

RESEARCH ARTICLE

The Effect of Systemic Hypertension on Prostatic Arterial Hemodynamics in Dogs with Benign Prostate Hyperplasia

Çağatay ESİN¹ (*) ¹ Department of Internal Medicine, Faculty of Veterinary Medicine, Ondokuz Mayıs University, TR-55200 Samsun - TÜRKİYE

(*) Corresponding authors:

Çağatay ESİN

Cellular phone: +90 546 2003326

E-mail: cagatay.esin@omu.edu.tr

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Abstract

This study aimed to examine how systemic hypertension impacts resistance indices in the prostate artery by comparing ultrasonographic assessments of the prostate gland between normotensive and hypertensive dogs with benign prostatic hyperplasia (BPH). Dogs presenting with symptoms such as frequent urination, painful urination, and blood in the urine, and diagnosed with BPH, were divided into two groups: normotensive and hypertensive, with each group consisting of ten dogs. Blood pressure measurements, as well as B-mode and Doppler ultrasonographic evaluations, were conducted. The mean age for the normotensive and hypertensive groups were 9.80±1.81 and 11.10±1.79 years, respectively. The mean weight for the normotensive and hypertensive groups were 27.60±6.02 and 29.00±4.00 kg, respectively. The mean prostate volume for the normotensive and hypertensive groups were 22.35±2.76 and 22.78±2.35 years, respectively (P=0.708). Dogs with BPH who also had hypertension exhibited significantly higher resistive indices in the prostate arteries compared to those with BPH who were normotensive (P<0.001). While the RI value was 0.76±0.03 in BPH dogs with hypertension, the RI value was 0.62±0.05 in normotensive BPH dogs (P<0.001). Finally, in veterinary practice, when dealing with a hypertensive patient, it is important to consider potential risk factors for prostatic vascular dysfunction. Additionally, the possibility of clinically significant BPH in hypertensive patients should be considered, and appropriate diagnostic tests should be conducted.

Keywords: Benign prostatic hyperplasia, Doppler ultrasonography, Hypertension, Resistive index

INTRODUCTION

Systemic hypertension (SH) refers to the abnormal and persistent increase in the pressure exerted by arterial blood on the vascular walls and the organs supplied by these vessels^[1]. In veterinary medicine, SH is classified into 3 categories. These are situational, secondary and idiopathic systemic hypertension^[2]. In current guidelines, normotensive systolic and diastolic pressure in cats and dogs are accepted as 120-130 and 60-90 mmHg, respectively^[3,4]. However, it has been reported that systolic pressure higher than 150 mmHg increases the risk of target organ damage. For this reason, senior life recommends measuring blood pressure in dogs and cats at some stage and performing detailed examination in all animals with blood pressure more than 150 mmHg^[5].

Benign prostatic hyperplasia (BPH) is the most common prostate disease affecting male dogs and develops spontaneously as glandular hyperplasia^[6,7]. It

is most often the result of aging and increased levels of dihydrotestosterone (DHT) in unspayed male dogs, which causes an increase in the size (hypertrophy) and number (hyperplasia) of prostate epithelial cells (hyperplasia: main mechanism in dogs), forming BPH^[8,9]. Methods used to diagnose BPH include anamnesis, clinical findings, physical examination, rectal palpation of the prostate contour, radiographic measurement of prostate size, ultrasonographic measurement of prostate volume and parenchyma, ultrasound-guided fine needle aspiration, and excisional biopsy^[10]. Since BPH and many other prostate diseases are associated with enlargement of the prostate, measuring prostate size is very important for diagnosis^[11]. Ultrasonography is the most important diagnostic method of choice to examine the prostate and allows assessing both the size of the gland and the homogeneity of its parenchyma^[12]. In addition, ultrasonographic examination provides information about the shape, contour, echogenicity and symmetry of the prostate and also provides information about



the adjacent soft tissue [13]. In recent years, the resistive index (RI) of the prostatic artery measured by Doppler ultrasonography has been used to evaluate patients with BPH, and RI has been reported to be increased in dogs with BPH [14-16].

Research in human medicine shows that systemic hypertension (SH) is involved in the etiology of BPH [17,18]. Additionally, BPH symptom scores have been reported to be higher in BPH patients with SH compared to healthy men [19]. The prevalence of SH and BPH are both emerging as a function of increasing age [18]. However, some studies have shown that, regardless of age, patients with symptoms of cardiovascular disease/atherosclerosis/hypertension are at much higher risk for BPH than those without the disease [20]. Systemic vascular dysfunctions may specifically affect the prostate gland [21]. The vascular system of the prostate is an important component of prostate growth and regulation, and therefore the idea was developed that dysfunction of blood flow in the prostate gland is involved in causing and controlling BPH [22].

The aim of this study was to find out whether there is a significant difference between the prostatic arterial resistive indexes of systemic hypertension dogs with BPH and the prostatic arterial resistive indexes of normotensive dogs with BPH. We hypothesized that the prostatic arterial resistive index would be significantly higher in systemic hypertension dogs with BPH than normotensive dogs with BPH.

MATERIALS AND METHODS

Ethical Statement

This study was approved by the Ondokuz Mayıs University, Animal Experiments Local Ethics Committee (Approval no: E-68489742-604.01-2400102486). In addition, an Informed Consent Form (for each patient) was obtained from dog owners.

Animal and Groups

Twenty dogs belonging to clients at the Ondokuz Mayıs University Veterinary Hospital were included in this study. In the control group, 10 patients with different breeds; the breeds were mixed-breed dogs (n=4), Golden retrievers (n=2), English setter (n=1), German pointer (n=1), Siberian husky (n=1), and Belgian shepherd (n=1). In the study group, 10 patients had different breeds; the breeds were mixed-breed dogs (n=3), Golden retrievers (n=2), German shepherds (n=3), and Labrador retrievers (n=2). Dogs presenting with symptoms such as frequent urination, painful urination, constipation, and blood in the urine, and diagnosed with BPH, were divided into two groups: normotensive BPH and hypertensive BPH group, with each group consisting of ten dogs. Also, the

study group (hypertensive BPH) consisted of 10 dogs with BPH diagnosed with hypertension that presented to our hospital with blood pressure problems (nervous system symptoms such as dilated eyes, depression, head tilt, weakness, heart murmurs, or abnormal heart rhythm symptoms). The control group (normotensive BPH) consisted of 10 dogs with BPH without any disease other than the diagnosis of BPH.

Hematological and serum biochemical analyses were performed on dogs to exclude infection, metabolic or other diseases. Four dogs with infection, metabolic or other diseases were excluded from the study. Limitations of this study are that the marker of BPH was not supported by biopsy and hormonal imbalances involving dihydrotestosterone (DHT), estrogen, and testosterone were not determined in the formation and progression of BPH.

Study Design

Inclusion in the hypertensive group (systemic hypertension) was determined based on documentation in the medical record of an elevated blood pressure in the range for systemic hypertension. Systolic blood pressure was measured in all dogs using the Doppler Blood Pressure System method (Vet-Dop2, USA, Vmed Technology, Washington) placed between the tarsal and metatarsal pad of the hind limb (Fig. 1). The final value of systemic blood pressure (SBP) was the mean value of 5 consecutive consistent measurements after, at least, 5 min acclimation period and before performing any other procedure. Systemic hypertension was classified as mild (150-159 mmHg), moderate (160-179 mmHg), or severe >180 mmHg [2]. Animals were included in the hypertensive group when SBP was ≥ 150 mmHg. The same investigator included dogs in the control group if they had a recorded normal blood pressure (less than 150 mmHg).

Prostatic ultrasonographic evaluation was performed from the abdominal region with a Mindray Vetus 9 color Doppler ultrasound device and a microconvex probe 6.5-7.5 MHz transducer. Dogs were placed in dorsal recumbency and caudal abdominal region was sheaved before ultrasonographic scanning [23]. Prostatic volume (PV) was evaluated by B-mode ultrasonography using the bladder as a window, measuring height and length in the sagittal plane and width in the axial plane (Fig. 2). PV was calculated using the formula: $PV \text{ (cm}^3\text{)} = 0.487 \times L \times W \times (DL + DT) : 2 + 6.38$ (L=length; DL=depth on longitudinal section; DT=depth on transverse section; W=width) [24]. The expected prostate volume (EPV) was used to predicted the prostatic volume according to the dog weight, i.e., a prostatic volume control for each dog body weight, considering the following formula: $EPV = 8.48 + (0.238 \times \text{Kg body$



Fig 1. Systolic blood pressure obtained while lying in a lateral position using Vet-Dop2. This dog's systolic blood pressure was 175

weight) [24,25]. Prostatic tissue perfusion and blood flow velocity of the prostatic artery were evaluated by Doppler ultrasonography (Fig. 3). Prostatic artery was scanned at the hypogastric abdominal region and located cranio-dorsal to the prostate gland [22,26,27]. The size of the sample volume, which determines Doppler information, was kept constant at 1 mm. Color flow Doppler was used to map the vessel and subsequently pulsed-wave Doppler was used to characterize the waveform. Blood sample volume was positioned at the artery center and all measurements were obtained with an angle of $\leq 60^\circ$, making proper angle correction whenever necessary. A total of 6 stable waves of the prostatic artery were obtained to calculate the average of each variable. Spectral waveform analysis was performed after the blood flow samplings were performed. Thereby, the mean values of RI, and PI ratio were calculated after 3 consecutive measurements were performed. The following blood flow velocity parameters were automatically calculated by the Doppler machine software, using mathematical formulas or Pourcelot index: peak systolic velocity (PSV), end diastolic velocity (EDV), resistance index [$RI=(PSV-EDV)/PSV$], pulsatility index [$PI=(PSV-EDV)/\text{mean velocity}$], time average maximum velocity (TAMAX) and peak systolic: diastolic velocity [$S/D=(PSV/EDV)$]. Analysis was performed always by only one analyzer.

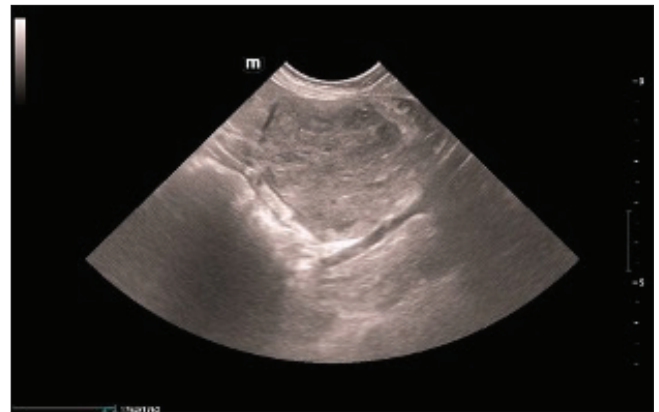


Fig 2. B-mode imaging of a benign prostatic hyperplasia. Hyperechoic parenchyma and enlarged prostate



Fig 3. Longitudinal ultrasound image obtained in right lateral recumbency using Mindray Vetus 9. This dog presented with systolic blood pressure of 180, and a prostatic arterial RI of 0.85

Statistical Analysis

The data were analyzed using the IBM SPSS Statistics for Windows (IBM Corp., Armonk, N.Y., USA). Means and standard deviation were obtained for the continuous variables. Quantitative data were assessed for normality using the Kolmogorov-Smirnov test, Shapiro-Wilk test, and direct data visualization methods. Quantitative data were compared between the study groups using independent t-test for normally distributed quantitative variables. P values less than 0.05 were considered significant. Correlations between measured variables were evaluated with Pearson correlation coefficient.

RESULTS

No significant difference was found between the groups in terms of age, weight and prostate volumes. However, there was a significant difference ($P<0.001$) in systolic and diastolic blood pressure between the hypertensive and normotensive BPH groups (Table 1).

When hemodynamic changes between the two groups were examined; PSV in the hypertensive BPH group was

Table 1. Age, weight, prostate volume and blood pressure findings of the control and study groups

Parameters	Normotensive BPH Group Mean±S.D.	Hypertensive BPH Group Mean±S.D.	P Value
Age (years)	9.80±1.81	11.10±1.79	0.548
Weight (kg)	27.60±6.02	29.00±4.00	0.124
PV (cm ³)	22.35±2.76	22.78±2.35	0.708
EPV (cm ³)	15.04±1.43	15.37±0.95	0.548
SBP (mmHg)	124.00±6.14	179.50±4.97	<0.001
DBP (mmHg)	84.00±3.94	103.00±6.32	<0.001

PV: prostatic volume; EPV: expected prostatic volume; DBP: diastolic blood pressure; SBP: systolic blood pressure

Table 2. Prostatic arterial Doppler hemodynamic findings of the control and study groups

Parameters	Normotensive BPH Group Mean±S.D.	Hypertensive BPH Group Mean±S.D.	P Value
PSV (cm/s)	16.21±2.15	23.03±3.42	<0.001
EDV (cm/s)	5.99±1.06	5.35±1.18	0.215
RI	0.62±0.05	0.76±0.03	<0.001
PI	1.06±0.11	1.34±0.07	<0.001

PSV: peak systolic velocity; EDV: end diastolic velocity; RI: Resistive Index; PI: Pulsatility Index

Table 3. Correlation of PV, PSV, EDV, RI and PI of benign prostatic hyperplasia dogs (n=20) with other parameters

Parameters	PV (cm ³)		PSV (cm/s)		EDV (cm/s)		RI		PI	
	r	P Value	r	P Value	r	P Value	r	P Value	r	P Value
Age (years)	-0.005	0.983	0.302	0.196	0.255	0.278	0.050	0.835	0.271	0.247
Weight (kg)	0.881*	<0.001	0.235	0.318	0.245	0.298	-0.027	0.910	0.032	0.893
SBP (mmHg)	0.109	0.647	0.833*	<0.001	-0.265	0.259	0.866*	<0.001	0.878*	<0.001
DBP (mmHg)	0.203	0.391	0.773*	<0.001	-0.186	0.434	0.740*	<0.001	0.748*	<0.001
PV (cm ³)	1	NA	0.212	0.369	0.180	0.448	0.014	0.952	0.162	0.496
PSV (cm/s)	0.212	0.369	1	NA	0.176	0.458	0.670*	0.001	0.752*	<0.001
EDV (cm/s)	0.180	0.448	0.176	0.458	1	NA	-0.603*	0.005	-0.275	0.240
RI	0.014	0.952	0.670*	0.001	-0.603*	0.005	1	NA	0.826*	<0.001
PI	0.162	0.496	0.752*	<0.001	-0.275	0.240	0.826*	<0.001	1	NA

* statistically significant; -: negative correlation; PV: prostatic volume; PSV: peak systolic velocity; EDV: end diastolic velocity; RI: Resistive Index; PI: Pulsatility Index; SBP: systolic blood pressure; DBP: diastolic blood pressure; NA: not applicable

higher than the normotensive BPH group, and this was found to be a significant difference (P<0.001). RI and PI were significantly higher (P<0.001) in the hypertensive BPH group than in the normotensive BPH group. No significant difference was found between the groups in terms of EDV (Table 2).

A positive correlation was found between weight and prostatic volume, systolic blood pressure and peak systolic

velocity, diastolic blood pressure and peak systolic velocity, systolic blood pressure and resistive index. Also positive correlation was found diastolic blood pressure and resistive index, peak systolic velocity and resistive index, systolic blood pressure and pulsatility index, diastolic blood pressure and pulsatility index, peak systolic velocity and pulsatility index, resistive index and pulsatility index. Resistive index and Pulsatility index were also positively

correlated with peak systolic velocity. It was noted that there was a negative correlation between the resistive index and end diastolic velocity (*Table 3*).

DISCUSSION

In this study, prostatic hyperplasia (PH) and prostatic arterial hemodynamics were investigated in hypertensive and normotensive dogs.

The relationship between SH and BPH first emerged in the field of human medicine in 1966 when the etiologic similarities of these two diseases were reported and has been studied for more than 50 years [17]. Furthermore, the pathogenesis of BPH is still unclear, possibly due to a number of complex mechanisms. This aspect is a current issue that is attracting the attention of more researchers.

Systemic hypertension appears to play a specific role in the pathogenesis of BPH through both static and dynamic components. Systemic vascular dysfunction can affect the prostate gland and cause dysfunction of blood flow in the prostate gland. Systemic hypertension has been proven to have a higher prevalence of BPH and lower urinary tract symptoms (LUTS) in humans, in various animal models and in epidemiologic studies [28].

Studies in human medicine have reported that prostatic arterial RI is higher in patients with hypertension than in normotensive men [29]. A previous study has shown that hypertensive men have more severe urinary tract symptoms and are more prone to prostatomegaly than normotensive men [30]. Hammarsten et al. [28] reported that individuals with treated hypertension had a larger prostate volume and higher BPH growth rate than normotensive individuals.

In addition, the relationship between SH and PH has also been supported by studies in veterinary medicine using animal models. Spontaneously hypertensive rats (SHR), an animal model of systemic hypertension, have been found to exhibit abnormal lower urinary tract function similar to patients with BPH [31]. In a different study, it was reported that SHR rats with prostatic hyperplasia had increased development of glandular epithelium of the prostate. SHR rats were found to develop BPH-like features in the absence of any inductive exogenous agent. Conversely, normotensive rats were reported not to develop such features [32].

Statistical differences were found between the targeted parameters in SH dogs in the study. There are many proposed mechanisms to link the development of hypertension and BPH, such as age and weight [18,33]. Weight and age were kept similar in the groups of dogs presented in the study. Age is associated with hypertension and BPH, as found in a previous study [18]. An age-related increase in BPH in dogs is also well known,

so age and weight differences were eliminated between the groups of dogs in the study to ensure that age and weight were not a factor in the development of BPH in hypertensive dogs [34]. In addition, a study has determined that there is a significant, age-independent relationship between BPH symptoms and hypertension. This finding points to a common pathophysiological factor for both disease states, such as increased sympathetic activity [19]. Consistent with previous findings, our current study showed that hypertension can often be accompanied by BPH or changes in prostatic arterial hemodynamics. In a 2023 study [29], patients with BPH and hypertension had significantly higher prostate artery resistance indices than normotensives with BPH. Even in patients with BPH and controlled hypertension, prostate artery resistance indices were still higher than normotensive men with BPH. The incidence of BPH may be significantly increased in dogs with hypertension. Prostatic arterial hemodynamics may be impaired in hypertensive dogs and it is suggested that hypertension may be an important factor influencing the incidence of BPH. We suggest future large-scale studies to further confirm our results.

In conclusion the studies presented, it was concluded that diabetes mellitus, hypertension, obesity, ischemic heart disease, excessive carbohydrate and fat intake, hyperinsulinemia, insulin resistance and dyslipidemia are risk factors in the development of BPH [29,33,35]. In addition, vascular dysfunctions are known to specifically affect the prostate gland [21]. In veterinary medicine, when confronted with a hypertensive patient, the possible presence of risk factors for dysfunction of the prostatic vascular system should be considered. The possibility of a clinically significant BPH in hypertensive patients should also be kept in mind and necessary examinations should be performed.

DECLARATIONS

Availability of Data and Materials: The datasets during and analysed during the current study available from the corresponding author (Ç. Esin) on reasonable request.

Funding Support: There is no funding source.

Competing Interest: The author declared that there is no conflict of interest.

Ethical Approval: This study was approved by the Ondokuz Mayıs University, Animal Experiments Local Ethics Committee (Approval no: E-68489742-604.01-2400102486).

Declaration of Generative Artificial Intelligence (AI): The author have declared that the article, tables and figure were not written/created by AI and AI-assisted technologies.

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