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Contrast-enhanced ultrasonographic characteristics of the diseased canine prostate gland

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ABSTRACT

The work was carried out on a total of 26 male dogs that on the basis of clinical examination, prostate ultrasound and prostate biopsy, were divided prospectively into four groups: (1) normal dogs (control group; n = 8); (2) dogs with benign prostatic hyperplasia (group BPH; n = 8); (3) dogs suffering from prostatitis (group prostatitis; n = 4); (4) dogs with prostatic tumors (group tumors; n = 6). The examination of the prostate by means of contrast medium and dedicated ultrasound system allowed a detailed qualitative and quantitative analysis of prostatic vessels in normal and diseased conditions, enabling the detection and characterization of different disease states, and quantification of parameters such as peak intensity of perfusion (%), arrival time of the contrast medium to its maximum value of video intensity (time to peak [TTP; seconds]), regional blood volume, regional blood flow, and mean transit time (MTT [seconds]). The hemodynamic indices TTP ($P < 0.01$) and MTT ($P < 0.001$) of diseased prostate groups were significantly lower than those in the normal prostate group although there were no differences among diseases. Optimal cutoff values were 31 seconds (Sensitivity: 72%; Specificity: 88%) and 47 seconds (Sensitivity: 100%; Specificity: 88%) while area under receiver operating characteristic curves were 0.86 ($P < 0.01$) and 0.97 ($P < 0.01$) for TTP and MTT, respectively. The qualitative evaluation of vascular patterns showed differences between normal and diseased prostate glands. The latter were characterized by an alteration of the normal vascular appearance consisting of loss of the subcapsular arterioles and lack of a centripetal vascular pattern. The qualitative aspect of the study highlighted the different vascular architecture between BPH, prostatitis, adenocarcinoma, and lymphoma. This study shows how contrast-enhanced ultrasound represents a valid and noninvasive method for highlighting and characterizing prostatic vasculature. Furthermore, it allows the operator to obtain qualitative and quantitative data that are useful for the diagnosis of selected prostatic diseases. In conclusion, contrast-enhanced ultrasound can be a valuable noninvasive diagnostic tool to improve the diagnostic accuracy of prostate diseases in the dog.

1. Introduction

Pathologic conditions affecting the canine prostate gland are frequently seen in small animal practice [1]. The most common prostatic diseases are benign prostatic hyperplasia (BPH), prostatitis, abscesses, cysts, paraprostatic cysts, and more rarely squamous metaplasia and neoplasia. In particular, BPH accounts for more than 50% of cases, whereas infection is less than 20%, neoplasia 7%, and squamous metaplasia less than 2% [2,3]. The common clinical signs of prostatic diseases include dysuria and hematuria, hemospermia/pyospermia, tenesmus, abdominal

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pain, stiff gait, and sepsis [4]. As the clinical signs often overlap, it is important to reach a definitive diagnosis before initiating treatment [1]. Moreover, subclinical prostatic disease appears to be common. Mukaratirwa and Chitura [5] reported a histologic prevalence of 75.6% of subclinical prostatic disorders in dogs dead for diseases not related to the prostate. In particular, the most common diseases comprising BPH (44.8%), prostatitis (23.6%), and prostatic neoplasia (3.6%).

Both the absence of specific signs and the high incidence of subclinical patients make it challenging to differentiate prostatic enlargement, infection, and neoplasia in dogs. Ultrasonography is the gold standard of the complementary diagnostic techniques used to assess the prostate. It allows differentiation of focal or diffuse heterogenous echogenicity, prostatomegaly, or cystic changes [6]. Furthermore, the size and appearance of the prostate can be determined and followed over time [7]. However, the ultrasonographic appearance of a prostatic cyst or abscess may be similar to prostatic carcinoma and diagnosis must be confirmed by prostatic fluid analysis and/or biopsy [8]. Doppler ultrasonography allows the evaluation of prostatic vasculature and blood flow in both physiological and pathologic conditions [9–11]. However, it is difficult to obtain an accurate assessment of the perfusion patterns at a microvascular level because of the Doppler's limitation in evaluating slow blood flow in microvessels or deep blood vessels [9]. The recent introduction of microbubble contrast agents for contrast-enhanced ultrasound (CEUS) and the development of contrast harmonic software have overcome these limitations. The microbubbles can perfuse the microcirculatory bed [12] and amplify the ultrasound signal [13]. In veterinary medicine, CEUS has been used primarily for the study of the liver [14], spleen [15], kidneys [16], pancreas [17], lymph nodes, and adrenal glands [18]. Analysis of the vascular pattern has been shown to allow differentiation between benign and malignant nodules in the liver of dogs [14].

The contrast agent distribution allows the evaluation and description of vascular perfusion, along with the quantification of hemodynamic parameters using dedicated image analysis software (Qontrast; Bracco, Milan, Italy). The quantitative hemodynamic parameters are the percentage increase in signal intensity (SI), from baseline intensity to maximal SI (peak intensity of perfusion [PPI; %]); the time of arrival of the ultrasound contrast agent to its maximum SI (time to peak [TTP; seconds]); the time lapse between half of the maximum SI of the contrast agent in the ascending phase of the curve (wash-in) and the same value of the SI in the descending phase (wash-out; mean transit time [MTT; seconds]); the integral of the video SI (%) changes during the extrapolated transition time without recirculation (regional blood volume [RBV]); and the ratio between regional blood volume and MTT (regional blood flow [RBF]).

A few publications describe the use of CEUS to investigate normal [19,20] and diseased [21,22] canine prostate glands. However, the contrast agent perfusion has not been assessed for all hemodynamic parameters. In these studies, the dogs underwent general anesthesia, which is known to modify blood flow hemodynamics. For example, the most significant cardiovascular effect of propofol is hypotension because of a decrease in cardiac output, myocardial contractility, ejection fraction, and systemic vascular resistance. Furthermore, all gas anesthetic agents depress myocardial contractility [23,24].

Consequently, we wished to analyze the qualitative prostatic vascular patterns in physiological and pathologic conditions of dogs not submitted to general anesthesia and to determine whether the quantitative hemodynamic indices could be used as markers for some prostatic diseases.

2. Materials and methods

2.1. Animals

All dogs used in this study were required to have informed owner consent, and all procedures were performed in accordance with the Italian laws on animal care. In this study, 26 male multibreed dogs were followed over 24 months (from October 2011 to September 2013). Eight dogs aged between 2 and 4 years, with an average weight of 29.3 kg, were considered clinically healthy with proven fertility. Eighteen dogs aged between 4 and 14 years, with an average weight of 25.1 kg, had a history of different prostatic diseases. The dogs recruited for this study underwent a standardized protocol that included clinical examination, serum chemistry profile, complete blood cell count and urinalysis (data not shown), CEUS and B-mode ultrasound examination of the prostate, and an ultrasound-guided biopsy of the prostate using a TruCut needle. On the basis of the clinical and histologic findings, the dogs were divided into different groups.

2.2. B-mode ultrasound examination

The dogs were positioned in lateral recumbency or in a quadrupedal position for examination. A B-mode ultrasound with linear (4–13 MHz) and microconvex transducers (6.6–8.0 MHz) was used to obtain scans of the prostatic gland. The prostate was evaluated according to its size, margins, echogenicity, echotexture, and integrity of the capsule.

2.3. Contrast-enhanced ultrasonography

All scanning procedures were performed without general anesthesia. The dogs were positioned in lateral recumbency, and a MyLab 70 XVision Gold machine equipped with contrast-tuned imaging technology module was used. To avoid rupture of the microbubbles, a linear transducer (3–8 MHz) with low mechanical index (0.13) was used. The ultrasound contrast agent used was the sulfur hexafluoride echo-signal enhancer (SonoVue Bracco system, Milano, Italia). In each dog, a bolus dose (0.03 mL/kg of body weight) of the freshly prepared contrast agent was rapidly infused into the cephalic vein through an 18-ga three-way valve catheter, and immediately followed by a 5-mL isotonic saline flush. Two experienced operators performed the procedures. The first operator injected the contrast medium through the catheterized vein, whereas the second performed the ultrasound scans.