

Value of specific history and physical examination findings and diagnostic test results for differentiation of benign from malignant prostate disease in dogs

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Abstract

Electronic medical records with a final diagnosis of prostate disease were retrieved from the electronic medical record system of a veterinary academic referral hospital. Data gathered included signalment, age at time of admission, clinical signs including gross hematuria, stranguria or dysuria, dripping of bloody fluid from the prepuce unassociated with urination, urinary incontinence and inappropriate urination, rectal tenesmus, and passage of ribbon-shaped stools, and signs of systemic disease. Presence of red blood cells (RBCs) and epithelial cells in urine sediment and of mineralization and regional lymph node enlargement on transabdominal ultrasound also were recorded. Ninety-nine cases were reviewed. The history and diagnostic findings determined to be significantly associated with benign prostatic hyperplasia/hypertrophy (BPH) rather than with prostatic neoplasia were being sexually intact ($p > 0.0001$) and dripping bloody fluid from the prepuce unassociated with urination ($p = 0.007$). The history and diagnostic findings determined to be significantly associated with prostatic neoplasia rather than with BPH were being castrated ($p < 0.0001$), stranguria or dysuria ($p < 0.0001$), rectal tenesmus ($p = 0.0009$), systemic signs of disease ($p = 0.004$), and mineralization of the prostate and regional lymph node enlargement visible with transabdominal ultrasound ($p < 0.0001$ and $p = 0.0002$, respectively).

Keywords: Prostate, neoplasia, benign prostatic hypertrophy, prostatitis, diagnosis

Introduction

Prostate disease is common in men and in dogs. Many pet owners are aware of diagnostic and treatment options for human prostate disease and expect their veterinarians to be aware of how those diagnostic tests and therapies work in dogs.

The canine prostate encircles the neck of the urinary bladder and is bounded dorsally by the rectum and ventrally by the symphysis pubis and ventral abdominal wall.¹ Histologically, it consists of two lobes separated by a median raphe; the lobes are separated into lobules made up of secretory epithelium and supportive tissue.¹ Blood supply is via the prostatic artery, with the dorsal and periurethral areas better vascularized than the ventral portion of the gland.² There is relatively little smooth muscle compared to the human prostate gland, with distinct differences in distribution and type of muscle at the bladder neck, and there is relatively more glandular tissue.^{3,4} The canine prostate gland is surrounded by a well defined capsule; histologic studies disagree as to whether a true capsule surrounds the human prostate.^{1,2,5}

Secretory function and increase in size of the prostate are androgen-mediated. A significant difference between human male and canine male populations in the United States in regards to prostate disease is intact status; very few men are castrated or have gonadal dysfunction such that they secrete no androgens, while 31.8% of dogs are castrated in the United States.⁶

Benign prostatic hypertrophy/hyperplasia is very common in men; more than 40% of men over 60 years of age have lower urinary tract signs associated with BPH.⁷ Benign prostatic hyperplasia/hypertrophy is the most commonly reported disorder of the prostate in dogs.⁸⁻¹⁰ It is well documented that 50% of intact male dogs have histologic evidence of BPH by five years of age.¹¹ Benign prostatic hyperplasia/hypertrophy has not been reported in castrated dogs. The primary metabolite of testosterone, dihydrotestosterone, is the androgen that mediates prostate hypertrophy and hyperplasia.^{12,13} In dogs, the prostate gradually increases in size until four to six years of age, plateaus, and then increases in size again until it begins to atrophy in very aged dogs.^{11,14,15} The increase in size associated with age is due to a decrease in androgen secretion in the face of continuing estrogen secretion.¹⁴ As the prostate increases in size, it may pull the urinary bladder forward into the abdominal cavity, making it difficult or

impossible to assess on digital rectal examination. The primary clinical sign of BPH in men is difficulty in completely emptying the urinary bladder. This clinical sign is less likely to develop in dogs because of the relative lack of activation of smooth muscle cells in the prostate compared to that in men, and subsequent lack of urethral constriction.¹⁶ Benign prostatic hyperplasia/hyperplasia in dogs more commonly is associated with increased size and secretory function of the gland and so has been reported to be evidenced clinically by dripping of bloody prostatic fluid from the urethra unassociated with urination, hematuria, rectal tenesmus, and passage of ribbon-shaped feces.¹⁷⁻²⁰

Prostatic neoplasia is the second leading cause of cancer-related death in men.²¹ There is histologic evidence of prostatic neoplasia in about one-third of men over 50 years of age and in 90% of men over 90 years of age.²¹ Overall incidence of prostatic neoplasia in dogs is reported as 0.7%.²² Prostatic neoplasia has been reported in intact and in castrated dogs; castration increases risk of development of prostatic carcinoma by a factor of two to four times.^{8,23-26} Prostatic neoplasia has a different biology in men than in dogs. Men develop an androgen-responsive, fairly benign form of prostatic cancer early, followed by a non-androgen-responsive, more aggressive form later in life. Dogs develop only non-androgen-responsive, aggressive prostatic neoplasia.²⁷ Growth pattern of prostatic neoplasia differs between castrated and intact dogs.²⁸ The association between castration and development of prostatic neoplasia in dogs has not been explained. Clinical signs reported in dogs with prostatic neoplasia include stranguria and dysuria, hematuria, rectal tenesmus, anorexia and weight loss, rear limb lameness, and polyuria and polydipsia.^{18-20,25,29-33}

Prostatitis is infection of the prostate gland and commonly occurs secondary to either BPH or neoplasia as those alterations in anatomy and function of the gland overcome mechanisms that prevent movement of normal bacterial flora from the distal urethra into the prostate. Prostatitis may be diffuse or may be localized as an abscess. Prostatic cysts also are reported, again varying from diffuse small cysts scattered throughout the gland, often associated with BPH, to large, localized cysts that may be within or outside the gland parenchyma.

In humans, evaluation for prostate disease by a physician is recommended for all men between the ages of 50 and 75 who have a life expectancy of at least ten years.³⁴ The recommended diagnostic tests are a complete history; digital rectal examination to evaluate prostate size, shape, and consistency, and to assess for pain; urinalysis; and assessment for serum concentration of prostate specific antigen (PSA).³⁵ This is recommended for all men, whether or not they are symptomatic, and further diagnostic testing, such as ultrasound and aspirate or biopsy of the prostate, are recommended only in men with symptoms of prostate disease or elevated PSA concentrations.

In dogs, evaluation of the prostate beyond digital rectal examination is not usually performed in asymptomatic animals. Diagnosis of prostatic disease includes a complete history; digital rectal examination to evaluate prostate size, shape, and consistency, and to assess for pain, remembering that the very enlarged prostate may be abdominal and difficult or impossible to assess by rectal examination; ultrasonography to evaluate internal architecture of the prostate and to guide collection of samples for cytology; and if infection is suspected, culture of prostatic fluid, collected by ejaculation or prostatic massage, or aspirates of the gland. Because prostatic fluid is secreted constitutively, with much running into the urinary bladder, urinalysis on samples collected by cystocentesis may provide information about the prostate. Prostate specific antigen is not used for diagnostic screening in dogs as it is not routinely identified in serum.³⁶ A related but distinct protein, canine prostate specific esterase, has been identified in the dog but concentrations in serum and seminal fluid have not been demonstrated to differ significantly between normal dogs and dogs with various prostate diseases.^{36,37}

The author has received many anecdotal reports from colleagues of clients arguing for unnecessary tests for prostate disease in their dogs based on information from their experience or the human medical literature. This retrospective study was an attempt to determine which factors gleaned from history, physical examination findings, and common diagnostic tests could be used to differentiate likely causes of disease and streamline the diagnostic process. The intent was not to circumvent cytologic or histopathologic assessment of the prostate, which is the gold standard for differentiation of disease types in the dog.

Materials and methods

Medical records were retrieved electronically using the system's embedded search mechanism. The search included male dogs of all breeds, intact or castrated, for any diagnosis containing all or portions of the word "prostate." Search terms included were abscess-prostate, adenocarcinoma-prostate, carcinoma-prostate, cyst-prostate, hypertrophy-prostate, prostatitis, and prostatomegaly. Data gathered included diagnosis, breed, and intact status and age at time of admission. Clinical signs noted by the owner or by a veterinarian during physical examination that were specifically recorded included gross hematuria, stranguria or dysuria, dripping of serosanguinous or hemorrhagic fluid from the prepuce unassociated with urination, urinary incontinence or loss of housetraining as evidenced by inappropriate urination, rectal tenesmus, and passage of ribbon-shaped stools. Also recorded were signs of systemic disease, such as lethargy, anorexia, or lameness.

Because it was not always clear how referring veterinarians had gathered data sent along with the patient, data were included from urinalysis and transabdominal ultrasound only if those tests were completed at the author's institution, to minimize variability. Recorded from urinalyses were number of RBCs and epithelial cells in the urine sediment. Recorded from transabdominal ultrasound reports were presence or absence of prostatic mineralization and regional lymph node enlargement. Cytologic diagnoses were included only if performed at the author's institution, again to minimize variability.

Categorical data were compared between groups using the χ^2 test or Fisher's exact two-tailed test, as appropriate. Non-categorical data were compared using ANOVA. Significance was set at $p < 0.05$.

Results

The initial search retrieved 183 medical records from 2002 to the present. Eighty-four cases were removed after initial evaluation. Twenty-three had been completed incorrectly by a clinician or had been coded incorrectly and did not pertain to prostate disease in dogs. Twenty-eight were removed due to an incomplete work-up, usually consisting only of a history and physical examination with any further diagnostics declined by the owner. Fifteen were cases with prostate disease secondary to a significant primary condition that would confound source of clinical signs or results of diagnostic tests; examples of these conditions were pyelonephritis, neoplasia of other organs or systems, immune-mediated thrombocytopenia or hemolytic anemia, infectious diseases including blastomycosis and tick-borne diseases, urolithiasis, and paraplegia with urinary and fecal incontinence. Ten cases had putative prostatic carcinoma and eight cases had putative BPH, with no cytologic confirmation. Diagnosis was based on parameters to be evaluated by this study so these cases were removed.

Ninety-nine cases were evaluated in detail. Diagnoses for all cases were verified by evaluation of cytology specimens collected by fine-needle aspirate or by histopathology after necropsy. Complete signalment, history and physical examination findings were recorded for all cases. Urinalysis was performed in 56 cases. All urine samples were collected by cystocentesis. Transabdominal ultrasound was performed in 90 cases.

Dogs of 44 breeds were identified. Breed size varied from toy to giant. Breeds most commonly represented were the Labrador retriever ($n=18$), English springer spaniel ($n=9$), Shetland sheepdog ($n=8$), golden retriever ($n=6$), and German shepherd dog ($n=5$). This reflects popularity of these breeds in the area and the clientele of the clinicians at the author's institution.

Fifty-seven dogs were diagnosed with prostatic carcinoma; differentiation was not consistently made between adenocarcinoma and transitional cell carcinoma. Twenty-nine dogs were diagnosed with BPH. Of the remaining dogs, eight were diagnosed with BPH with overlying prostatitis, two with carcinoma with overlying prostatitis, and one each with BPH with an intraprostatic cyst BPH with an ossified intraprostatic abscess, and a periprostatic cyst. Statistical comparisons were made between the dogs diagnosed with carcinoma and BPH.

Difference in intact status as an aid in differentiation of disease type is significant, with $p < 0.0001$. Benign prostatic hyperplasia/hypertrophy was more common in intact than in castrated dogs; all 29 dogs diagnosed with BPH were intact. Prostatic carcinoma was more common in castrated than in

intact dogs; 54 of 57 dogs with carcinoma were castrated (94.7%). Mean age at diagnosis did not vary significantly between dogs diagnosed with BPH (7.9 ± 2.9 years [mean \pm SD]) and those diagnosed with carcinoma (10.2 ± 1.9 years).

Hematuria was defined grossly, either by owner description or as evidenced during urine collection, or by noting of RBCs in the urine sediment. Hematuria was noted as a clinical sign in 12 of 29 dogs with BPH (41.3%) and in 18 of 57 dogs with carcinoma (31.6%). Number of RBCs in urine sediment in dogs with BPH was on average much lower than that in dogs with carcinoma (3.3 ± 8.0 in 18 dogs versus 32.8 ± 28.8 in 28 dogs). Presence or absence of hematuria did not vary significantly between groups by either definition. Stranguria (painful urination) and dysuria (difficult or painful urination) were considered synonymous. Stranguria/dysuria was significantly more common in dogs with carcinoma (40.4% of 57 dogs) than in dogs with BPH (0 of 29 dogs; $p < 0.0001$). Dripping of serosanguinous or hemorrhagic fluid from the prepuce unassociated with urination was significantly more common in dogs with BPH (41.4% of 29 dogs) than in dogs with carcinoma (14.0% of 57 dogs; $p = 0.007$). Urinary incontinence and inappropriate urination did not differ significantly between the two groups; this clinical sign was reported in 10.3% of the dogs with BPH and in 15.8% of the dogs with carcinoma. Number of epithelial cells in urine sediment was higher in dogs with carcinoma (4.14 ± 3.6 , $n=28$) than in dogs with BPH (0.5 ± 0.8 , $n = 18$) but this difference was not significant.

Rectal tenesmus is straining to pass stool, which may be of varying consistency. In this population two of 29 dogs with BPH (6.9%) were reported to have tenesmus while 24 of 57 dogs with carcinoma (42.1%) were reported to have tenesmus. This difference is significant ($p = 0.0009$). Associated with this is passage of ribbon-shaped stools. None of the dogs with BPH and seven of the dogs with carcinoma (12.3%) were reported to pass soft, ribbon-shaped stools. This difference is not significant ($p = 0.09$). General systemic signs of disease that were reported included anorexia and weight loss, lethargy, hindlimb weakness and ataxia, and abdominal pain. These signs were significantly more common in dogs with carcinoma (35.1%) than in dogs with BPH (6.9%; $p=0.004$).

Mineralization of the prostatic parenchyma and regional lymph node enlargement were assessed using transabdominal ultrasound. Mineralization was noted in 32 of 49 dogs with carcinoma (65.3%) and in none of the 29 dogs with BPH; this difference is significant ($p < 0.0001$). Regional lymph node enlargement was noted in 24 of the dogs with carcinoma (49.0%) and in three of the dogs with BPH (10.3%); this difference also is significant ($p = 0.0002$).

Discussion

The primary limitations to this study were the study population and limitations in retrieving data based on varying use of the electronic medical record. The study was conducted at a veterinary teaching hospital. Dogs with BPH are less likely to be referred for diagnosis or care than are dogs with less common or higher morbidity prostate disorders, including prostatic neoplasia. It is possible that the results of this study reflect increased severity of disease in this specific population of dogs. The electronic medical record is a standard software product (Universal Veterinary Information System [UVIS]) and despite the fact that all faculty and house officers are trained to use the medical record in a specific way, historical data and laboratory results were saved in varying sites within the record. It is possible that not all data were found by the author, although a considerable amount of effort was put into completely evaluating all material available for each case.

Benign prostatic disease has not been reported in castrated dogs and was not identified in this study.^{20,38} Any dog that has been castrated at least three months prior to presentation should have prostatic atrophy and no clinical signs suggestive of prostatic disease.^{39,40} Any castrated male dog with prostatomegaly should be considered to have neoplasia. Similarly, dogs with stranguria or dysuria as a component of prostate disease should be considered to have neoplasia. Smooth muscle is not activated in dogs with prostate disease so any urethral obstruction is due to invasion of the urethra by neoplastic tissue.¹⁶ Because many owners will elect euthanasia at the time of diagnosis of prostatic neoplasia, definitive diagnosis by collection of samples for cytology or histopathology is strongly recommended. Techniques for collection of fine-needle aspirate cytology specimens and biopsy specimens for

histopathology have been described.⁴¹ Fine-needle aspirate is less invasive and correlates with histopathology diagnosis in 80% of cases.⁴²

The other parameters listed were significant in this study but were present in dogs with either condition. Some, for example mineralization of the prostatic parenchyma, also may be associated with prostatitis, which was not evaluated in this study, or with undiagnosed concurrent disease.^{39,43-45} Intact status of the dog and presence or absence of stranguria/dysuria are strong predictors permitting initial differentiation of BPH from prostatic neoplasia in dogs.

The history and diagnostic findings determined to be significantly associated with BPH rather than with prostatic neoplasia in dogs in this study were being sexually intact and dripping bloody fluid from the prepuce unassociated with urination. The history and diagnostic findings determined to be significantly associated with prostatic neoplasia rather than with BPH were being castrated, stranguria or dysuria, rectal tenesmus, systemic signs of disease, and mineralization of the prostate and regional lymph node enlargement visible with transabdominal ultrasound. Knowledge of these parameters guides further diagnostic testing and therapy (Figure).

Figure. Diagnostic key for dogs with prostatic enlargement and history of clinical signs suggestive of prostatic disease:

1. The dog is intact. Go to step 2.
- 1'. The dog was castrated \geq 3 months ago. Go to step 3.
2. The dog has any of the following clinical signs: stranguria/dysuria, rectal tenesmus, systemic signs of disease, mineralization of the prostate, regional lymph node enlargement. Go to step 3.
- 2'. The dog does not have any of the above clinical signs. Go to step 4.
3. The dog most likely has prostatic neoplasia. Overlying prostatitis may be present. Cytology or biopsy specimens should be collected for definitive diagnosis. Therapy is palliative.⁴⁶
4. The dog most likely has BPH. Cytology or biopsy specimens should be collected for definitive diagnosis. Overlying prostatitis may be present and should be assessed by culture of prostatic fluid or tissue. Castration is the most effective therapy for BPH. Medical therapy with finasteride is described.⁴⁶

References

1. Evans HE, Christensen GC: The urogenital system. In: Evans HE, ed. Miller's anatomy of the dog. Philadelphia: WB Saunders: 1993. p. 514-515.
2. Stefanov M, Martin-Alguacil N, Martin-Orti R: Distinct vascular zones in the canine prostate. *Micro Res Tech* 2000;50:169-175.
3. Stolzenburg J-U, Schwalenberg T, Do M, et al: Is the male dog comparable to human? A histological study of the muscle systems of the lower urinary tract. *Anat Histol Embryol* 2002;31:198-205.
4. Razvi HA, Muschter K, Anson JC, et al: Alteration of laser-tissue interaction with the 805 nm diode laser using indocyanine green in the canine prostate. *Las Surg Med* 1996;19:184-189.
5. Ayala AG, Ro JY, Babaian R, et al: The prostatic capsule: Does it exist? *Am J Surg Pathol* 1989;13:21-27.
6. Trevejo R, Yang M, Lund EM: Epidemiology of surgical castration of dogs and cats in the United States. *J Am Vet Med Assoc* 2011;238:898-904.
7. Chute CG, Panser LA, Girman CJ, et al: The prevalence of prostatism: a population-based survey of urinary symptoms. *J Urol* 1993;150:85-89.
8. Teske E, Naan EC, van Dijk EM, et al: Canine prostate carcinoma: Epidemiological evidence of an increased risk in castrated dogs. *Mol Cell Endocrinol* 2002;197:251-255.
9. Sjogren I, Sateri H: Prostate diseases of the dog—a retrospective study. *Svensk Vet* 1985;37:183-186.
10. 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.
11. Berry SJ, Strandberg JD, Saunders WJ, et al: Development of canine benign prostatic hyperplasia with age. *Prostate* 1986;9:363-373.
12. Issacs JT, Coffey DS: Changes in dihydrotestosterone metabolism associated with the development of canine benign prostatic hyperplasia. *Endocrinology* 1981;108:445-453.
13. Russell DW, Wilson JD: Steroid 5alpha reductase: two genes / two enzymes. *Ann Rev Biochem* 1994;63:25-61.
14. Brendler CB, Berry SJ, Ewing LL, et al: Spontaneous benign prostatic hyperplasia in the Beagle. Age-associated changes in serum hormone levels, and the morphology and secretory function of the canine prostate. *J Clin Invest* 1986;71:1114-1123.

15. Berry SJ, Coffey DS, Ewing LL: Effects of aging on prostate growth in Beagles. *Am J Physiol* 1986;250:R1039-1046.
16. Bruengger A, Bartsch G, Hollinger BE, et al: Smooth muscle cell of the canine prostate in spontaneous benign hyperplasia, steroid induced hyperplasia and estrogen or tamoxifen treated dogs. *J Urol* 1983;130:1208-1210.
17. Read RA, Bryden S: Urethral bleeding as a presenting sign of benign prostatic hyperplasia in the dog: A retrospective study (1979-1993). *J Am Anim Hosp Assoc* 1995;31:261-267.
18. Thrall MA, Olson PN, Freemyer FG: Cytologic diagnosis of canine prostatic disease. *J Am Anim Hosp Assoc* 1985;21:95-102.
19. Barsanti JA, Finco DR: Evaluation of the techniques for diagnosis of canine prostatic diseases. *J Am Vet Med Assoc* 1984;185:198-200.
20. Krawiec DR, Heflin D: Study of prostatic disease in dogs: 177 cases (1981-1986). *J Am Vet Med Assoc* 1992;200:1119-1122.
21. Garnick MB: The dilemmas of prostate cancer. *Sci Am* 1994;270:72-81.
22. Merlo DF, Rossi L, Pellegrino C, et al: Cancer incidence in pet dogs: Findings of the animal tumor registry of Genoa, Italy. *J Vet Intern Med* 2008;22:976-984.
23. Bryan JN, Keeler MR, Henry CJ, et al: A population study of neutering status as a risk factor for canine prostate cancer. *Prostate* 2007;67:1174-1181.
24. Obradovich J, Walshaw R, Goullaud E: The influence of castration on the development of prostatic carcinoma in the dog. *J Vet Intern Med* 1987;1:183-187.
25. Bell FW, Klausner JS, Hayden DW, et al: Clinical and pathological features of prostatic adenocarcinoma in sexually intact and castrated dogs: 31 cases (1970-1987). *J Am Vet Med Assoc* 1991;199:1623-1630.
26. Sorenmo KU, Goldschmidt M, Shofer F, et al: Immunohistochemical characterization of canine prostatic carcinoma and correlation with castration status and castration time. *Vet Comp Onco* 2003;1:48-56.
27. LeRoy BE, Northrup N: Prostate cancer in dogs: Comparative and clinical aspects. *Vet J* 2009;180:149-162.
28. Lai C-L, van den Ham R, van Leenders G, et al: Histopathological and immunohistochemical characterization of canine prostate cancer. *Prostate* 2008;68:477-488.
29. Durham SK, Dietze AE: Prostatic adenocarcinoma with and without metastasis to bone in dogs. *J Am Vet Med Assoc* 1986;188:1432-1436.
30. Leav I, Ling GV: Adenocarcinoma of the canine prostate. *Cancer* 1968;22:1329-1345.
31. Lee-Parritz DE, Lamb CR: Prostatic adenocarcinoma with osseous metastases in a dog. *J Am Vet Med Assoc* 1988;192:1569-1572.
32. Hargis AM, Miller LM: Prostatic carcinoma in dogs. *Compend Contin Educ Pract Vet* 1983;5:647-653.
33. Basinger RR, Rawlings CA, Barsanti JA, et al: Urodynamic alterations associated with clinical prostatic diseases and prostatic surgery in 23 dogs. *J Am Anim Hosp Assoc* 1989;25:385-392.
34. United States Preventive Services Task Force: Screening for prostate cancer. Available at: <http://www.uspreventiveservicestaskforce.org/uspstf08/prostate/prostaters.htm>, Accessed July 25, 2011.
35. Roehrborn CG, Bartsch G, Kirby R, et al: Guidelines for the diagnosis and treatment of benign prostatic hyperplasia: a comparative, international overview. *Urology* 2001;58:642-650.
36. Bell FW, Klausner JS, Hayden DW, et al: Evaluation of serum and seminal plasma markers in the diagnosis of canine prostatic disorders. *J Vet Intern Med* 1995;9:149-153.
37. Dube JY, Lazure C, Tremblay RR: Dog prostate arginine esterase is related to human prostate specific antigen. *Clin Invest Med* 1986;9:51-54.
38. Krawiec DR: Canine prostate disease. *J Am Vet Med Assoc* 1994;204:1561-1564.
39. Bradbury CA, Westropp JL, Pollard RE: Relationship between prostatomegaly, prostatic mineralization, and cytologic diagnosis. *Vet Radiol Ultrasound* 2009;51:167-171.
40. O'Shea JD: Studies on the canine prostate gland. I. Factors influencing its size and weight. *J Comp Pathol* 1962;72:321-331.
41. Root Kustritz MV: Collection of tissue and culture samples from the canine reproductive tract. *Theriogenology* 2006;66:567-574.
42. Powe JR, Canfield PJ, Martin PA: Evaluation of the cytologic diagnosis of canine prostatic disorders. *Vet Clin Pathol* 2004;33:150-154.
43. Feeney DA, Johnston GR, Klausner JS, et al: Canine prostatic disease—comparison of ultrasonographic appearance with morphologic and microbiologic findings: 30 cases (1981-1985). *J Am Vet Med Assoc* 1987;190:1027-1034.
44. Feeney DA, Johnston GR, Klausner JS, et al: Canine prostatic disease—comparison of radiographic appearance with morphologic and microbiologic findings: 30 cases (1981-1985). *J Am Vet Med Assoc* 1987;190:1018-1026.
45. Vignoli M, Russo M, Catone G, et al: Assessment of vascular perfusion kinetics using contrast-enhanced ultrasound for the diagnosis of prostatic disease in dogs. *Reprod Domest Anim* 2011;46:209-213.
46. Smith J: Canine prostatic disease: a review of anatomy, pathology, diagnosis, and treatment. *Theriogenology* 2008;70:375-383.