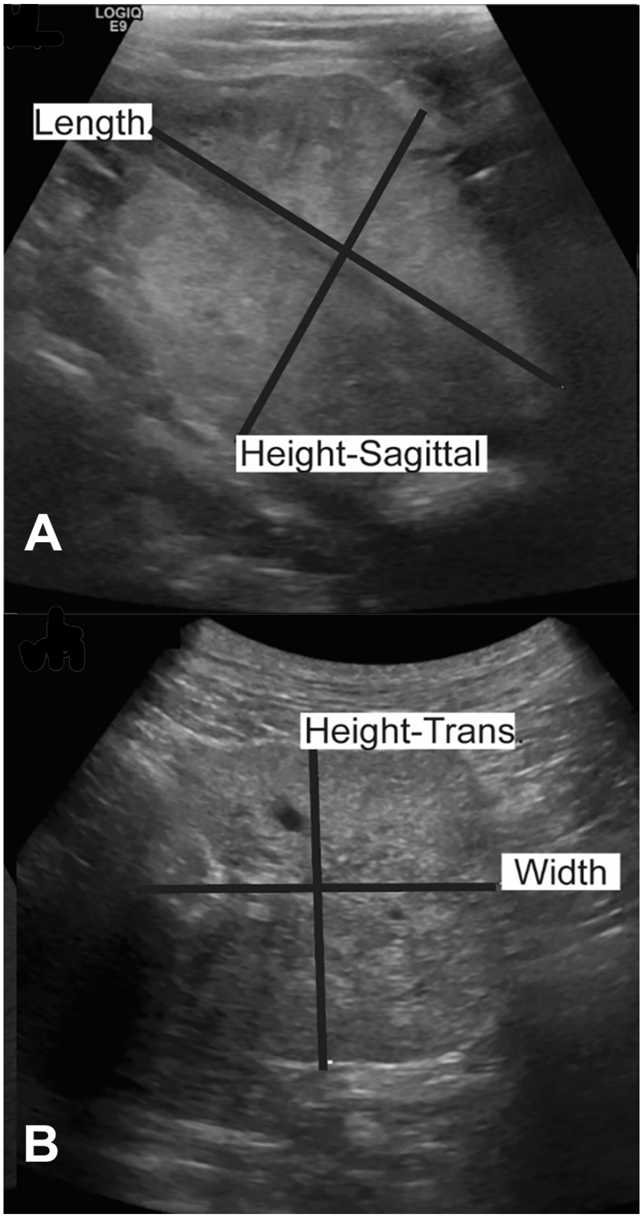

Figure 1. Ultrasonographic measurement of the prostate using electronic calipers in a (A) sagittal view and (B) transverse view

The median age at diagnosis of BPH was 8 years, ranging from 1 to 14 years in this population of dogs. Dogs weighed 3 - 68 kg with a median of 34 kg. Eight of the cases were Labrador Retrievers, 2 were Bernese Mountain Dogs, and remaining breeds were represented by a single case: Border Collie, Rough Coated Collie, Pomeranian, Poodle, Field Spaniel, Flat Coated Retriever, German Shorthaired Pointer, Golden Retriever, Spinone, Greater Swiss Mountain Dog, Leonberger, Mastiff, Newfoundland, Small Musterlander, and a Labrador/German Shepherd mix.

Clinical signs

Nine of 25 dogs with BPH were asymptomatic (ZSI-BPH score 11). Fourteen dogs diagnosed with BPH had mild clinical signs (median ZSI-BPH score 14.5, range; 12 - 22). Two dogs had moderate clinical signs (ZSI-BPH score 26). The mild clinical signs included anorexia, < 1 day (n = 2), anorexia < 1 week (n = 2), weight loss light (n = 1), weight loss moderate (n = 2), regular, but difficult and painful defecation (n = 2), urination with weaker or interrupted flow (n = 1), urination with very weak or interrupted flow (n = 1), urinary retention with urinary drip or paradoxal urinary incontinence (n = 1), urinary incontinence (n = 4), urethral leakage (n = 1), and hematuria (n = 7). The moderate clinical signs included anorexia for > 1 week (n = 1), urinary retention with urinary drip or paradoxal urinary incontinence (n = 2), urinary incontinence (n = 2), urethral leakage (n = 2), hematuria (n = 1). Overall, the median ZSI- BPH score was 12 (range; 11 - 26). Results of all ZSI-BPH categories are summarized (Table 1).

Prostatic palpation, ultrasonographic findings, and size

The results of DRE and prostatic ultrasonographic echotextures are summarized (Table 2) for this group of dogs clinically diagnosed with BPH. Only 17/25 dogs had DRE performed and the prostate was not assessed during rectal in 1 dog and prostates were not palpable in 5 dogs. When DRE was performed and prostate was described, the majority of descriptions were incomplete. All dogs had ultrasonographic performed; however, many were described as 'normal BPH' rather than descriptions of echotexture, and many echotexture descriptions were incomplete.

The P-CS expressed as volume per kg body weight ranged from 0.21 to 3.31 cm^3/kg with a median volume of 1.60 cm^3/kg. Compared to P-ES, 16 had P-CS smaller than their expected volume. Only 9 cases had prostates that were > P-ES. Also, there was no correlation between prostate volume per kg body weight and total ZSI-BPH score ($r = -0.0016$. 95% confidence interval – 0.4068 to – 0.4042, $p = 0.9940$, Figure 2).

Medical records were reviewed for dogs with BPH and total ZSI-BPH calculated based on scoring 11 criteria from 1 to 4 with possible total ZSI-BPH scores of 11 - 44.[14] P-CS was calculated using ultrasonographic imaging of each dog's prostate. Electronic calipers were used to measure length, width, and height along a sagittal and, when available, transverse plane in ultrasonographic still images (Figure 1). Ultrasonographic measurements were used to calculate prostate volume (length x width x (height sagittal + height transverse)/2) x 0.523).[15] In the absence of transverse views, the sagittal height was used in our calculations in place of both the width and the mean of the sagittal and transverse heights. Prostate volume expressed as volume per kg body weight was calculated as P-CS/ BW. Relationship ($r = -0.0016$, 95% confidence interval – 0.4068 to – 0.4042, $p = 0.9940$) between prostate volume per kg body weight and clinical sign severity (ZSI-BPH) is depicted (Figure 2).

Prostatic cytology, bacterial culture, and urinalysis

Cytology and/or bacterial culture was a selection criterion for

Table 1. Zambelli Symptom Index at diagnosis of dogs with a clinical diagnosis of benign prostatic hyperplasia

Anorexia	Absent (20) 1 day (2) 1 day to 1 week (2) > 1 week (1)
Weight loss	Absent (22) Light (1) Moderate (2) Severe (0)
Dyschezia /tenesmus (severity)	Absent (23) Regular, but difficult and painful defecation (2) Irregular, difficult and painful defecation (0) Defection impossible or absent in some days (0)
Dysuria (severity)	Absent (20) Urination with weaker or interrupted flow (1) Urination with very weak or interrupted flow (1) Urinary retention with urinary drip or paradoxal urinary incontinence (3)
Urinary incontinence	Absent (19) Present (6)
Urethral leakage (amount)	Absent (22) Few drops (2) Many drops (1) Stains on floor (0)
Urethral leakage (frequency)	Absent (22) Since 1 to 7 days (1) Since 7 to 15 days (1) Since > 15 days (1)
Hematuria (amount)	Absent (17) Sometimes pinkish urine (3) Pinkish urine (2) Red urine (3)
Hematuria (frequency)	Absent (17) 1 episode per year (4) 2 to 3 episodes per year (3) >3 episodes per year (1)
Hematuria (duration)	Absent (18) Since 1 to 7 days (5) Since 7 to 15 days (1) Since > 15 days (1)
Total severity score	Asymptomatic (9) Mild (14) Moderate (2) Severe (0)

our study. One dog had cytology alone performed, 18 had bacterial culture alone performed, and 6 had both types of sampling performed. Complete urinalysis was not a selection criterion for our study but was done in a subset of dogs (n = 19).

Cytological evaluation of the prostate, aspirates (n = 3) and wash (n = 4), were described and reviewed by a board-certified clinical pathologist. Aspirates were moderately to highly cellular and consisted of a homogeneous population of prostatic cells in a background of blood cells. Cells were arranged in flat sheets in all 3 specimens with no evidence of neoplasia, inflammation, or infection. The cytologic diagnosis was consistent with benign prostatic hyperplasia. Prostatic wash specimens were acellular to poorly cellular on direct smear. A cytocentrifuged specimen in all 4 cases described epithelial cells consistent with urogenital or transitional epithelium. None of the prostatic wash samples identified signs of neoplasia or infection. Only 1/4 cases had inflammation noted and it was characterized as lymphocytic and plasmacytic inflammation.

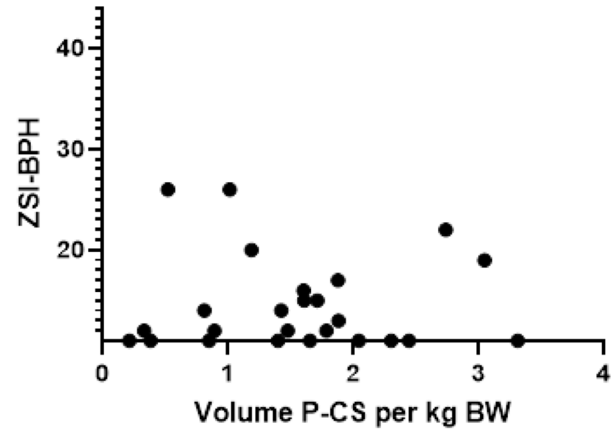

Figure 2. Volume calculated size (P-CS) per kg body weight (BW) and Zambelli's symptom index for benign prostatic hyperplasia (ZSI-BPH); each dog represents 1 dog

Twenty-four dogs had bacterial cultures performed. Samples cultured included urine collected via cystocentesis (n = 5), catheter (n = 4), or void (n = 11), and/or prostatic wash fluid (n = 6). Two dogs had both urine and prostatic fluid cultures performed. Positive bacterial urine cultures occurred in 4 dogs with *Escherichia coli* (*E. coli*) (> 100,000 CFU/ml) isolated in all 4 cases. All 4 cultures were susceptible to nitrofurantoin, tetracycline, and TMP-sulfa antibiotics. One was resistant to ciprofloxacin and another resistant to amoxicillin/clavulanate. Three of 4 dogs that had a culture confirmed bacteriuria also had urinalysis, and interestingly, only 2 dogs had bacteria on the urine sediment.

Nineteen dogs had urinalysis. Urine was collected via catheter (n = 3), cystocentesis (n = 6), and void (n = 10). Results of the urinalysis including color, turbidity, specific gravity, pH, WBCs, RBCs, transitional cells, protein, casts, crystals, bilirubin, ketones, glucose, and sperm are summarized (Table 3).

Treatment and outcome

Nine of our 25 cases had a minimum of 2-month follow-up. Three dogs were asymptomatic at the time of initial clinical evaluation and never developed clinical disease requiring treatment over 1 - 2 years of follow-up available. Remaining 6 dogs

Table 2. Description of prostate palpation based on digital rectal examination (DRE) and prostatic ultrasonographic echotextures of dogs with a clinical diagnosis of benign prostatic hyperplasia

Digital rectal examination of prostate (n = 11)†		**Ultrasonographic prostatic echotextures (n = 25)**	
Shape	Symmetrical (6) Asymmetrical (2) Not described (3)	**Shape**	Symmetrical (11) Asymmetrical (1) Not described (13)
Margin	Smooth (1) Irregular (1) Not described (9)	Diffuse **echopattern**	Homogenous (1) Heterogenous (13) Not described (11)
Discomfort	Painful (0) Nonpainful (6) Not described (5)	**Echotexture**	Hyperechoic (10) Hypoechoic (0) Not described (15)
		Intra-prostatic structures	Hyperechoic structures (3)* Hypoechoic structures (3)* Anaechonic structures (6)* Absent/Not described (16)

*Note: some had structures of multiple echogenicity
†No rectal examination was performed in 8 dogs, prostate was not assessed during rectal examination in 1 dog, prostate was not palpable in 5 dogs

Table 3. Urinalysis of dogs clinically diagnosed with benign prostatic hyperplasia

Urine color	Slightly yellow (2), Yellow (9), Dark yellow (3), Amber (3), Red tinged (1), Dark red (1)
Turbidity	Clear (5), Slightly hazy (3), Hazy (3), Cloudy (8)
Specific gravity	Range: 1.014 - 1.054, Median: 1.027
pH	Range: 6 - 8.5, Median: 7.5
WBCs	Absent (1), Rare (6), 1 - 5/hpf (6), 5 - 10/hpf (1), 10 - 25/hpf (1), 25 - 50/hpf (1), 50 - 100/hpf (2), TNTC (1)
RBCs	Absent (5), Rare (2), 1 - 5/hpf (4), 5 - 10/hpf (1), 10 - 25/hpf (0), 25 - 50/hpf (1), 0 - 100/hpf (4), TNTC (2)
Protein	Absent (1), Trace (2), 1+ (5), 2+ (5), 3+ (3), 4+ (3)
Transitional epithelial cells	Present (16), Absent (3)
Casts	Absent (15), Granular (4), Hyaline (1), Cellular (1)
Sperm	Present (13), Present (13), Absent (6)
Bilirubin	Positive (8), Negative (11)
Ketones	Positive (0), Negative (19)
Crystals	Absent (13), Amorphous (3), Bilirubin (1), Triple phosphate (2)
Glucose	Absent (18), Trace (1)†

*Four dogs with proteinuria had a follow-up urine protein: creatinine ratio (median: 2.055; range: 0.04 - 19.78)
† no evidence of hyperglycemia
hpf (high power field); TNTC (too numerous to count)

with BPH had clinical disease (e.g. hematuria, stranguria, dysuria, pollakiuria, or urinary accidents) at initial clinical evaluation and were treated with oral antibiotics (n = 5), prazosin 2 mg (0.1 mg/kg) once every 8 hours (n = 1), finasteride 5 mg (0.2 mg/kg) once daily (n = 1), and/or megestrol 20 mg (0.6 mg/kg) once daily (n = 1). Oral antibiotic treatments for confirmed or suspected secondary prostatitis included amoxicillin (500 mg [15 mg/kg] once every 12 hours [n = 1]), doxycycline (300 mg [9 mg/kg] twice daily (n =1), trimethoprim/sulfamethoxazole (480 mg [14 mg/kg]) twice daily (n = 1), enrofloxacin (272 mg [10 mg/kg] once daily [n = 1]), and ciprofloxacin (750 mg [24 mg/kg] once daily [n =1]). The dog treated with finasteride alone had resolution of clinical signs within 2 months before case was lost to follow-up.

The 5 remaining dogs with clinical signs at initial presentation failed medical treatment and did not have resolution of clinical signs at any point during follow-up despite incremental decreases in their prostate size. After failing medical treatment, 2 dogs were castrated. Both dogs experienced incomplete prostatic involution, based on follow-up ultrasonographic, and had persistent lower urinary tract signs that were treated symptomatically with intermittent antibiotics based on documented bacteriuria (n = 2). One of the 2 dogs treated for bacteriuria responded well to antibiotics and had a negative urine culture after treatment, whereas the other dog had persistent bacteriuria despite antibiotic treatment. Additional supportive medications prescribed chronically in 1 dog including oral prazosin 2 mg (0.1 mg/kg) and bethanechol 20 - 25 mg (0.6 - 0.7 mg/kg) once every 8 hours.

Discussion

Purpose of this retrospective medical record review was to describe canine BPH in a clinical population of client-owned dogs. It is important to note that this review took place at an institution that treats BPH patients through the internal medicine department and does not routinely perform semen collection in dogs. Therefore, semen and/or prostatic fluid analysis, that can be a helpful diagnostic tool for BPH, were not included in this study. It is also important to note that we used a diagnostic tool for clinical signs of BPH retrospectively rather than prospectively. It is possible that not all clinical signs we scored were noted in the record. It is also possible that not all clinical signs were assessed in each patient. Therefore, our ZSI-BPH scores may be low estimates of true clinical sign severity.

As expected, most dogs with BPH experienced only mild clinical signs or remained asymptomatic. When mild to moderate clinical signs were present, they included: urinary incontinence, urethral leakage, dysuria, hematuria, tenesmus, and dyschezia.

Prostatomegaly is considered the hallmark feature of canine BPH and is often the sole measure for determining efficacy of treatments. However, we observed that there was no correlation between prostate size and severity of clinical signs in our population. Further, a comparison of P-ES to P-CS suggests that the majority of cases (18/25) had prostates that were equal to or smaller than expected rather than enlarged. These findings suggest that prostate enlargement alone should not be used to identify patients with BPH. CPSE assays may be a more predictive diagnostic tool as they are highly predictive of a cytologic diagnosis of BPH in dogs.[16]

Our finding that the majority of cases (18/25) had prostates that were equal to or smaller than expected rather than enlarged suggests that subjective prostatic enlargement may be over diagnosed in intact male dogs. This may be in part due to the fact that in the US most dogs are neutered at a young age and many practitioners are not accustomed to examining prostates in intact male dogs, therefore they may perceive the prostate of an aged intact male as enlarged when it is of an appropriate size for that dog's age and weight. Implementing a standard practice of measuring the prostate volume using ultrasonographic and comparing it to the calculated expected prostatic size based on body weight and age, as done in this study and a previous study,[16] may be a more objective measure to use to establish an ultrasonographic diagnosis of prostatic enlargement in intact male dogs.

We determined the prevalence of concurrent bacterial infection in our population as an indicator of concurrent prostatitis and potential etiology of urinary dysfunction in dogs with BPH. Only 4 of the dogs with bacterial urine cultures and/or cytology performed cases had a positive bacterial culture. In all 4 cases *E. coli* was isolated in high numbers (> 100,000 CFU/ml). Interestingly, 18/19 cases that had urinalysis performed had pyuria and 11/19 had pyuria with ≥ 1 - 5 WBC per hpf (high power field) suggesting the presence of lower urinary tract inflammation in majority of cases, despite only 3 of these dogs, having confirmed and documented bacteriuria via bacterial culture. Prostate inflammation is strongly correlated with symptom severity in men and is associated with relapse of symptoms following treatment.[17-20] Prostatic inflammation is also correlated with prostatic fibrosis in men[20-22] and we have previously identified an increase in prostatic collagen with age in intact male dogs[23] and a shift in the cell type producing collagen 1a1 with age in intact male dogs.[24] The clinical finding of WBCs in the urine of dogs with BPH in the absence of bacteriuria may indicate an area for further study to determine if prostate inflammation predicts ZSI-BPH severity.

The majority of cases with follow-up at this tertiary veterinary care facility were comprised of complicated cases that failed standard BPH treatments. Only 2 cases with follow-up elected castration and both cases had persistent UTIs and urinary signs. In fact, only 1 of the 6 cases with follow-up that presented with urinary signs improved following treatment, pointing to a need for further study of treatments' efficacy in reducing clinical signs for BPH and for BPH with concurrent UTI in dogs. We recently characterized a uropathogenic *E. coli* mouse model of prostate infection and inflammation[25] that holds promise for testing of optimal treatments for dogs and men with both BPH and concurrent uropathogenic *E. coli* infection.

Overall, this study demonstrated the presence of clinical signs other than prostatomegaly in dogs with BPH. Clinical signs of BPH using ZSI-BPH scoring did not correlate with prostatic size. Objective determinations of prostatomegaly are lacking in intact male dogs and prostatomegaly associated with BPH may be over diagnosed in dogs. Concurrent bacterial infections of the prostate were infrequent in this population of dogs with BPH but based on urinalysis findings clinical lower urinary tract inflammation may be present in majority of patients. There is a need for future studies to develop additional diagnostic tests for BPH in dogs that do not rely so heavily on prostatic size, determine the influence of prostatic inflammation on severity of clinical signs, and determine treatments that not only reduce prostate size but also alleviate concurrent clinical signs including urinary dysfunction.

Acknowledgement

Funded by National Institutes of Health grants: TL1 TR002375, T35 OD011078, F30 DK122686, U54 DK104310 and University of Wisconsin-Madison, School of Veterinary Medicine. The content is solely the responsibility of the authors and does not necessarily represent the official views of the National Institutes of Health.

Conflict of interest

None to declare.

References

1. Johnston SD, Kamolpatana K, Root-Kustritz MV, et al: Prostatic disorders in the dog. Anim Reprod Sci 2000;60-61:405-415.
2. Smith J: Canine prostatic disease: a review of anatomy, pathology, diagnosis, and treatment. Theriogenology 2008;70:375-383.
3. Polisca A, Troisi A, Fontaine E, et al: A retrospective study of canine prostatic diseases from 2002 to 2009 at the Alfort Veterinary College in France. Theriogenology 2016;85:835-840.
4. Berry SJ, Strandberg JD, Saunders WJ, et al: Development of canine benign prostatic hyperplasia with age. Prostate 1986;9:363-373.
5. Palmieri C, Lean FZ, Akter SH, et al: A retrospective analysis of 111 canine prostatic samples: histopathological findings and classification. Res Vet Sci 2014;97:568-573.
6. Franciosi M, Koff WJ, Rhoden EL: Correlation between the total volume, transitional zone volume of the prostate, transitional prostate zone index and lower urinary tract symptoms (LUTS). Int Urol Nephrol 2007;39:871-877.
7. Lepor H: Landmark studies impacting the medical management of benign prostatic hyperplasia. Rev Urol 2003;5(Suppl 5):S28-S35.
8. Christensen BW: Canine prostate disease. Vet Clin North Am Small Anim Pract 2018; 48:701-719.
9. Mukaratirwa S, Chitura T: Canine subclinical prostatic disease: histological prevalence and validity of digital rectal examination as a screening test. J S Afr Vet Assoc 2007;78: 66-68.
10. Huggins C, Clark PJ: Quantitative studies of prostatic secretion : II. The effect of castration and of estrogen injection on the normal and on the hyperplastic prostate glands of dogs. J Exp Med 1940;72:747-762.
11. Sirinarumitr K, Johnston SD, Kustritz MV, et al: Effects of finasteride on size of the prostate gland and semen quality in dogs with benign prostatic hypertrophy. J Am Vet Med Assoc 2001;218:1275-1280.
12. Angrimani DSR, Francischini MCP, Brito MM, et al: Prostatic hyperplasia: vascularization, hemodynamic and hormonal analysis of dogs treated with finasteride or orchiectomy. PLoS One 2020;15:e0234714.
13. Angrimani DSR, Bicudo LC, Llamas Luceño N, et al: Does finasteride treatment for benign prostatic hyperplasia influence sperm DNA integrity in dogs? Basic Clin Androl 2020;30:39.
14. Zambelli D, Cunto M, Gentilini F: Validation of a model to develop a symptom index for benign prostatic hyperplasia in dogs. Reprod Domest Anim 2012;47(Suppl 6):229-231.
15. Ruel Y, Barthez PY, Mailles A, et al: Ultrasonographic evaluation of the prostate in healthy intact dogs. Vet Radiol Ultrasound1998;39:212-216.
16. Pinheiro D, Machado J, Viegas C, et al: Evaluation of biomarker canine-prostate specific arginine esterase (CPSE) for the diagnosis of benign prostatic hyperplasia. BMC Vet Res 2017;13:76. DOI 10.1186/s12917-017-0996-5.
17. Bushman WA, Jerde TJ: The role of prostate inflammation and fibrosis in lower urinary tract symptoms. Am J Physiol Renal Physiol 2016;311:F817-F21.
18. Roehrborn C: The impact of acute or chronic inflammation in baseline biopsy on the risk of progression in the MTOPS study (abstract). Eur Urol Suppl 2005;4:5.
19. Torkko KC, Wilson RS, Smith EE, et al: Prostate biopsy markers of inflammation are associated with risk of clinical progression of benign prostatic hyperplasia: findings from the MTOPS Study. J Urol 2015;194:454-461.
20. Macoska JA, Uchtmann KS, Leverson GE, et al: Prostate transition zone fibrosis is associated with clinical progression in the MTOPS study. J Urol 2019;202:1240-1247.
21. Ma J, Gharaee-Kermani M, Kunju L, et al: Prostatic fibrosis is associated with lower urinary tract symptoms. J Urol 2012;188:1375-1381.
22. Rodriguez-Nieves JA, Macoska JA: Prostatic fibrosis, lower urinary tract symptoms, and BPH. Nat Rev Urol 2013;10:546-550.
23. Ruetten H, Wegner KA, Romero MF, et al: Prostatic collagen architecture in neutered and intact canines. Prostate 2018;78:839-848.
24. Ruetten H, Cole C, Wehber M, et al: An immunohistochemical prostate cell identification key indicates that aging shifts procollagen 1A1 production from myofibroblasts to fibroblasts in dogs prone to prostate-related urinary dysfunction. PLoS One 2020;15:e0232564.
25. Ruetten H, Sandhu JK, Mueller B, et al: A uropathogenic E. coli UTI89 model of prostatic inflammation and collagen accumulation for use in studying aberrant collagen production in the prostate. Am J Physiol Renal Physiol 2020;320:F31-F46.