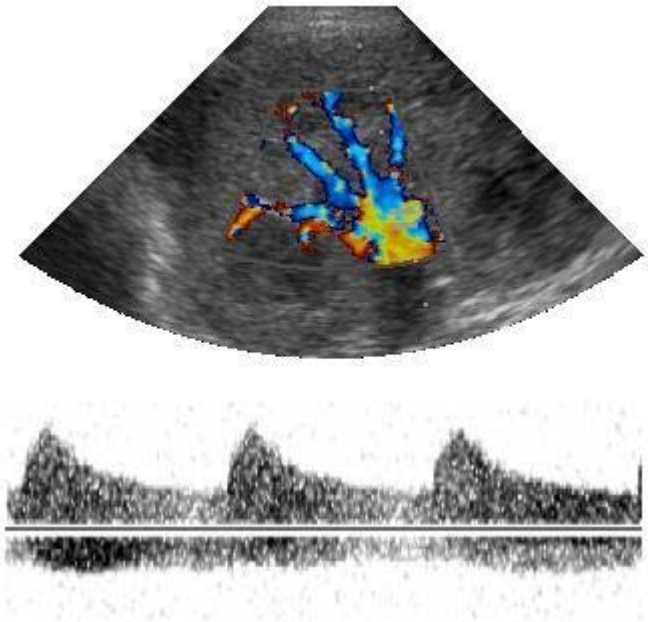
VASCULAR RESISTANCE DETERMINATION WITH DOPPLER ULTRASOUND IN CANINE AND FELINE DISEASE

(DETERMINACIÓ DE RESISTÈNCIA VASCULAR MITJANÇANT ECOGRAFIA DOPPLER EN PATOLOGIA CANINA I FELINA)



PhD Thesis

Rosa Novellas Torroja

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Departament de Medicina i Cirurgia Animals

Facultat de Veterinària

Universitat Autònoma de Barcelona

VASCULAR RESISTANCE DETERMINATION WITH DOPPLER ULTRASOUND IN CANINE AND FELINE DISEASE

(DETERMINACIÓ DE RESISTÈNCIA VASCULAR MITJANÇANT ECOGRAFIA DOPPLER EN PATOLOGIA CANINA I FELINA)

Memòria presentada per

Rosa Novellas Torroja

per a optar al grau de

Doctor en Veterinària

Directora de la tesis: Yvonne Espada Gerlach

Yvonne Espada Gerlach, Professora Titular del Departament de Medicina i Cirurgia Animals de la Facultat de Veterinària de la Universitat Autònoma de Barcelona

CERTIFICO:

Que la tesi doctoral que porta per títol: *VASCULAR RESISTANCE DETERMINATION WITH DOPPLER ULTRASOUND IN CANINE AND FELINE DISEASE, (DETERMINACIÓ DE RESISTÈNCIA VASCULAR MITJANÇANT ECOGRAFIA DOPPLER EN PATOLOGIA CANINA I FELINA)*, de la que n'és autora la llicenciada en Veterinària **Rosa Novellas Torroja**, s'ha realitzat a la Facultat de Veterinària de la Universitat Autònoma de Barcelona sota la meva direcció.

I perquè així consti, a efectes de ser presentada com a Tesi Doctoral per a optar al títol de Doctor en Veterinària, signo aquest certificat.

Bellaterra, 17 d'octubre de 2007

Agraïments

Vull donar les gràcies a totes les persones que han fet possible aquesta tesis, tant a les que hi han participat activament com les que simplement han estat amb mi i m'han recolzat fent que això arribés a bon port.

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Index

Abbreviations

ALKP: alkaline phosphatise

ALT: Alanine amino transferasa

ARF: acute renal failure

CRF: chronic renal failure

DM: diabetes mellitus

GGT: gamma glutamil transferasa

HA: hyperadrenocorticism

HR: heart rate

PI: pulsatility index

PKD: polycystic kidney disease

RI: resistive index

SBP: systolic blood pressure

TAMX: time average maximum velocity

Introduction

Organs with a rich arterial blood supply such as the kidneys, the eyes, the heart, and the brain are more sensitive to blood pressure changes.

Renal disease and hypertension are intimately related. Renal disease can lead to sodium and water retention and resultant extracelular fluid volume expansion. This increases cardiac output producing systemic hypertension. Furthermore, activation of the renin-angiotensin-aldosterone system and other neurohormonal disorders common in renal disease may further elevate systemic arterial blood pressure. On the other hand, high blood pressure causes glomerular hypertension and hyperfiltration, proteinuria, and arteriosclerosis completing this vicious cycle through self-perpetuating renal damage.[1]

In the eye, lesions associated with hypertension are typically a result from failure in vascular autoregulation of the retinal arteries. In response to increases in blood pressure, retinal arterioles undergo vasoconstriction. With chronic vasoconstriction, vascular smooth muscle cells have diminished contractile function and develop fibrous changes. Progressive degenerative changes in the vessel wall lead to rupture of the endothelial and muscle cells, with leakage of blood and serum into the retinal tissue and account for the effusive lesions characteristic of hypertensive retinopathy.[2]

Evaluating the relationship between arterial blood pressure and peripheral vascular resistance in the kidney and the eye in animals with hypertension or with diseases related with hypertension may be of interest to assess if correlation exists between hypertension and increased vascular

resistance. Peripheral vascular resistance can be indirectly evaluated by Doppler ultrasonography.

1. *Doppler ultrasonography*

Ultrasonography is an imaging diagnostic technique widely used in small animal clinical practice. Ultrasound is characterized by sound waves with a frequency higher than the upper range of human hearing (20 kHz).[3] It is characterized by being a non-invasive cheap technique that can be usually performed without chemical restrain.

B-mode (brightness mode) ultrasound provides information about shape architecture, location, and size of body structures. It also permits evaluation of moving structures such as the heart or gastrointestinal tract and it is used to guide fine needle aspirations or biopsy. It is, however, a low sensitive and specific technique because if a lesion is not seen, pathology can not be ruled out in some conditions and the ultrasonographic appearance of many lesions is not specific. Obtaining a histological sample is necessary, in many cases, to reach a definitive diagnosis.

Colour Doppler, power Doppler, pulsed wave Doppler and contrast enhanced ultrasonography may be helpful to differentiate and further characterize some lesions. Doppler ultrasound provides information about the presence or absence of flow within a tubular structure and therefore makes differentiation between vascular and non-vascular structures possible. Flow

appearance also provides information about the type of vessel (arterial *versus* venous), flow direction and its relative or absolute velocity. Velocity may be quantified and its variations through the cardiac cycle recorded.

1.1. Doppler effect

The Doppler effect was described by Johann Doppler in 1842 and results from the shift in sound frequency that a sound wave experiments when the transmissor and / or the receptor of the sound are moving with respect to the propagation media. During ultrasound examination, the sound wave is transmitted by the transducer and when it interacts with the moving blood cells, the frequency shifts and comes back to the transducer with a higher frequency (if the flow is towards the transducer) or a lower frequency (if the flow is away from the transducer). The difference between the frequency of the transmitted and the reflected sound is called Doppler shift. The Doppler shift will be higher with increasing velocity[4] (Figure 1).

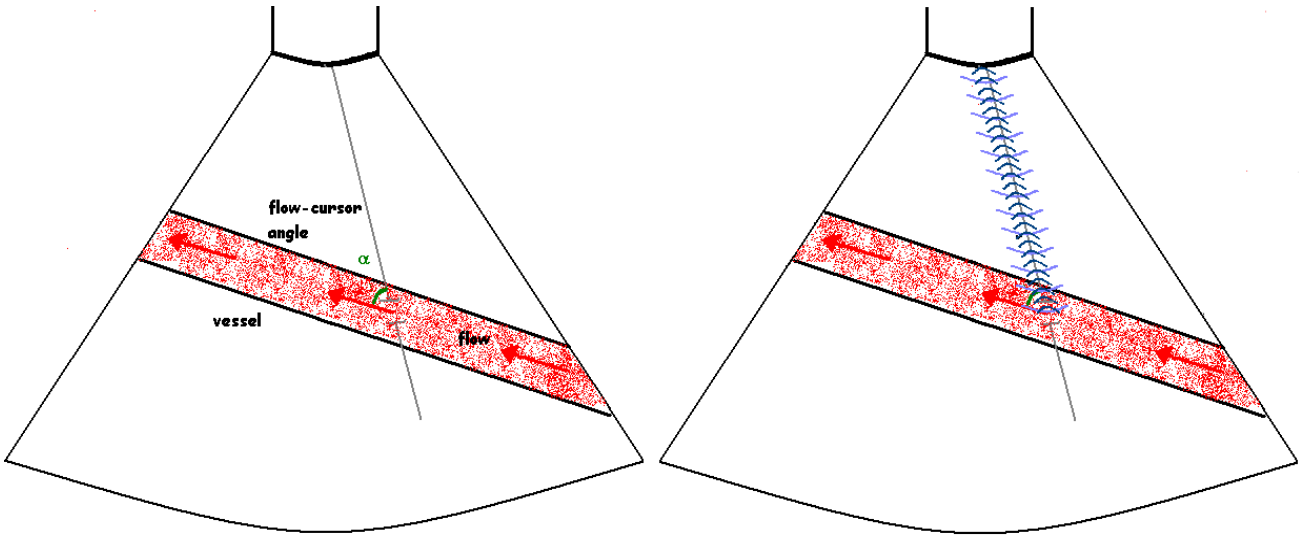

Figure 1. Pulsed Doppler ultrasound applied in a vessel.

When the direction of reflector movement forms an angle with respect of the transducer axis, the Doppler shift (f_s) is calculated as:

$$f_s = f_t - f_r = f_t \, 2.u.cos\theta / c$$

where

f_t is the transmitted frequency

f_r is the received frequency

c is the ultrasound velocity (considered constant in soft tissues, 1540 m/s)

u is the blood velocity, and

θ is the angle between the beam and flow direction.

This equation is usually rearranged to calculate blood cells velocity:

$$u = f_s \, c \, / \, 2 f_t \, cos\theta$$

This velocity is displayed with pulsed Doppler as a spectrum where velocity is set in the vertical axis and time is displayed in the horizontal axis.

Flow measurements providing indirect information of peripheral vascular resistance can be obtained from this spectral display. Some indices have been developed to estimate vascular resistance and to evaluate and compare Doppler waveforms. These indices can be calculated from ratios

including peak systolic velocity, end diastolic velocity, and mean velocity through the cardiac cycle (or time averaged maximum velocity)[5] (Figure 2).

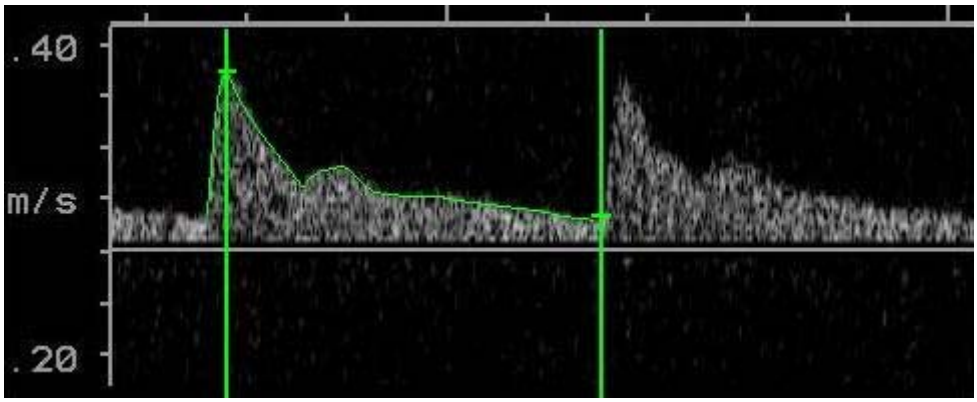

Figure 2. Pulsed Doppler display showing determination site for peak systolic velocity (cursor at the left of the image), end diastolic velocity (cursor at the right of the image) and mean velocity through the cardiac cycle (continuous line delineating the waveform).

The resistive (or Pourcelot) index and the pulsatility index are two of the indices most commonly used.

Resistive index is calculated as:

$$RI = \frac{V_{max} - V_{min}}{V_{max}}$$

And ***pulsatility index*** is calculated as:

$$PI = \frac{V_{max} - V_{min}}{V_{mean}}$$

where

Vmax is the maximum velocity

Vmin is the minimum velocity

Vmean is the mean velocity

These indices can be used to assess vascular resistance within arteries from many organs and provide useful information to differentiate some diseases. For instance, evaluation of the celiac and cranial mesenteric artery has been used in food allergy studies.[6] Resistive and pulsatility indices have also been used to characterize different types of lesions in lymph nodes[7] or superficial tumours[8] and to assess ocular vasculature in dogs with glaucoma.[9] Several studies have also evaluated the benefit of using these indices in renal and urinary abnormalities.

1.2. Renal Doppler ultrasound

The kidney is a well-vascularised organ receiving about 20% of the cardiac output. Many renal diseases have an important vascular component and some systemic diseases, such as hypertension, are mediated by the vascular control system of the juxtaglomerular apparatus. This fact makes the kidney a suitable organ to be evaluated by Doppler, because it is expected for the renal and renovascular diseases to cause changes in the vascular supply, microvascular circulation, and venous return.[10]

The dorsal longitudinal placement of the transducer at the paralumbar region provides an excellent angle for Doppler evaluation of the renal, interlobar and arcuate arteries[4] (Figure 3).

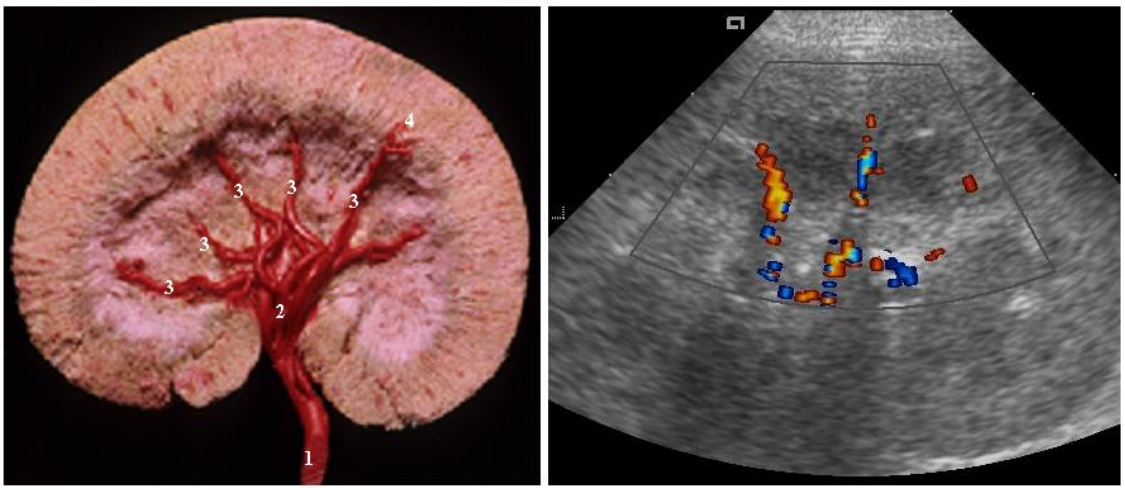

Figure 3. A, Anatomic reconstruction of the renal arterial vasculature (Courtesy of J. Ruberte and A. Carretero) 1: renal artery, 2: segmental arteries, 3: interlobar arteries, 4: arcuate arteries. B, Colour Doppler ultrasound of the longitudinal dorsal view of the kidney.

Resistive and pulsatility indices can be calculated from renal arteries, interlobar arteries, and arcuate arteries although some studies in animals suggested that many pathologies induce more marked alterations in blood flow resistance in more distal arterial branches of the kidney.[11] Therefore, Doppler waveforms obtained from arcuate arteries have potentially more clinical relevance in kidney disease. In one study comparing the indices from three different locations in the kidney vasculature, values obtained from interlobar-arcuate location were more consistent and therefore considered to be more desirable for clinical approach.[12]

Different factors can produce increased renal resistive and pulsatility indices. When vascular resistance increase, either due to obstruction or vasoconstriction, diastolic blood flow is reduced to a major degree than systolic

flow.[13] This results in a relatively higher decrease of the end diastolic velocity than of the peak systolic velocity, increasing RI and PI.

RI can increase with different abnormalities in absence of renal disease. In human medicine, increased renal RI has been related with systemic hypotension, extreme heart rates, and presence of perinephric and subcapsular fluid.[11] Negative relationship also exists between RI of segmentary renal arteries and heart rate.[14]

Sedative and anaesthetics can also modify vascular indices. Administration of atropine, diazepam, acepromacine, and ketamine in healthy dogs resulted in a significant decrease in renal RI, which was considered to be due to ketamine positive chronotropic effect.[15] However, in cats, administration of atropine, acepromacine, and ketamine resulted in obtaining similar values to those for non-sedated cats.[16] In another study, increased RI and PI were recorded in cats anaesthetised with isofluorane. The direct effect of the inhalatory anaesthetic on renal autoregulation, reducing the renal blood flow and the glomerular filtration rate was suggested as the explanation for this effect.[17]

1.2.1. Renal resistive and pulsatility indices in dogs and cats

Several studies have described RI and PI in normal dogs and cats.[15-20] Normal values slightly differ among the studies. Some authors suggest an upper maximum value of 0.70 for both cats[16] and dogs,[19] which is also the limit used in human medicine.[21] Others suggest an upper limit value of 0.73 for dogs [8,22] and

of 0.71 for cats.[22] Renal PI values could not be found for non-sedated normal dogs. An upper limit value of 1.06 for the PI is obtained from a study in normal cats.[17]

Obtaining intrarenal RI is useful to confirm renal disease during ultrasound examination in dogs and cats in which B-mode ultrasonographic appearance of the kidney is normal or when parenchymal hyperechogenicity is the unique finding.[22]

RI and PI have also been used in renal or urinary disease studies in dogs and cats.[18, 19, 22-26] In these studies, increased RI have been reported in dogs and cats with acute or chronic renal failure.[22, 23]

RI and PI have also been used to evaluate renal vascular response to different degrees of hypovolemia in dogs[27] and to assess outcome in cats with renal transplantation.[20, 28]

1.2.2. Renal resistive and pulsatility indices in human beings

In human medicine renal RI and PI have been commonly used in patients with renal and hepatic disease, diabetes mellitus and hypertension.

RI has been used as a predictor of renal failure reversibility in human patients, being the RI significantly higher in patients with persistent renal failure than in those with recovered renal function.[29] Higher RI and PI have also been reported in association with a faster decline in renal function.[30]

In patients with liver disease increased RI and PI have also been reported. RI showed a correlation with glomerular filtration rate and with arterial blood pressure in cirrhotic patients and it was also useful as a prognostic indicator of the disease.[31] In patients with liver disease, the indices have also been correlated with some biochemical parameters, such as bilirubin, albumin, and creatinine levels and prothrombin time.[32]

High RI and PI values are also reported in diabetic patients with renal impairment[33,34] or in people with diabetes mellitus but with normal renal function.[35] In some studies, RI and PI showed a correlation with serum creatinine concentration, creatinine clearance rate, serum glucose concentration, cholesterol levels, presence of microalbuminuria, arterial blood pressure, patient age, and duration of the disease.[35-40]

Increased RI has been related with early hypertensive renal damage and correlated with systemic blood pressure.[41] Increased RI values have also been reported to correlate with systemic blood pressure and duration of the disease in patients with hypertension.[42]

1.3. Ocular Doppler ultrasound

Doppler ultrasound permits visualization and analyses of the type of flow from different orbital and ocular vessels. An advantage of eye and orbital Doppler ultrasound is that most of the vessels in this region run nearly parallel to the ultrasound beam, providing ideal conditions for velocity studies.

Ocular vessels that can be visualized are the long posterior ciliary arteries, the short posterior ciliary arteries, the anterior ciliary artery, and retinal or cilioretinal primary arteries.

The anterior ciliary artery enters the anterior sclera dorsomedial and dorsolateral, caudal to the limbus; the long posterior ciliary artery is visualized in either the 3 or the 9 o'clock positions within the sclera.[43]

Excessive external pressure from the transducer may increase intraocular pressure during ultrasound examination and therefore can affect subsequent blood flow velocity and indices measurement. To minimize this effect, a lateral approach through the non-osseous portion of the canine orbit has been described.[44]

In veterinary ophthalmology RI and PI have been used in dogs with glaucoma.[9] Increased values were found in Beagles with primary open angle glaucoma in comparison to normal animals. The effect of amlodipine in the RI has also been reported, showing significantly reduced values after treatment.[45]

In human medicine, increased extraocular RI has been reported in patients with primary hypertension.[46, 47]

2. Arterial blood pressure and hypertension in dogs and cats

Arterial blood pressure results from the interaction between cardiac output and total peripheral resistance. Cardiac output (volume expelled per minute) is equal to the heart rate times the stroke volume, which in turns depends on preload and contractility. All the factors associated with renin-angiotensin-aldosterone system will have an important role in total peripheral resistance.[48]

Different methods can be used to evaluate arterial blood pressure. Indirect methods are usually most used in clinical practice because, although they are not always good predictors for the direct values,[49] they are non-invasive. Oscillometric and Doppler methods are the most commonly used indirect methods.

Although oscillometric method is currently used in dogs and cats, it is not always easy to obtain measurements. In one study comparing three blood pressure measurement methods (oscillometric, Doppler, and plethysmography) in anaesthetized cats, oscillometric method proved to be less accurate and efficient to obtain blood pressure measurements and it tended to underestimate blood pressure.[50]

The major limitation of the Doppler technique is accurate measurement of diastolic pressure, which relies on subjective determination of a sudden muffling of the Doppler signal.[51]

Systolic blood pressure in dogs depends on age, breed, sex, temperament, exercise regime, and diet.[52] However, as a general guideline, the following limits can be considered in both dogs and cats when considering hypertension (systolic / diastolic):[53]

Mild hypertension	>150/95
Moderate hypertension	>160/100
Severe hypertension	>180/120

Differing from human beings, in who primary hypertension is the most common form of hypertension, in dogs and cats, secondary hypertension is the most frequent type. Causes of hypertension include renal failure,[54] hyperadrenocorticism,[55, 56] diabetes mellitus,[57] hyperthyroidism, pheochromocytoma, hyperaldosteronism, and hepatic disease.[52]

Objectives

1. To obtain normal values for both intrarenal and ocular RI and PI in non-sedated clinically normal dogs and cats.

2. To obtain values for intrarenal and ocular RI and PI in clinically normal dogs sedated with a sedative protocol suitable for ill animals and to evaluate if it causes significant changes in the indices.

3. To determine RI and PI in intrarenal and ocular vessels in dogs and cats with diseases that may be associated with hypertension and assess their relationship with systolic blood pressure.

4. To investigate possible correlation between renal or ocular RI and PI and hematologic and biochemical parameters in animals with disease.

Studies

1. Novellas, R., Espada, Y., Ruiz de Gopegui, R. Doppler ultrasonographic estimation of renal and ocular resistive and pulsatility indices in normal dogs and cats. Veterinary Radiology and Ultrasound 2007; 48: 69-73.

2. Novellas, R., Ruiz de Gopegui, R., Espada, Y. Effects of sedation with midazolam and butorphanol on resistive and pulsatility indices in healthy dogs. Veterinary Radiology and Ultrasound 2007; 48: 276-280.

3. Novellas, R., Ruiz de Gopegui, R., Espada, Y. Increased renal vascular resistance in dogs with hepatic disease, The Veterinary Journal (2007), doi:10.1016/j.tvjl.2007.07.026

4. Determination of renal vascular resistance in dogs with diabetes mellitus and hyperadrenocorticism.

5. Determination of renal vascular resistance and blood pressure in dogs and cats with renal disease.

6. Determination of vascular resistance in the long posterior ciliary artery in dogs and cats with disease.

Published studies

1. Doppler ultrasonographic estimation of renal and ocular resistive and pulsatility indices in normal dogs and cats

DOPPLER ULTRASONOGRAPHIC ESTIMATION OF RENAL AND OCULAR RESISTIVE AND PULSATILITY INDICES IN NORMAL DOGS AND CATS

ROSA NOVELLAS, YVONNE ESPADA, RAFAEL RUIZ DE GOPEGUI

Resistive index (RI) and pulsatility index (PI) are indirect measurements of blood flow resistance that may be used to evaluate vascular changes in renal and ophthalmologic diseases. To our knowledge, no reports are available describing values for renal and ocular PI index in the unsedated dog and ocular RI and PI indices in the unsedated cat. The purpose of this study was to measure normal values for both intrarenal and ocular RI and PI within the same subject in unsedated clinically normal dogs and cats. Twenty-seven dogs and 10 cats were considered healthy by means of physical examination, CBC, biochemical profile, urinalysis, and ultrasonography. Systolic blood pressure was measured by Doppler ultrasonography. Intrarenal and ocular arteries were scanned by pulsed Doppler ultrasonography to calculate RI and PI. No significant differences were noted between the values obtained for the right vs. the left kidney and eye. The upper values of these indices were calculated as mean + 2 standard deviations resulting in 0.72 and 1.52 for dog renal RI and PI; 0.7 and 1.29 for cat renal RI and PI; 0.76 and 1.68 for dog ocular RI and PI; and 0.72 and 1.02 for cat ocular RI and PI.
Veterinary Radiology & Ultrasound, Vol. 48, No. 1, 2007, pp 69–73.

Key words: cat, dog, Doppler ultrasonography, pulsatility index, resistive index.

Introduction

DUPLEX DOPPLER ULTRASONOGRAPHY provides real-time anatomic and dynamic vascular flow information. It permits blood flow measurements to provide indirect information about peripheral vascular resistance. Information about vascular impedance cannot be obtained from absolute velocity; thus, indices have been developed to evaluate and compare Doppler wave forms. These indices are velocity ratios obtained by pulsed wave Doppler ultrasonography. The resistive index (RI) and the pulsatility index (PI) provide information on expression of the resistance to blood flow within an artery.

Renal-pulsed wave Doppler waveforms can be obtained in the renal artery, or in interlobar or arcuate arteries. However, the most severe alterations in resistance occur at distal arterial branches (arcuate or interlobar).[1] The RI and PI have been used to evaluate changes in vascular resistance due to urinary obstruction,[2,3] diuretic effects,[4] acute and chronic renal failure,[3] and congenital dysplasia.[5] Sedation[6] or anesthesia[7] may also modify these indices. In humans, the RI and the PI are related to the severity and progression of chronic renal failure.[8] They are also related to systolic pressure, age, and end organ damage in patients with essential hypertension.[9]

Doppler ultrasonography may also be used to evaluate ocular and orbital vascular flow velocities and characteristics. Doppler imaging of the ophthalmic vasculature is possible in many ocular and retrobulbar vessels including the external and internal ophthalmic artery, anterior ciliary artery, short and long ciliary arteries, and primary retinal arteries.[10] Resistive and pulsatility indices have been used to evaluate ocular vascular resistance in canine glaucoma[11] and the effects of systemic antihypertensive therapy.[12] Increased ocular RI was reported in humans with essential hypertension,[13] and in patients receiving antihypertensive treatment. Hypertension alters vascular resistance in the kidney and eye in humans as well as animals.

Renal and ocular RI in the dog and renal RI and PI in the cat have been characterized in unsedated normal animals.[2,4,5,7,14,15] We found no report describing normal values obtained for both renal and ocular PI in unsedated, clinically normal, dogs and ocular RI and PI in unsedated, healthy cats. The purpose of this study is to present normal values for both intrarenal and ocular RI and PI within the same subject in non-sedated clinically normal dogs and cats.

Materials and Methods

Animals

Twelve adult healthy mixed-breed dogs and 10 adult healthy mixed-breed cats presented to the Veterinary Teaching Hospital for routine surgery (ovariohysterectomy or orchiectomy); vaccination and physical examination were included. Owner consent was obtained before ultrasonography. Fifteen clinically normal adult Beagle dogs

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owned by the veterinary faculty were also scanned. In all, there were 27 dogs with a mean age of 4.3 years (range 1–8 years) and 10 cats with a mean age of 7.8 years (range 8 months–12 years). The animals were judged as clinically normal based on physical examination, CBC, serum biochemical profile, urinalysis, and abdominal and ocular ultrasonography findings.

Arterial Blood Pressure Measurement

Systolic blood pressure was determined before other interventions and, after 5–10 min, was allowed to adapt to the environment. Systolic blood pressure was measured with a Doppler device* (8 MHz transducer). The measurement was performed with the animals in left recumbency and the cuff placed on the proximal tarsus to compress the cranial tibial artery. Three measurements were obtained in each animal, as previously described,[16] and the mean value was computed.

Renal Doppler Ultrasonography

Triplex Doppler ultrasonography was performed with an Acuson Computed sonography 128/XP or an Acuson Aspen ultrasound machine. Hair was clipped and acoustic gel† was applied to the skin. The animals were fasted for 12 h and they were in right or left lateral recumbency to scan the nondependent kidney. Different transducers and frequencies (V7 sector multifrequency 5–7 MHz, C7 convex multifrequency 4–5–7 MHz, and L7 multifrequency 7–10 MHz) were used depending on animal weight and renal depth. Color Doppler was used to visualize the intrarenal vasculature. Subsequent pulsed Doppler interrogation from one of the arteries was obtained with a sample width of 1.5–4 mm and a frequency of 4–7 MHz. The smallest scale that displayed the flow without aliasing was selected. The mean RI and PI for each kidney were determined by averaging a total of nine Doppler waveforms from the interlobar or arcuate arteries (Fig. 1) at three separate locations (cranial pole, mid-portion, and caudal pole, three waveforms at each) as previously described.[2,14]

The RI and PI were calculated automatically by the software of the ultrasound machine, after manual delimitation of peak systolic velocity, end diastolic velocity, and time average maximum velocity (TAMX) as follows:

$$\mathrm{RI} = (\text{peak systolic velocity}) - (\text{end diastolic velocity})/(\text{peak systolic velocity})$$

$$\mathrm{PI} = (\text{peak systolic velocity}) - (\text{end diastolic velocity})/(\mathrm{TAMX})$$

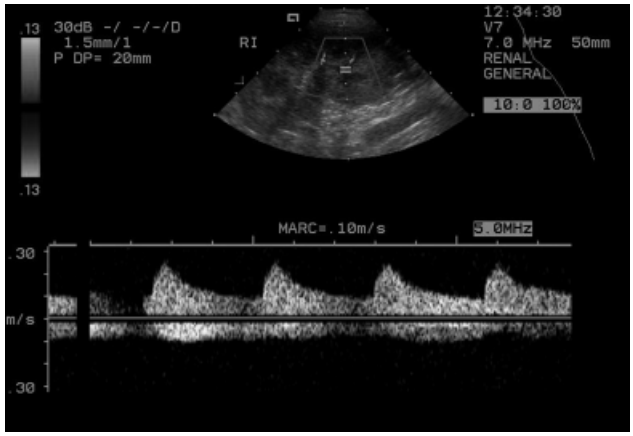

FIG. 1. Color Doppler visualization of renal vasculature and pulsed Doppler volume sample location in an interlobar artery.

Ocular Doppler Ultrasonography

Before sonography, topical ocular anesthesia—oxibuprocaine and tetracaine‡—was administered and sterile coupling gel§ was applied. Different transducers (linear multifrequency 7–10 MHz, sector multifrequency 5–7 MHz, linear multifrequency 9–11 MHz) were applied. Images were obtained with the animal in sternal recumbency and the probe directly on the cornea. The long posterior ciliary artery was visualized with color Doppler in either the 9 or the 3 o'clock positions within the sclera (Fig. 2), depending on which vessel was most easily visualized or had a better quality Doppler image. The long posterior ciliary artery was easy to visualize as previously described.[10,15] Pulsed Doppler (5–7 MHz) was applied with a sample volume between 1.5 and 3 mm. When three to five similar-appearing waveforms were obtained, the mean was calculated from three RI and PI in each eye.

Femoral Doppler Ultrasound

Right femoral Doppler ultrasound was obtained with the animal in right lateral recumbency. The artery was located by palpation. Femoral waveforms were obtained with pulsed Doppler ultrasound, and three measurements of pulse rate were calculated by the machine software applications. The mean of these values was used as the pulse rate of the animal.

Statistical Analysis

Mean comparison tests were used to examine for differences between right and left renal values, between cranial

*Vet BP Doppler Ultrasound Blood Flow Detector, Sonomed Ltd., Warsaw, Poland.

†Polaris II ultrasonic gel, GE Medical Systems, Leanhard Long Gmbtl, Austria.

‡Colircusí anestésico doble; Alcon Cusí SA, Barcelona, Spain.

§Ultrasound transmission gel, Sterile R. Aquasonic 100, Parker Laboratories Inc.

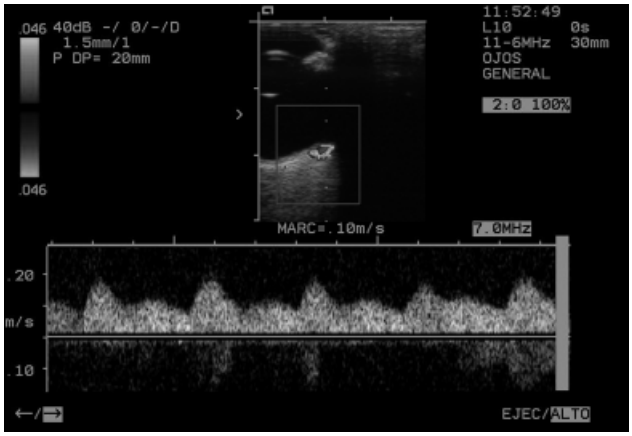

FIG. 2. Color Doppler visualization of ocular vasculature and pulsed Doppler volume sample location in the ciliary artery.

pole, mid-portion or caudal pole, or between the right and left eyes. When values were normally distributed, paired Student's *t*-tests were performed. If values were not normally distributed, a nonparametric test (Wilcoxon's rank sum test) was used. The values of RI, PI, systolic pressure, and pulse rate obtained in the Beagles were compared with the healthy non-Beagle dogs using Student's *t*-test (normally distributed values) or a Mann–Whitney U-test (non-normal values). Determinants of correlation (Pearson's for normal distribution or Spearman's for non-normal distribution) were used to determine for a relationship between RI, PI and systolic pressure, and pulse rate. Statistical significance was defined as $P < 0.05$.

Results

Resistive and Pulsatility Indices

Intrarenal arterial values were obtained in all animals but all nine values were not acquired in the right kidney in four dogs of the non-Beagle group due to their larger mass. The values of the cranial pole in the right kidney were the most difficult to obtain due to difficulties in acquiring satisfactory Doppler signals from deep locations. With regard to the ciliary artery, it was not possible to acquire all values in two dogs due to lack of cooperation during the examination. In some animals, pulsed Doppler registration was more difficult and time consuming due to panting. In cats, all values were obtained except for one cat, in which it was not possible to obtain indices in one eye and for the left renal cranial pole due to poor cooperation.

Even though acclimatization time for both dogs and cats was allowed before blood pressure measurement, some animals still appeared excited during blood pressure measurement, and exhibited excess body motion during blood pressure determinations and ultrasound examination, which occurred more frequently in Beagle dogs and cats.

TABLE 1. Mean Renal and Ocular RI and PI in Each Group of Dogs and in Cats

	Kidney		Eye	
	RI	PI	RI	PI
Non-Beagle	0.62 ± 0.04	1.16 ± 0.18	0.60 ± 0.06	1.07 ± 0.16
Beagle	0.63 ± 0.03	1.14 ± 0.13	0.64 ± 0.05	1.21 ± 0.22
All Dogs	0.62 ± 0.04	1.15 ± 0.15	0.63 ± 0.06	1.15 ± 0.21
Cats	0.62 ± 0.04	1.02 ± 0.12	0.55 ± 0.05	0.79 ± .08

RI, resistive index; PI, pulsatility index.

No difference was found between right and left kidney indices, between the different locations in each kidney, or between right and left ocular indices (Table 1). No differences were found between the two groups of dogs, so all 27 dogs were grouped for quantification of normal dog values.

Systolic Blood Pressure and Pulse Rate

The mean systolic blood pressure was 126 ± 15 mmHg for non-Beagle dogs, 165 ± 20 mmHg for Beagle dogs, and 152 ± 25 mmHg for cats. Significant differences were found between systolic blood pressure of non-Beagle dogs and the Beagle dogs. The mean pulse rate was 111 ± 33 ppm for non-Beagle dogs, 102 ± 17 ppm for Beagle dogs, and 190 ± 41 ppm for cats. No statistically significant difference was found between the groups of dogs.

No significant correlation was found between systolic blood pressure or pulse rate with PI or RI.

Discussion

Both RI and PI provide an indirect measure of arterial resistance by means of a ratio between peak systolic, end diastolic, and mean velocities of spectral Doppler vascular flow waveform. RI reaches its theoretical upper limit of 1 if the diastolic velocity is 0. The pulsatility index is more sensitive than the RI to differentiate abnormal waveforms because it considers the mean velocity throughout one cycle. To perform the Doppler exam, the angle between the Doppler beam and the blood flow must be kept below 60° to obtain a reliable velocity measure. One advantage of these indices over absolute measurements of velocity is that the insonation angle does not need to be known and small or tortuous vessels can be evaluated.[17] Owing to the pulsate nature of blood flow, velocity, and wave distribution constantly change. Waveforms are also affected by cardiac output, gravitational orientation, exercise, stress, and digestion.[17] Systemic hypotension, markedly decreased heart rate, and subcapsular or perinephric fluid collection have been associated with increased renal RI in humans.[1] No animal in this study had hypotension or bradycardia. In addition, subcapsular or perinephric fluid was not observed. Differences in RI with aging have been found in humans, with higher values both in children and elderly

individuals than in adults.[18] In the present study, such age-induced differences were not found due to the similar age of the animals.

The intrarenal RI values obtained in this study in unsedated dogs and cats are similar to those obtained in other studies in unsedated dogs[2,4,5] and cats,[7,14] and in sedated cats.[19] Urinary obstruction or vasoconstriction can increase renal vascular resistance.[2,5] When an increase in vascular resistance occurs, diastolic blood flow is reduced to a greater degree than systolic blood flow.[20] Then, the relatively greater decrease in end diastolic velocity than in peak systolic velocity causes an elevation in RI and PI. It is necessary to establish the upper limit for RI and PI to identify an abnormally increased vascular resistance. The upper limit (calculated as mean + 2 standard deviations) for RI differs slightly in different studies. Some suggest an upper value of 0.70 for cats[19] and dogs,[5] which is the same value proposed as a limit for normal mean intrarenal RI in humans.[21] Others suggest an upper value of 0.73 for dogs[2,3] and of 0.71 for cats.[3] Similarly, we suggest an upper limit for the RI of 0.72 for dogs and an upper value of 0.70 for cats.

We suggest an upper intrarenal PI of 1.52 in unsedated dogs. In cats, our PI differs from that in a previous study[7] where the mean was 0.80 ± 0.13 and the upper limit was 1.06. In our study, the upper limit for PI in cats was 1.29.

We suggest an upper value of 0.76 for canine ocular RI. This value and its corresponding normal range are lower than those previously described (0.68 ± 0.07).[15] External pressure from the transducer may increase intraocular pressure during the examination, and it will affect subsequent measurements of blood flow velocity and RI.[15] To minimize external pressure on the eye in a previous study,[15] ultrasonographic images were obtained by a lateral approach through the lateral orbital ligament. Different examination techniques between studies may explain reported differences in RI. No reports describing normal ocular PI in nonsedated dogs or ocular RI or PI in nonsedated cats were found. We suggest an upper value of 1.68 for ocular PI in the dog, and values of 0.72 and 1.02 for ocular RI and PI, respectively, in the cat.

Systolic pressure in Beagles was significantly higher than in non-Beagle dogs. This finding has also been described in unsedated untrained Beagle dogs, with a mean value of 164 mmHg.[22] Normal arterial pressure is breed specific in dogs.[23] Although acclimation was allowed, some Beagles were still excited and exhibited excessive subject body motion during blood pressure evaluation and ultrasound examination. Beagle dogs were less acclimated to interactions with people than were the non-Beagle dogs. Stress-related factors can increase arterial blood pressure, mimicking hypertension.[24] We considered these high blood pressure values as resulting from stress. Then, differences between breeds and different stress levels may be the cause of the different systolic blood pressure values obtained. Ideally, to rule out pathologic hypertension, repeated blood pressure measurements over multiple days should be determined. The objective of this study was to compare blood pressure with vascular indices at the same time.

Our results suggest that there is no correlation between the ocular or renal indices and blood pressure in normal animals, even when stress induces transitory hypertension.

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2. Effects of sedation with midazolam and butorphanol on resistive and pulsatility indices in healthy dogs

EFFECTS OF SEDATION WITH MIDAZOLAM AND BUTORPHANOL ON RESISTIVE AND PULSATILITY INDICES IN HEALTHY DOGS

ROSA NOVELLAS, RAFAEL RUIZ DE GOPEGUI, YVONNE ESPADA

Resistive index (RI) and pulsatility index (PI) are indirect measurements of blood flow resistance that may be measured by pulsed wave Doppler ultrasonography. Chemical restrain may potentially alter the indices although it is required to perform ultrasonography in some patients. The purpose of this study was to describe values for both intrarenal and ocular RI and PI within the same subject in clinically normal dogs sedated with a midazolam and butorphanol combination and evaluate if there are any significant changes between sedated and nonsedated dogs. Fifteen healthy Beagle dogs were studied by Duplex Doppler interrogation in interlobar or arcuate arteries of the kidney and long posterior ciliary artery. Pulse rate and systolic blood pressure were also determined. All measurements were recorded before and after the administration of a sedative combination of midazolam (0.2 mg/kg) and butorphanol (0.2 mg/kg). Mean comparison tests (paired *t*-tests or Wilcoxon's rank-sum test) were used to determine if any significant differences existed between right and left renal values or right and left ocular values. A correlation study (Pearson or Spearman) was applied between RI, PI, and systolic pressure, and pulse rate. RI and PI were significantly higher in sedated Beagles than in unsedated Beagles. There was neither correlation between index and systolic blood pressure nor pulse rate. In conclusion, provided that normal RI and PI increase in sedated animals, then reference ranges should be higher when sedated—healthy or ill—animals are evaluated. *Veterinary Radiology & Ultrasound, Vol. 48, No. 3, 2007, pp 276–280.*

Key words: dog, Doppler ultrasonography, pulsatility index, resistive index, sedation.

Introduction

DUPLEX DOPPLER ULTRASONOGRAPHY provides real time anatomic and dynamic vascular flow information, including information about peripheral vascular resistance. Information about vascular impedance can not be obtained from absolute velocity, thus, indices have been developed to evaluate and compare Doppler wave forms. These indices are velocity ratios obtained by pulsed wave Doppler ultrasonography. The resistive index (RI) and the pulsatility index (PI) provide information on expression of the resistance to blood flow within an artery.

Altered RI and PI have been reported in dogs and cats with renal disease. Increased renal RI and PI due to urinary obstruction have been described.[1,2] The increased RI difference between obstructed and nonobstructed contralateral kidneys after mannitol administration was useful for identification of unilateral urethral obstruction.[3] Increased renal RI in dogs and cats with acute and chronic renal failure and congenital dysplasia has also been reported.[2,4] Some sedatives and anesthetics may modify the RI and PI. A combination of atropine, diazepam, acepromazine, and ketamine reduced the renal RI in healthy dogs.[5] However, in cats sedated with a combination of atropine, acepromazine, and ketamine, a renal RI value similar to that obtained in unsedated cats or dogs was observed.[6] Increased renal RI and PI in cats anaesthetized with isofluorane has also been reported.[7]

In people, the RI and the PI are related to the severity and progression of chronic renal failure.[8] They are also related to systolic pressure, age, and end-organ damage in patients with essential hypertension.[9]

RI and PI have been used to evaluate ocular vascular resistance in canine glaucoma[10] and the effects of systemic antihypertensive therapy.[11] Increased ocular RI was reported in humans with essential hypertension,[12] and in patients receiving antihypertensive treatment. Studies reporting measurement of the renal or ocular indices in hypertensive animals have not been found.

Measurement of renal and ocular RI and PI is particularly interesting in animals with renal disease and hypertension. These animals are frequently geriatric and may have concomitant heart or liver disease. Sedatives may be contraindicated in these patients. The combination of midazolam and butorphanol is commonly used to sedate ill or

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critical animals in our institution if chemical restraint is required. The purpose of this study is to present values for intrarenal and ocular RI and PI in clinically normal dogs sedated with midazolam and butorphanol and evaluate if there are any significant changes between sedated and nonsedated dogs.

Materials and Methods

Animals

Fifteen clinically normal adult Beagle dogs (nine females and six males, from 2.5 to 8 years) owned by the Veterinary Faculty were studied. The animals were judged to be clinically normal based on physical examination, complete blood count (CBC), serum biochemical profile, urinalysis, and abdominal and ocular ultrasonography. The animals were housed in standard cages and provided with water *ad libitum* and a canine adult maintenance diet, following the rules and regulations of the Animal Welfare Committee of the Autonomous University of Barcelona.

Arterial Blood Pressure Measurement

Systolic blood pressure was determined before other interventions and after 5–10 min for adaptation to the environment. Systolic blood pressure was measured with a Doppler device (Vet BP Doppler Ultrasound Blood Flow Detector* 8 MHz transducer). The measurement was done with the animals in left lateral recumbency and the cuff placed on the proximal aspect of the tarsus to compress the cranial tibial artery. Three measurements were obtained in each animal, as previously described,[13] and the mean value computed.

Renal Doppler Ultrasonography

Triplex Doppler ultrasonography was performed with an Acuson Aspen ultrasound machine. Hair was clipped and acoustic gel (Pollaris II ultrasonic gel†), applied to the skin. The animals were fasted for 12 h and they were in right or left lateral recumbency to scan the nondependent kidney. A V7 sector transducer operating at 6 MHz frequency was used. Color Doppler was used to visualize the intrarenal vasculature. Subsequent pulsed Doppler interrogation from one of the arteries was obtained with a sample width of 1.5 mm and a frequency of 5 MHz. All Doppler flow spectra recorded for analysis consisted of at least three consecutive similar-appearing wave forms. The mean RI and the PI for each kidney was determined by averaging a total of nine Doppler waveforms from the interlobar or arcuate arteries at three separate locations

*Sonomed Ltd, Warsaw, Poland.
†GE Medical Systems, Leanhard Long Gmbtl A6020, Austria.

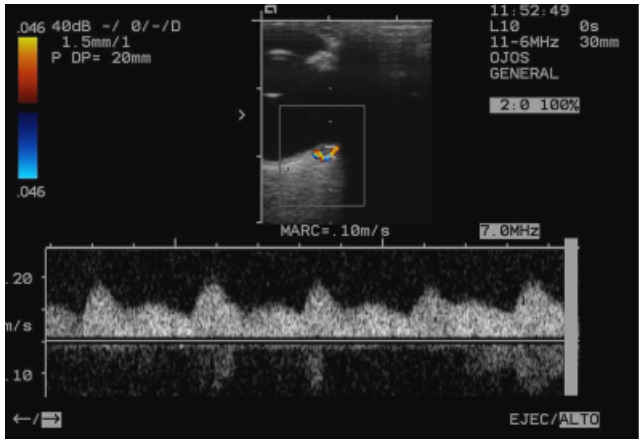

FIG. 1. Ocular triplex Doppler ultrasound showing sample volume placement.

(cranial pole, midportion, caudal pole; three waveforms at each) as described previously.[1,14]

The RI and PI were calculated using ultrasound machine software, after entering peak systolic velocity, end diastolic velocity, and time average maximum velocity (TAMX), as follows:

$$\text{RI} = (\text{peak systolic velocity}) - (\text{end diastolic velocity})/(\text{peak systolic velocity})$$

$$\text{PI} = (\text{peak systolic velocity}) - (\text{end diastolic velocity})/(\text{TAMX})$$

Ocular Doppler Ultrasonography

Before sonography, topical ocular anesthesia consisting of oxibuprocaine and tetracaine‡ was administered and sterile coupling gel§ applied. A L10 linear transducer operating at 11 MHz was used. Images were obtained with the animal in sternal recumbency and the probe directly on the cornea. The long posterior ciliary artery was visualized with color Doppler in either the 9 or 3 o'clock positions within the sclera (Fig. 1), depending on which vessel was most easily visualized or had a better quality Doppler image. Pulsed Doppler (7 MHz) was applied with a sample volume of 1.5 mm. When three similar appearance waveforms were obtained, the mean RI and PI was calculated for each eye.

Femoral Doppler Ultrasound

Right femoral Doppler ultrasound was obtained with the animal in right lateral recumbency. The artery was located by palpation. Femoral waveforms were obtained with pulsed Doppler ultrasound and three measurements

‡Colircusí anestésico doble. Alcon Cusí SA, Barcelona, Spain.
§Ultrasound transmission gel. Sterile R. Aquasonic 100. Parker Laboratories Inc.

of pulse rate were calculated by the machine software applications. The mean of these values was used as the pulse rate of the animal.

Sedation Protocol

After all measurements were performed, 0.2 mg/kg of midazolam¶ and 0.2 mg/kg of butorphanol‖ were administered intramuscularly. All measurements described above were repeated in the sedated dogs.

Statistical Analysis

Mean comparison tests were used to examine for differences between right and left renal values or between right and left eyes. When values were normally distributed paired Student's *t*-tests were performed. If values were not normally distributed, a nonparametric test (Wilcoxon's rank-sum test) was used. The same tests were used for comparison of indices, systolic blood pressure, and pulse rate before and after sedation. Determinants of correlation (Pearson's for normal distribution or Spearman's for nonnormal distribution) were used to examine for a relationship between RI, PI and systolic pressure, and pulse rate. Statistical significance was defined as $P < 0.05$.

Results

Resistive and Pulsatility Indices

The renal and ocular RI and PI were acquired in all dogs except one in which the values for the long posterior ciliary artery could not be obtained due to lack of cooperation during the examination. In some animals, pulsed Doppler registration was more difficult and time consuming due to panting. Even though acclimatization time for dogs was allowed before blood pressure measurement, some animals still were excited during blood pressure measurement, and had excess body motion during ultrasound examination.

No difference was found between right and left kidney indices or between right and left ocular indices; therefore, mean values were obtained as combination of right and left kidney and eye measurements, respectively. RI and PI values for Beagles before and after sedation are given in Table 1. Indices were significantly higher after sedation ($P < 0.001$). In pulsed Doppler ultrasonography of the sedated Beagles, a reduction of the diastolic velocity was observed in comparison with unsedated dogs both in intrarenal (Fig. 2) and ocular waveforms.

Systolic Blood Pressure and Pulse Rate

Significant differences were found between systolic blood pressure before (165 ± 20 mmHg) and during (149 ± 22 mmHg) sedation ($P = 0.004$). Pulse rate was not different between the groups. No significant correlation was found between systolic blood pressure or pulse rate and the indices.

TABLE 1. Mean Values (± Standard Deviation) for Renal and Ocular Resistive and Pulsatility Indices in Unsedated and Sedated Dogs

	Kidney ($n = 15$)		Eye ($n = 14$)	
	RI	PI	RI	PI
Unsedated	0.63 ± 0.03	1.14 ± 0.13	0.64 ± 0.05	1.21 ± 0.22
Sedated	0.73 ± 0.03*	1.56 ± 0.22*	0.73 ± 0.05*	1.60 ± 0.27*

RI, resistive index; PI, pulsatility index. *Significant difference ($P < 0.001$) between values in sedated and nonsedated dogs.

Discussion

Normal values for the renal RI before sedation were similar to previous studies in normal nonsedated dogs.[1,3,4] Our values obtained for ocular RI are lower than previously reported.[15] External pressure from the transducer may increase intraocular pressure during the examination, and it will affect subsequent measurements of blood flow velocity and RI.[15] To minimize external pressure on the eye in the previous study, images were obtained by a lateral approach through the lateral orbital ligament. This different examination technique between studies may explain the reported differences in RI. The values obtained in unsedated Beagles were not statistically different from those obtained by the present authors in a previous study.[16]

Systemic hypotension, markedly decreased heart rate, and subcapsular or perinephric fluid collection have been associated with increased renal RI in humans.[17] A negative relationship between renal RI and heart rate was also observed in humans.[18] None of the animals of this study had hypotension or bradycardia. In addition, subcapsular or perinephric fluid was not found.

Polypnea or panting increases patient movement and, consequently, the motion of arteries during Doppler interrogation. As a result, the examination becomes prolonged and difficult. In such instances, particularly when the patient is aggressive or difficult to handle, sedation facilitates ultrasonography.

Anesthetic agents may alter systemic and renal hemodynamics and subsequently affect vascular resistance indices. Statistically significant lower intrarenal RI in dogs sedated with a combination of atropine, acepromazine maleate, diazepam, and ketamine hydrochloride has been observed in comparison with unsedated dogs.[5] The authors of that study suggested that these lower values were presumably due to the positive chronotropic effect of ketamine hydrochloride.

Measurement of renal and ocular RI and PI is especially interesting in animals with renal failure or urinary

¶Dormicum; 5 mg/ml. Roche Farma, S.A. Madrid, Spain.
‖Turbogesic; 10 mg/ml. Fort-Dodge Veterinaria, S.A. Girona, Spain.

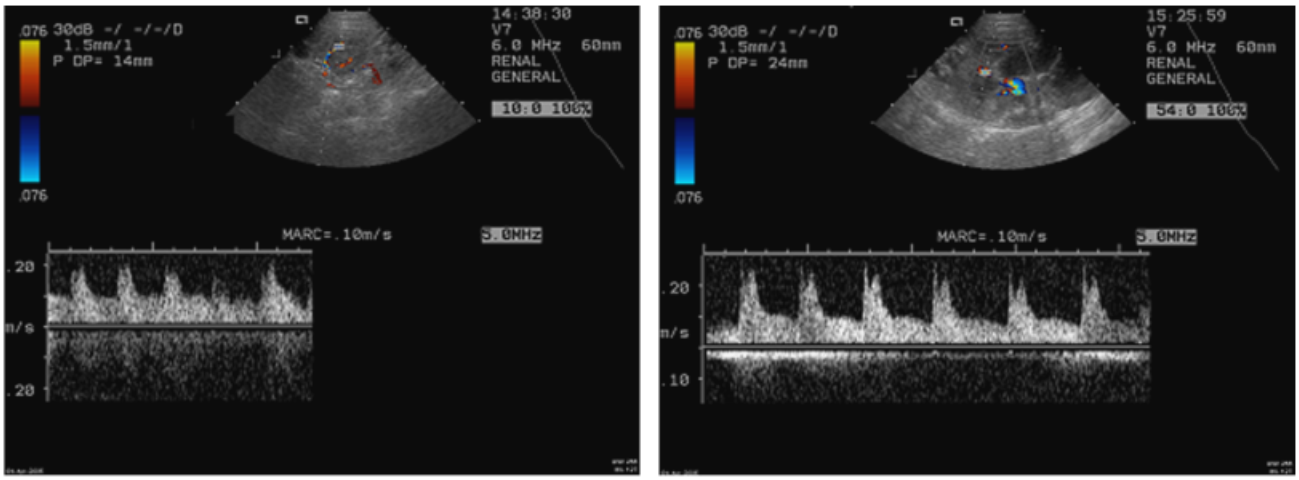

FIG. 2. Renal triplex Doppler ultrasound of the same animal before (A) and after sedation (B). A more accentuated reduction of the diastolic velocity is seen in comparison to unsedated dogs.

obstruction. In animals with chronic renal failure the administration of active renal excreted drugs, such as ketamine in cats, should be avoided.[19] Animals with renal disease are commonly older and may have concomitant heart or liver disease. In clinically normal animals, ketamine increases heart rate, cardiac output, and arterial pressure. Thus, ketamine has to be used with caution in animals with heart disease.[19] Phenothiazides should also be administered with caution in animals with liver disease, especially those with hepatic encephalopathy, as they may have a decreased seizure threshold. Phenothiazides are also contraindicated in patients with hypotension or hypovolemia secondary to severe renal disease.[20] Then, the selection of sedatives with minimal adverse effects is mandatory in patients that require renal vascular sonography. It has been reported that the combination of midazolam and butorphanol has minimal cardiopulmonary effects.[21] Hemodynamic and cardiovascular stability makes opiate use appropriate for sedation of animals with renal disease.[20] As a result, the combination of midazolam and butorphanol was chosen for the present study.

Midazolam combined with butorphanol is a neuroleptoanalgesia technique consisting of the combined use of a benzodiazepine sedative and an opiate analgesic. In healthy animals its sedative effect is moderate or mild, relatively large differences in effects may be observed between individuals, and some dogs may have excitation during the first 30 min.[22] In the present study, different effects between individuals were observed. Some animals were more excited after sedation. It has been reported that this combination may induce a marked decrease in mean arterial pressure and a mild reduction of heart rate.[21] In the present study, arterial blood pressure in Beagles was significantly lower after sedation and pulse rate did not significantly differ from the unsedated Beagles. In addition, statistically significant differences were also found between renal and ocular indices before and after sedation.

The heart rate correlates inversely with renal RI.[18] In the present study, such a relationship was not detected. Some animals had decreased pulse rate during sedation but no statistically significant differences were found before and during sedation.

In humans sedated with midazolam, a downward trend in renal blood flow and an upward trend in renal vascular resistance, estimated as mean arterial pressure and renal blood flow ratio, were observed.[23] In addition, the increase in RI and PI was associated with reduction of renal blood flow.[24] The midazolam effect on renal blood flow observed in this study may be the cause of the observed increase in renal and ocular PI and RI.

Conclusions

In conclusion, renal and ocular RI and PI increased in healthy dogs when a combination of midazolam and butorphanol was used. Then, reference ranges should be increased when clinical patients are evaluated using this sedation protocol. Then, normal sedated dogs have renal RI and PI below 0.79 and 2.00, respectively, and ocular RI and PI below 0.83 and 2.14, respectively.

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3. Increased renal vascular resistance in dogs with hepatic disease

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Increased renal vascular resistance in dogs with hepatic disease

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Abstract

Doppler ultrasound is a non-invasive technique that can be used to estimate vascular resistance by calculation of resistive index (RI) and pulsatility index (PI). Liver disease may increase renal RI and PI, and in humans with liver disease the indices are monitored to attain prognostic information. Systemic hypertension has been found in dogs with hepatic disease and is also related to increased renal vascular resistance in humans. The aim of this study was to examine renal vascular resistance increases in dogs with hepatic disease and to ascertain whether these may be related to blood pressure increases and biochemical parameters. Twenty dogs with hepatic disease were evaluated. The mean renal RI, PI, and systolic blood pressure were significantly higher than in normal animals. A positive correlation was found between the indices and alkaline phosphatase but not with systolic blood pressure. In conclusion, renal vascular resistance may increase in dogs with hepatic disease and in this study was above the limit value in 50% of the animals.

Keywords: Dog; Liver; Resistive index; Pulsatility index; Hypertension

Introduction

Duplex Doppler ultrasound is a reliable technique for assessing renal haemodynamics, providing both real time anatomic and blood flow dynamic information. Obtaining pulsed wave Doppler spectra may also provide information about peripheral vascular resistance. The resistive index (RI) and pulsatility index (PI) are calculated from blood flow velocity waveform analysis and are widely accepted as indicators of vascular resistance. Renal RI and PI have been reported in normal dogs (Nyland et al., 1993; Morrow et al., 1996; Rivers et al., 1997; Novellas et al., 2007) and different pathologies in both human and veterinary medicine have been shown to alter these indices. Increased renal vascular resistance, evaluated by means of RI and or PI, has been described in both dogs and cats with renal disease (Nyland et al., 1993; Morrow et al., 1996; Rivers et al., 1997; Choi et al., 2003).

In humans, RI and PI have been found to be related to the severity and progression of chronic renal failure (Petersen et al., 1997). They are also related to systolic pressure, age and end organ damage in the kidney in patients with systemic hypertension (Pontremoli et al., 1999). Increased renal RI and PI have been reported in many studies of human hepatic disease. For example, RI correlated significantly with glomerular filtration rate and arterial blood pressure in cirrhotic patients and it was also a predictive value for survival (Maroto et al., 1994). RI and PI have been reported to correlate with some biochemical parameters such as serum levels of bilirubin, albumin, prothrombin time, and creatinine (Koda et al., 2000).

Renal dysfunction can occur in patients with established liver disease without other causative factors. Early clinical detection of renal disease with conventional tests is difficult because the serum creatinine level does not increase until late in the course of the disease. An early change that does occur in these patients is intense renal cortical vasoconstriction with elevation of renal arterial resistance that may be detectable using Doppler ultrasound (Platt et al., 1992; Colli et al., 1993).

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Hepatic disease has been reported to be a cause of systemic hypertension in an epidemiological study of canine blood pressure (Bodey and Michell, 1996). The mechanisms involved in the development of systemic hypertension in dogs with hepatic disease are not clear, but a loss of hepatic activation of medullipin, a renally secreted vasodepressor lipid, has been suggested. Unfortunately no more studies in animals with hepatic disease assessing hypertension or its possible causes have been found. Renal involvement in dogs with hepatic disease has not been recorded but if the cause of systemic hypertension in dogs with hepatic disease could be related to a lack of vasodepressor effect, we postulate that this could be detected as increased renal vascular resistance and a rise in RI and PI may be found. To the authors' knowledge no studies have been undertaken to evaluate the possible relationship between vascular resistance, blood pressure, and biochemical parameters in dogs with hepatic disease.

The aim of this study was to determine whether renal vascular resistance increases in dogs with hepatic disease and if this could be related to the presence of arterial hypertension. We also evaluated whether a correlation with biochemical parameters could be found in dogs, as it is seen in human patients.

Materials and methods

Twenty dogs attending the Veterinary Teaching Hospital of the Autonomous University of Barcelona with hepatic disease were included in the study. Physical examination, complete blood cell count, biochemical profile (including total bilirubin, calcium, cholesterol, creatinine, phosphate, glucose, total protein, urea, sodium chloride, alanine amino transferase (ALT), creatine kinase, alkaline phosphatase (ALKP), gamma glutamil transferase (GGT), and proteinogram), urinalyses and complete abdominal ultrasound were performed on each animal.

When possible, liver cytology, biopsy or post-mortem examination was undertaken. The final diagnosis of liver disease was based on liver histology in 10 animals and on liver cytology in two; in the remaining eight dogs the diagnosis was based on clinical, biochemical and diagnostic imaging findings.

Systolic blood pressure was determined before other interventions and after 5–10 min adaptation to the environment. Systolic blood pressure was measured with a Doppler device (Vet BP Doppler Ultrasound Blood Flow Detector, Sonomed; 8 MHz transducer). The measurement was performed with the animal in left lateral recumbency and the cuff placed on the proximal aspect of the tarsus to compress the cranial tibial artery. Three measurements were obtained for each animal, as previously described (Stepien and Rapoport, 1999), and the mean value computed.

Hair was clipped and acoustic gel (Polaris II ultrasonic gel, GE Medical Systems) was applied to the skin. The animals were placed in right or left lateral recumbency to scan the uppermost kidney. A multifrequency sector transducer operating at 6 or 7 MHz was used. Once the kidney was located using B-mode ultrasound, colour Doppler was used to visualize the intra-renal vasculature. Subsequent pulsed Doppler interrogation from one of the interlobar or arcuate arteries was obtained with a sample width of 1.5–2 mm and a frequency of 5 MHz. The smallest scale that displayed the flow without aliasing was selected. The mean RI and PI for each kidney were determined by averaging a total of nine Doppler wave forms from the arteries (Fig. 1) at three separate locations, as previously described (Nyland et al., 1993; Pollard et al., 1999).

The RI and PI were calculated automatically by the software of the ultrasound machine (Acuson Computed sonography 128/XP or an Acuson Aspen), after manual delimitation of peak systolic velocity, end diastolic velocity and time average maximum velocity (TAMX) (Fig. 2), as follows:

RI = (peak systolic velocity) – (end diastolic velocity)/(peak systolic velocity)

PI = (peak systolic velocity) – (end diastolic velocity)/(TAMX)

Heart rate was also calculated from the renal pulsed Doppler wave forms by the software of the machine.

Blood pressure and renal index values previously obtained from 27 mixed breed healthy dogs (Novellas et al., 2007) were used as normal values for comparison with animals with liver disease. Values were obtained using the same technique and by the same operators to avoid variation.

Statistical analysis was performed using a statistical package for social sciences (SPSS computer package). The indices, heart rate, arterial pres-

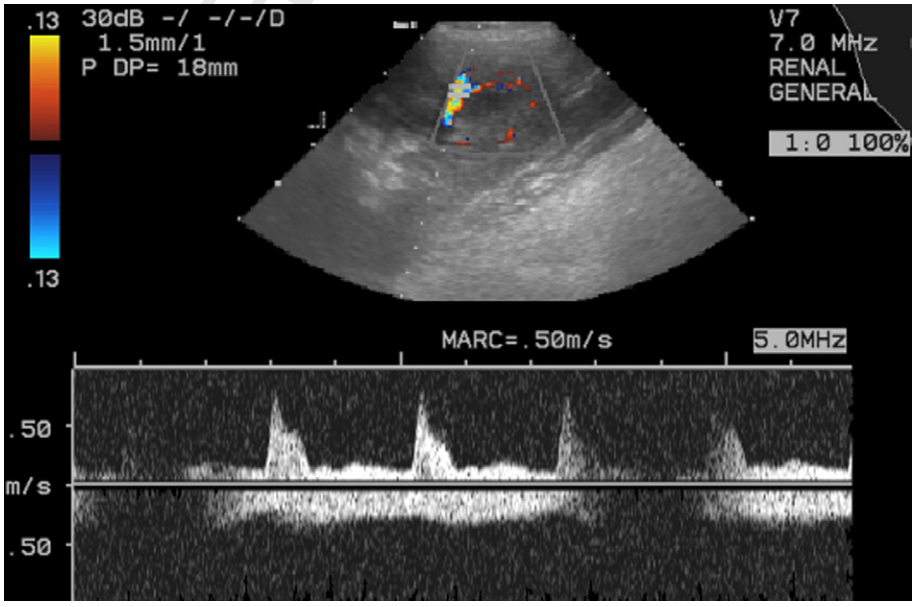

Fig. 1. Doppler ultrasound image showing sample location (interlobar artery) and pulsed wave spectral Doppler in one dog with hepatic disease.

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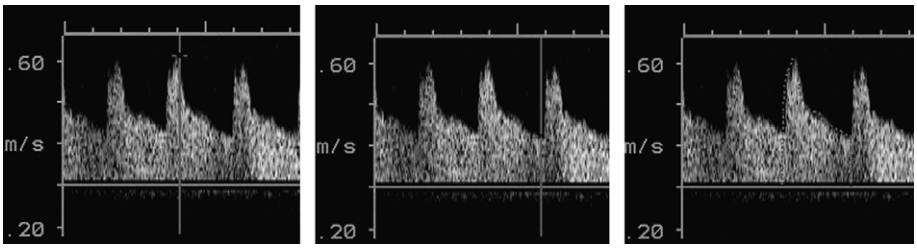

Fig. 2. Pulsed Doppler waveform showing delimitation for peak systolic velocity, end diastolic velocity and time-averaged maximum velocity (from left to right, respectively).

sure, and age were found to have a normal distribution using a Shapiro–Wilk test, and parametric tests were applied. The values of RI and PI of the animals with liver disease were compared with the values previously obtained in the group of healthy dogs by Student's t test. A Pearson correlation was applied to determine relation of RI or PI to blood pressure and biochemical parameters (creatinine, urea, ALT, ALKP, cholesterol, total bilirubin, and total protein). Statistical significance was defined as $P < 0.05$.

Results

Thirteen female and seven male dogs of different breeds (three Yorkshire terriers, three Dobermans, two Catalan Sheepdog, one Scottish terrier, one Schnauzer, one German Pointer, one Chow-chow, one Cocker Spaniel, one Fox Terrier, one Dalmatian, one German Shepherd and four crossbreds) of mean age 9.9 years (range 4–17 years) were evaluated. Seven cases were diagnosed as hepatic neoplasia (one hepatic carcinoma, one non-differentiated sarcoma, one lymphoma, one hepatocellular adenoma, and three metastatic neoplasias) and five had hepatopathy (one chronic toxic hepatitis, one cirrhosis, one non-specific hepatitis, one multifocal purulent hepatitis, and one colangiohepatitis) based on histopathological diagnosis. The remaining eight cases, in which cytology, biopsy or post-mortem study was not possible, were presumptively diagnosed as neoplasia (three) or hepatopathy (three chronic hepatopathy, and two acute toxic hepatopathy) based on clinical history, biochemical profile (increased ALT, ALKP, cholesterol, GGT, bilirubin and decreased albumin), and diagnostic imaging results.

Five of the twenty animals presented with peritoneal effusion of the three dogs diagnosed with neoplasia, one had bladder leiomyosarcoma diagnosed by biopsy with a concomitant liver mass, the second had ultrasonographic findings consistent with liver masses with concomitant splenic masses, and the third presented with hepatomegaly, multiple liver nodules and ascites. In the two dogs with acute toxic hepatopathy, clinical, biochemical and ultrasonographic changes (hypoechogenic parenchyma) appeared after cephalexin or trimethoprim-sulfa administration. The remaining three animals with chronic hepatopathy presented with clinical and biochemical changes of long duration, and imaging findings were consistent with chronic lesions (small, hyperechoic liver with nodules).

Mean RI and PI values for each animal are given in Table 1. A statistically significant difference was found between mean RI, PI and systolic blood pressure of the dogs with hepatic disease and the healthy dogs (Fig. 3). The cut-off upper values for normal RI and PI were also obtained from the healthy dogs (mean + 2 SD) as 0.72 for RI and 1.52 for PI. Based on these upper limits, seven dogs had high mean RI values and 10 had high mean PI values. Of the three dogs that had high PI but normal RI, the RI was in the upper limit of the normal values. The remaining 10 dogs had RI and PI values within normal limits. Three of the five animals with ascites had increased RI and/or PI. However, the small number studied made further statistical analyses unreliable.

Table 1
Resistive index (RI), pulsatility index (PI), and systolic blood pressure (SBP) values from dogs with liver disease

Dog	RI	PI	SBP (mm Hg)
1	0.74[a]	1.73[a]	165
2	0.71	1.44	161
3	0.64	1.24	202
4	0.72	1.72[a]	100
5	0.84[a]	2.13[a]	140
6	0.63	1.16	132
7[b]	0.67	1.24	138
8	0.77[a]	1.93[a]	133
9	0.75[a]	1.81[a]	173
10	0.62	1.12	157
11	0.70	1.54[a]	111
12[b]	0.59	1.01	167
13	0.61	1.13	141
14	0.70	1.31	150
15	0.66	1.44	146
16[b]	0.74[a]	1.79[a]	128
17	0.75[a]	1.73[a]	181
18	0.79[a]	2.10[a]	145
19[b]	0.72	1.43	148
20[b]	0.70	1.56[a]	148

[a] Values above normal limits.
[b] Animals with ascites.

Seven animals presented with increased systolic blood pressure, defined as arterial blood pressure > 150 mm Hg (Kraft and Egner, 2003) (Table 1). Three of these dogs had increased RI and PI. A significant correlation was found between ALKP and RI and PI ($r = 0.58$, $P = 0.012$; $r = 0.80$, $P < 0.001$, respectively). No further correlation was found between the indices and arterial blood pressure, heart rate, or other biochemical parameters.

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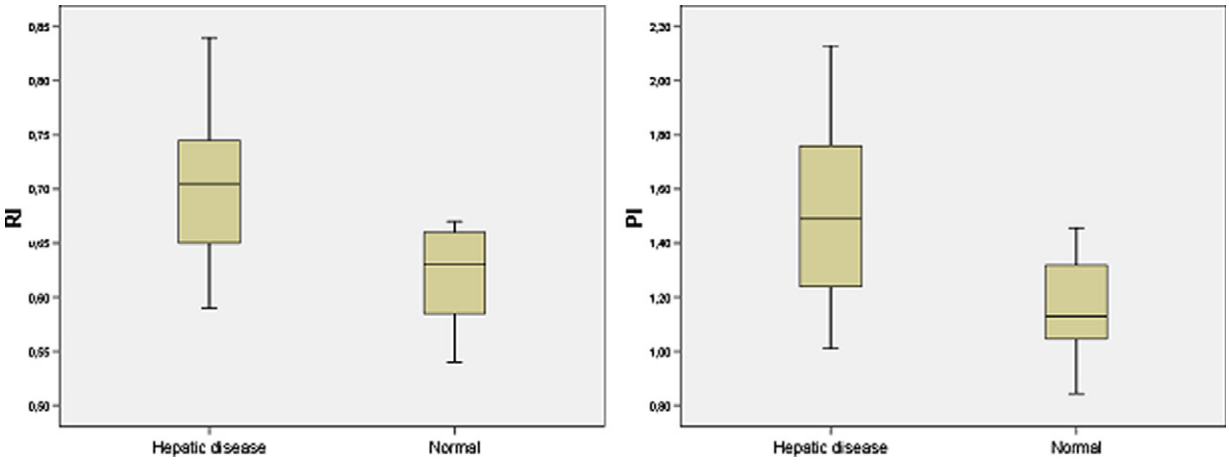

Q2 Fig. 3. Whisker-plot of the resistive index (RI) and pulsatility index (PI) distribution in normal animals and those with liver disease.

Discussion

Proposed normal upper limit values for renal RI in dogs differ slightly between previous studies from 0.70 to 0.73 (Nyland et al., 1993; Morrow et al., 1996; Rivers et al., 1997). Values obtained under the same conditions and by the same authors in a group of healthy non-sedated dogs were used as upper normal limits for renal RI (0.72) and PI (1.52) (Novellas et al., 2007) in the present study.

RI and PI are used in human and veterinary medicine as indicators of vascular resistance. When vascular resistance increases either due to obstruction or vasoconstriction, diastolic blood flow is reduced to a larger degree in comparison to systolic blood flow (Rifkin et al., 1987). This fact is reflected as a higher decrease in end diastolic velocity than in peak systolic velocity and, therefore, increased RI and PI.

In human medicine, RI and PI have been related with the severity and progression of chronic renal failure (Petersen et al., 1997). A positive correlation of RI with systolic pressure, age and end organ damage of the kidney has also been reported (Pontremoli et al., 1999). Increased RI has been reported in dogs with urethral obstruction (Nyland et al., 1993) and in cats with obstructive renal disease (Rivers et al., 1997). Other renal diseases including acute and chronic renal failure (Rivers et al., 1997), congenital dysplasia (Morrow et al., 1996) or acute tubular necrosis have also shown increased RI (Daley et al., 1994).

Several studies in human patients with chronic liver disease have shown that renal arterial resistance is increased in cirrhotic patients with ascites (Colli et al., 1993). Renal RI increases as liver disease progresses (Rendón et al., 2000) related to the severity of cirrhosis and renal blood flow (Sacerdoti et al., 1993; Maroto et al., 1994), and is considered useful as a prognostic indicator of the disease (Maroto et al., 1994; Platt et al., 1994). This increased renal RI is seen even in the absence of any apparent renal dysfunction (Colli et al., 1993).

Early clinical detection of renal impairment in hepatic disease is difficult with conventional tests because the serum creatinine level does not increase until late in the course of the disease. Doppler ultrasonography may detect an increase in renal vascular resistance in patients with moderately severe cirrhosis when technetium-99*m*-diethylene triamine pentaacetic acid scintigraphy is normal (Al-Kareemy et al., 1998) and it also may identify subgroups of non-azotemic patients with hepatic cirrhosis that were at higher risk of subsequently developing kidney dysfunction and hepatorenal syndrome (Platt et al., 1994). The incidence of increased RI among patients with liver disease varies from 36% to 59% (Platt et al., 1992, 1994; Pompili et al., 1999; Colli et al., 1993). A similar incidence was found in our animals.

In human patients with peritoneal effusion, higher RI and PI have been reported in comparison with findings from non-ascitic patients (Sacerdoti et al., 1993; Celebi et al., 1997; Rendón et al., 2000). Five animals in our study presented with ascites and three of these had increased RI and/or PI. However, the small numbers made further statistical analyses unreliable.

Portal hypertension in human hepatic disease is associated with hyperdynamic circulation, which is characterized by hypervolemia, high cardiac output, arterial hypotension, and low peripheral vascular resistance. These circulatory abnormalities are thought to be secondary to splanchnic arteriolar vasodilatation related to portal pressure increase. To counteract the effect of the splanchnic arteriolar vasodilatation on the systemic circulation, a homeostatic response mediated by the sympathetic nervous system, renin–angiotensin system and other vasoconstrictors, increases vascular resistance in other regions such as skin, muscle (Maroto et al., 1993), brain (Guevara et al., 1998), and kidney (Platt et al., 1992; Colli et al., 1993; Sacerdoti et al., 1993; Maroto et al., 1994; Rendón et al., 2000). Middle cerebral, central retinal and renal RI have been shown to correlate with plasma renin activity as well as norepinephrine and aldosterone concentrations (Guevara et al., 1998; Koda et al., 2000). Increased renal vascular resistance was also found in 50% of our animals.

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In human patients, resistive and pulsatility indices have been reported to correlate with some biochemical parameters, such as serum concentrations of bilirubin, albumin, prothrombin time, and creatinine, but not with serum levels of aspartate aminotransferase or ALT (Koda et al., 2000). In the present study, a significant correlation was found between ALKP and both RI and PI. RI and PI were also seen to correlate with arterial pressure and heart rate in people (Mostbeck et al., 1990; Platt, 1992), but no relationship between them was found in the present study. An age related factor has also been described in humans, in which higher RI and PI were found in children and the elderly (Terry et al., 1992). No correlation was found between age and RI or PI in the animals in our study.

PI may be more accurate in differentiating abnormal wave forms because it incorporates mean velocity in its calculation. In human patients with chronic liver diseases, PI was shown to correlate more closely with bilirubin, Child-Pugh score, and plasma levels of neurohumoral factors (plasma renin activity, aldosterone, and norepinephrine) compared to RI, and was therefore recommended to be used as an indicator for renal vascular resistance (Koda et al., 2000). However, other studies found no advantage in measuring PI in addition to RI (Colli et al., 1993). In our study, only three animals presented with increased PI and a normal RI, although in each of these cases RI was near or just at the upper limit value (0.7 in two animals and 0.72 in the other). The correlation found between the indices and the ALKP was higher for PI.

Systemic hypertension has been described in dogs with liver diseases (Bodey and Michell, 1996) and was also found in 35% of the animals in our study. As a decreased vasopressor effect has been suggested as a possible cause of hypertension in those animals, we postulated that this could be also the reason for the increased renal vascular resistance in the kidney. RI and PI values were above normal in some animals indicating the presence of this increased resistance. However a correlation between indices and blood pressure was not found in our study.

Conclusions

On the basis of this study, we conclude that renal vascular resistance, evaluated by means of RI and PI, does increase in some dogs with hepatic disease. A correlation between ALKP and the renal indices could be found in dogs with hepatic disease. Systolic hypertension was found in 35% of the animals although no correlation was found between systolic blood pressure and the two indices. Further studies with a larger group of animals may help to elucidate whether a relationship exists between renal indices and arterial pressure. Such work should also be helpful in assessing the correlation of RI and PI with other parameters, such as neurohumoral factors, or their predictive value for severity and prognosis.

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Annexes

1. Determination of renal vascular resistance in dogs with diabetes mellitus and hyperadrenocorticism

Abstract

Diabetes mellitus (DM) and hyperadrenocorticism (HA) are causes of hypertension in dogs. Mechanisms that induce hypertension in these diseases are related with increased vascular peripheral resistance. Renal RI and PI are related with hypertension and diabetes in human patients and are used as indicators of disease severity. The aims of the study were to assess renal vascular resistance in dogs with DM and/or HA, since may develop hypertension due to their disease, and evaluate the possible relationship between the indices, blood pressure, and biochemical parameters. Nineteen dogs with HA and/or DM were included in the study. When compared with values for healthy dogs means RI, PI, and systolic blood pressure were higher in the group of dogs. Correlation was found between both indices and blood glucose. In conclusion, renal vascular resistance was higher in dogs with DM and/or HA.

Keywords: dog; resistive index; pulsatility index; hyperadrenocorticism, diabetes mellitus.

Introduction

Endocrine diseases such as hyperadrenocorticism (HA) and diabetes mellitus (DM) in dogs are known causes of secondary hypertension (Dukes 1992, Bodey and Michell 1996, Struble and others 1998). Hypertension was found in 46% of diabetic dogs (Struble and others 1998) and is described in 50% to 86% of dogs with HA (Ortega and others 1996, Nichols 1997, Goy-Thollot and others 2002). Mechanisms that induce hypertension in these diseases are usually related to increased vascular peripheral resistance (Littman 2000).

Duplex Doppler ultrasound provides both real time anatomic and blood flow dynamic information by obtaining pulsed wave Doppler spectra. Resistive index (RI) and pulsatility index (PI) are calculated from blood flow velocity waveform analysis and are widely accepted as indicators of vascular resistance. Renal RI and PI are widely used in human medicine to assess renal vascular resistance in pathologies involving increased blood pressure, hemodynamic alterations, or renal disease. Resistive and PI are related to severity and progression of chronic renal failure (Petersen and others 1997). They are also related to systolic pressure, age and kidney end organ damage in patients with hypertension (Pontremoli and others 1999). Higher values of RI and PI are also found in human diabetic patients with renal impairment (Sperandeo and others 1996, Casadei and others 2003). Significant increase in renal RI was also described in people with DM and normal renal function (Derchi and others 1994). In humans, renal RI and PI were reported to correlate with serum creatinine concentration, creatinine clearance rate, patient age, duration of diabetes, blood pressure, blood glucose, cholesterol levels, and the presence of

microalbuminuria (Kim and others 1992, Brkljacic and others 1994, Derchi and others 1994, Platt and others 1994, Ishimura and others 1997, Sari and others 1999). These indices also allow the early detection of human patients affected by DM, who show renal vascular involvement without alterations of other ultrasound parameters (Casadei and others 2000).

Normal values for renal RI and PI have been reported in normal dogs and cats (Nyland and others 1993, Morrow and others 1996, Rivers and others 1996, Rivers and others 1997a, Mitchell and others 1998, Pollard and others 1999, Novellas and others 2007). Increased RI and or PI have been described in dogs and cats with different renal diseases (Nyland and others 1993, Morrow and others 1996, Rivers and others 1997b, Choi and others 2003).

Studies evaluating the possible relationship of renal RI and PI and blood pressure in dogs with HA or DM could not be found. The aims of this study were: (1) assess renal vascular resistance in dogs with DM and/or HA and, thereby, which were at risk of developing hypertension due to their disease, and (2) evaluate the possible relationship between the indices, blood pressure, and biochemical parameters.

Material and methods

Nineteen dogs attending the Veterinary Teaching Hospital of the Autonomous University of Barcelona with DM and/or HA were included in the study. The diagnosis was based on clinical, biochemical and diagnostic imaging findings.

Physical examination, complete blood cell count, biochemical profile (including total bilirubin, calcium, cholesterol, creatinine, phosphate, glucose, total protein, urea, sodium chloride, alanine amino transferase (ALT), creatine kinase, alkaline phosphatase (ALKP), gamma glutamyl transferase (GGT), and proteinogram), urinalyses, and complete abdominal ultrasound were performed in the animals. Diabetes mellitus diagnosis was based on clinical signs and persistent fasting hyperglucemia and glucosuria. Hyperadrenocorticism diagnosis was based on clinical signs, laboratory abnormalities and adrenal gland ultrasonography. Diagnosis was confirmed by compatible ACTH stimulation test and low-dose dexamethasone suppression test; in addition high-dose dexamethasone suppression test was performed in 1 case.

Systolic blood pressure was determined before other interventions and after 5 to 10 minutes for adaptation to the environment. Systolic blood pressure was measured with a Doppler device (Vet BP Doppler Ultrasound Blood Flow Detector, Sonomed Ltd, 8 MHz transducer). The measurement was done with the animals in left lateral recumbency and the cuff placed on the proximal aspect of the tarsus to compress the cranial tibial artery. Three measurements were obtained in every animal, as previously described (Stepien and Rapoport 1999) and the mean value computed.

Hair was clipped and acoustic gel (Polaris II ultrasonic gel, GE Medical Systems) was applied to the skin. The animals were placed in right or left lateral recumbency to scan the uppermost kidney. A multifrequency sector transducer operating at 6 or 7 MHz was used. Once the kidney was located using B-mode

ultrasound, colour Doppler was used to visualize the intrarenal vasculature. Subsequent pulsed Doppler interrogation from one of the interlobar or arcuate arteries was obtained with a sample width of 1.5 to 2 mm and a frequency of 5 MHz. The smallest scale that displayed the flow without aliasing was selected. The mean RI and PI for each kidney was determined by averaging a total of nine Doppler wave forms from the arteries (Fig. 1) at three separate locations as previously described (Nyland and others 1993, Pollard and others 1999).

The RI and PI were calculated automatically by the software of the ultrasound machine (Acuson Computed sonography 128/XP or an Acuson Aspen), after manual delimitation of peak systolic velocity, end diastolic velocity and time average maximum velocity (TAMX), as follows:

RI = (peak systolic velocity) – (end diastolic velocity) / (peak systolic velocity)

PI = (peak systolic velocity) – (end diastolic velocity) / (TAMX)

Heart rate was also calculated from the renal pulsed Doppler wave forms by the software of the machine.

When possible, follow up values were recorded, repeating all the measurements detailed above in the animals.

Blood pressure and renal indices previously obtained from 27 mixed breed healthy dogs and 10 healthy cats (Novellas and others 2007) were used

for comparison as a control group. Values were obtained using the same technique and by the same operators to avoid variation due to this factors.

Statistical analysis was performed with a Statistical Package for Social Sciences (SPSS computer package). The indices, heart rate, and arterial pressure were found to have a normal distribution using a Shapiro-Wilk test, therefore parametric tests were applied. The values of RI and PI of the animals with DM and/or HA were compared with the values of the healthy dogs group following a Student's *t* test. A Pearson correlation study was applied to determine relation of RI or PI to blood pressure and biochemical parameters. Statistical significance was stated as $P < 0.05$.

Results

Twelve females and 7 males of different breeds (8 crossbreed, 3 Yorkshire terriers, 2 Poodles, 2 Boxers, 1 miniature Schnauzer, 1 Shih-Tzu, 1 Doberman, and 1 Catalan Sheepdog) were evaluated in this study. Twelve animals presented with HA, 3 presented with DM, and 4 with both HA and DM. The mean age was 11 years (SD= 1.87).

Revaluation was possible in five dogs. Three of them presented HA and two presented both HA and DM. Three dogs were revaluated once and two were revaluated twice. Mean follow up time was 5.7 months (range 0.5-17 months).

Mean results for RI, PI, blood pressure, and heart rate for the 19 diseased and 27 healthy dogs are given in table 1.

No statistically significant difference was found between the right and the left kidney indices, so a mean value of both kidneys was used for comparison. A statistically significant difference was found between renal RI, PI (Fig. 2) of the group of the diseased dogs and the group of normal dogs. The cut off upper values for normal RI and PI were calculated as mean + 2SD from the healthy dogs and stated as 0.72 for RI and 1.52 for PI. Based on these upper limits, 2 dogs had high mean PI and 3 other dogs had both high mean RI and PI. As regards the two dogs that had high PI but normal RI, the RI was in the upper limit of the normal values (0.72 and 0.71, respectively).

A statistically significant difference was also found between heart rate and systolic blood pressure of the group of the diseased dogs and the group of normal dogs. Ten of the nineteen animals presented hypertension, stated as systolic blood pressure > 150 mmHg (Kraft and Egner 2003). Four of these dogs had increased RI and PI.

Number and percentage of increased RI, PI, and hypertension for different disease group are given in table 2.

If groups with different pathology were considered, none of the three animals with DM alone presented indices values above the upper limits; 2/12 dogs with HA alone had increased values; and 3/4 animals with both DM and HA presented increased values.

As regarding blood pressure, 0/3 with diabetes, 8/12 with HA and 2/4 with DM and HA presented hypertension.

In five animals follow up was possible. Measurements were repeated twice in three dogs and three times in two dogs. Three of the animals (two with HA and 1 with DM and HA) presented increased values in the second evaluation and one also in the third. All these three animals had had normal renal RI and PI in the first measurement. One of the other two dogs had HA and presented normal values both in the first and second evaluation. The fifth animal, (with DM and HA) had presented increased RI and PI values in the previous evaluation but showed decreased or equal values in the subsequent determinations. This dog was the only animal which was under angiotensin converting enzyme inhibitors (ACEIs) treatment in the 2 follow up measurements. On the second evaluation, all five animals presented hypertension but none of the two was hypertensive in the third measurement.

Statistically significant correlation was found between blood glucose and RI (r = 0.573, p=0.032) and PI (r = 0.585, p=0.028), and between age and RI (r = 0.484, p=0.036).

Discussion

Diabetes mellitus and HA cause hypertension in human and animals. Mechanisms that induce hypertension in human diabetic patients are related with diabetes-induced alterations such as sodium retention, vasculopathy and nephropathy (Weidman and others 1993). Sympathetic nerve hyperactivity is also important in the pathogenesis of hypertension; it stimulates renin-angiotensin system activity, promotes sodium reabsorption, and increases heart

rate, stroke volume and peripheral vascular resistance, thus inducing hypertension (Perin and others 2001). Possible mechanisms associated with hypertension in diabetic dogs include disturbed lipid metabolism leading to reduced vascular compliance and generalized glomerular hyperfiltration or an immune-mediated microangiopathy affecting basement membranes (Dukes 1992). Vasculopathy leads to peripheral vessel changes and vasoconstriction (Kraft and Egner 2003).

Pathogenesis of hypertension in HA results from the interplay between several pathophysiological mechanisms regulating plasma volume, peripheral vascular resistance and cardiac output, which are all increased. Glucocorticoids causes hypertension through several mechanisms: their intrinsic mineralcorticoid activity; activation of the renin-angiotensin system; enhancement of cardiovascular inotropic and pressor activity of vasoactive substances; and causing suppression of the vasodilator systems. Glucocorticoids may also induce changes that increase cardiac output, total peripheral resistance and renovascular resistance, leading to chronic hypertension. Insulin resistance seems to contribute to the hypertension of HA (Magiakou and others 2006). Increased elevation in blood pressure in response to catecholamines has been demonstrated in dogs with induced hyperadrenocorticism (Martinez and others 2005).

Resistive and pulsatility indices are used in human and veterinary medicine as indicators of vascular resistance. When vascular resistance increases either due to obstruction or vasoconstriction, diastolic blood flow is reduced to a higher degree in comparison to systolic blood flow (Rifkin and

others 1987). This fact is reflected as a higher decrease in end diastolic velocity than in peak systolic velocity and, therefore, increased RI and PI.

Resistive and PI are related to the severity and progression of chronic renal failure in human patients (Petersen and others 1997). They are also related to systolic pressure, age, and end organ damage in the kidney in people with hypertension (Pontremoli and others 1999). Higher renal PI and RI values are described in human patients with DM and nephropathy (Brkljacic and others 1994, Sperandeo and others 1996). Diabetes mellitus patients with normal renal function also showed a significant increase in RI in comparison with controls (Derchi and others 1994).

We found increased renal RI and PI in our group of diabetic and HA patients in comparison to the healthy group, suggesting that increased vascular resistance occurs in these animals. Correlation between renal RI and PI and blood pressure has been described in human diabetic patients (Brkljacic and others 1994, Derchi and others 1994). However, this relationship was not found in the dogs of our study. It has also been observed in human studies an inverse relationship between RI in intrarenal arteries and heart rate (Mostbeck and others 1990). In our study, the heart rate was higher in the disease group than in the healthy group; this fact may potentially have falsely decreased RI and PI in the disease group. Renal RI and PI were also reported to correlate with serum creatinine concentration, creatinine clearance rate, patient age, duration of diabetes, blood glucose and cholesterol levels (Kim and others 1992, Brkljacic and others 1994, Derchi and others 1994, Platt and others 1994, Ishimura and others 1997, Sari and others 1999). We found a correlation between both RI and

PI and blood glucose concentration in our animals. Hyperglycaemia activates intrarenal rennin-angiotensin-aldosterone, leading to a stimulation of the local production of angiotensin II, which increases renal vascular resistance and reduces renal blood flow (Arima and Ito 2003). A correlation between age and RI was also found in our dogs.

Three of the four animals with concurrent DM and HA had RI and PI values above the normal limit at first evaluation; the fourth animal presented increased values in the follow-up measurement. Only two dogs in the HA group and no dog in the diabetic group had increased values at first examination. Follow up was possible in three animals with HA revealing normal values in two of them (although higher than in the first evaluation); the third one developed diabetes and presented increased RI and PI in the two follow up measurements. This seems to indicate that increased vascular resistance could be more frequent in animals with both diseases. The fact that more factors increasing renovascular resistance are interacting at the same time in these animals could explain this observation.

A tendency for RI and PI values to increase was seen with time in three of the dogs with follow up measurements. As RI and PI correlate with duration of disease in human (Derchi and others 1994, Ishimura and others 1997), the tendency we have observed in our animals could be indicative of similar effects in dogs. One dog with DM and HA showed lower values in the subsequent measures. This animal was treated with enalapril during these measures. As ACEIs have shown to reduce intrarenal vascular resistance in diabetic patients

(Taniwaki and others 2003), this could be the cause for the decreasing indices values.

Presentation of hypertension in our dogs with HA with or without concomitant diabetes in our study was between the ranges previously described for dogs with HA (Ortega and others 1996, Nichols 1997, Goy-Thollot and others 2002). On the other hand hypertension was not found in any of the dogs with diabetes alone. Prevalence of hypertension in dogs with diabetes in other studies is controversial. Whereas in one study 46% of the dogs presented hypertension (systolic blood pressure > 160mmHg) (Struble and others 1998) in another study no differences were found between systolic blood pressure of the diabetic dogs and the control group. Moderate systolic hypertension was found in 29% of diabetic but also in 18% of control dogs and severe hypertension was found in only 1 diabetic dog (Manczur and others 2006).

Differing from what has been described in humans, no correlation has been found between renal indices and systolic blood pressure in our study. This fact suggests that different mechanisms may be acting in each species.

Obvious limitations of this study are the small number of animal evaluated and the follow up in a limited number of cases. Further studies with larger number of patients will be required to confirm the presence of increased RI and PI in these patients and the relationship of these indices with the evolution of the disease.

Conclusion

In conclusion, increased renal vascular resistance has been found in dogs with HA and DM. Significant correlation was found between the indices and glucose blood concentration, but no relation between blood pressure and renal indices was seen. More studies with a larger number of animals will elucidate if this is a consistent finding. Furthermore, the utility of these values in the prognostic and progression of the disease needs to be further investigated.

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Tables

Table 1. Mean RI, PI, systolic blood pressure, and heart rate of healthy and disease dogs.

Group	RI	PI	Heart rate (bpm)	Blood pressure (mmHg)
Healthy group	0.62 ± 0.04	1.15 ± 0.15	106 ± 24	126 ± 14
Disease group	0.68 ± 0.07[a]	1.37 ± 0.28[a]	125 ± 37[a]	171 ± 47[a]

[a] Significant differences.

Table 2. Number and percentage of dogs with increased renal indices (RI and/or PI) and hypertension.

Group	Increased indices		Hypertension	
	n	%	N	%
Dogs				
All (n=19)	5	26	10	53
DM (n=3)	0	0	0	0
HA (n=12)	2	17	8	67
DM & HA (n=4)	3	75	2	50

Figures

Figure 1. Triplex Doppler ultrasound image showing a spectral intrarenal arterial waveform.

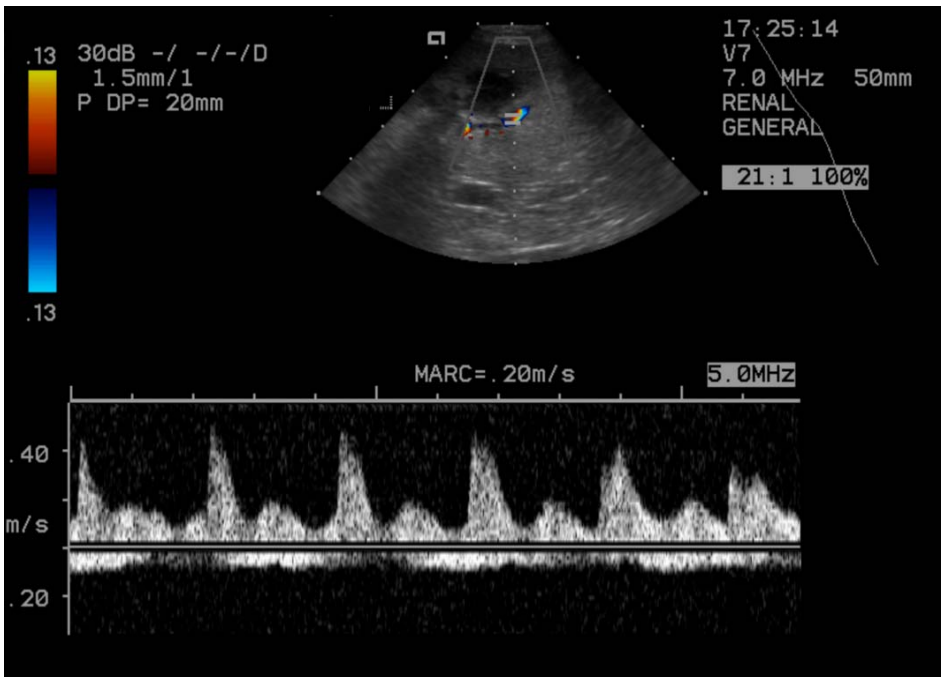
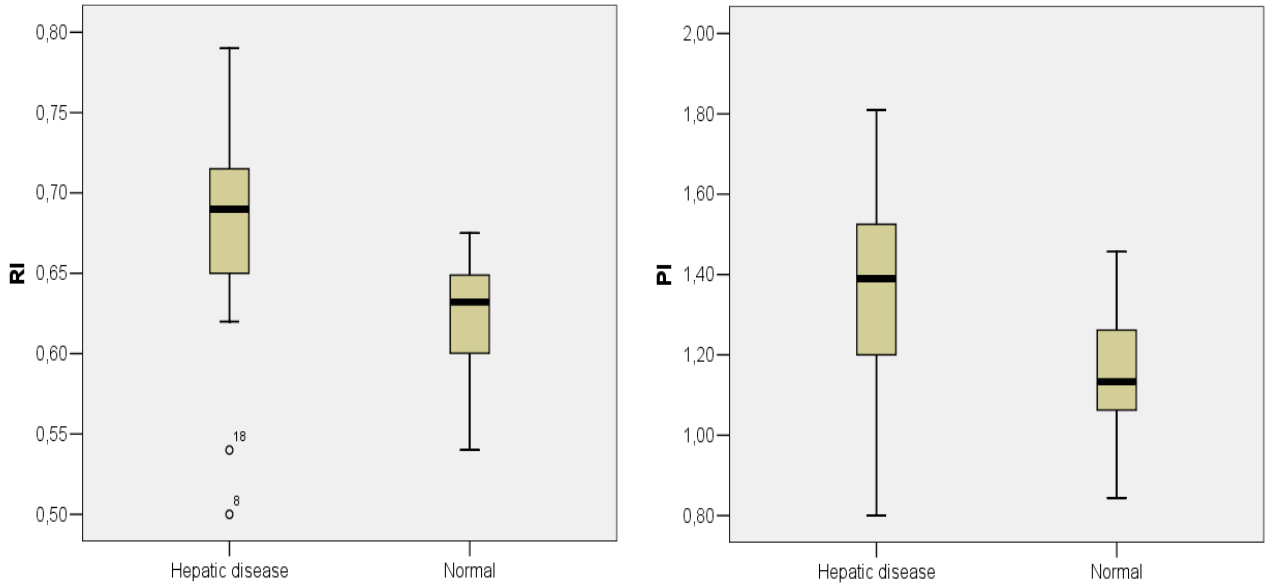


Figure 2. Whisker–plot of the resistive (RI) and pulsatility (PI) indices distribution in normal and in animals with disease.



2. Determination of renal vascular resistance and blood pressure in dogs and cats with renal disease

Abstract

Systemic hypertension is common in dogs and cats with renal disease. Increased intrarenal vascular resistance may play a role in the development of hypertension as a result of renal disease. Intrarenal vascular resistance can be evaluated by means of resistive index (RI) and pulsatility index (PI) obtained with Doppler ultrasound. RI was reported to be associated with early hypertensive renal damage and also to correlate with systemic blood pressure in human patients. The aim of this study was to assess renal vascular resistance in dogs with renal disease and to investigate the possible relationship between renal RI and PI with systolic blood pressure and biochemical parameters in dogs and cats with renal disease. Fifty three dogs and 22 cats with renal disease were included in the study. Significant differences were found between RI and PI of the healthy animals and the renal disease group. Significant correlation was found between the indices and red blood cell count, packed cell volume, creatinine, and urea. No relationship could be found between renal RI and PI and systolic blood pressure. RI and PI may be used in the evaluation and follow up of many renal diseases.

Key words: dog, cat, kidney, pulsatility index, resistive index

Introduction

Systemic hypertension is commonly observed in dogs and cats with renal disease and it has been reported to occur in 60% to 69% of cats with renal failure (Kobayashi et al., 1990) and 31% to 93% of dogs with renal failure (Cowgill and Kallet, 1986; Jacob et al., 2003; Cortadellas et al., 2006).

The kidney not only participates in the development and persistence of hypertension but it is also injured by hypertension. Sustained systemic hypertension may result in renal injury such as glomerulosclerosis, glomerular atrophy, and proliferative glomerulonephritis, due to transmission of increased blood pressure to the glomerular capillary bed (Bartges et al., 1996; Brown and Henik., 1998). Dogs with renal failure and higher systolic blood pressure have been reported to be more likely to develop uremic crisis, to die, and to undergo greater decrease in renal function (Jacob et al., 2003). In another study of canine induced renal failure, the more hypertensive dogs had significantly lower glomerular filtration rate values, higher urine protein:creatinine ratios, and higher renal lesions scores than less hypertensive dogs (Finco, 2004).

Possible mechanisms involved in hypertension related to renal disease are: failure to excrete Na and water resulting in increased extracellular fluid volume; increased renin-angiotensin-aldosterone system; increased production of renopressor substances or decreased production of renodepressor substances; anaemia, resulting in increased cardiac output; and hyperparathyroidism. Once hypertension has developed, it will accelerate the renodestructive process, resulting in glomerulosclerosis and further loss of

nephrons, stablishing a vicious cycle (Dukes, 1992). Increased intrarenal vascular resistance as a result of glomerulosclerosis may play a role in the development of hypertension as a result of renal disease (Dukes, 1992; Van de Sandt et al., 2003).

The normal renal arteries have low resistance to blood flow, seen as high continuous diastolic flow, which gradually decreases during diastole (Szatmari et al., 2001). This vascular pattern can be evaluated by mean of pulsed Doppler ultrasound that may also provide information about vascular resistance using calculations such as resistive (RI) and pulsatility indices (PI). Duplex Doppler evaluation of intrarenal RI may be useful as an aid in confirmation of renal disease in dogs and cats in which the gray scale sonographic appearance of the kidney is unremarkable or when increased relative renal cortex echogenicity is the sole renal parenchymal abnormality observed (Rivers et al., 1997).

RI and PI in normal dogs and cats have been described (Nyland et al., 1993; Morrow et al., 1996; Rivers et al., 1996; Rivers et al., 1997; Mitchell et al., 1998; Pollard et al., 1999; Novellas et al., 2007). They have also been used in studies of renal and urinary tract disease in dogs and cats (Nyland et al., 1993; Daley et al., 1994; Morrow et al., 1996; Rivers et al., 1996; Rivers et al., 1997; Choi et al., 2001; Choi et al., 2003), and to evaluate renal transplantation in both cats (Pollard et al., 1999) and dogs (Nyland et al., 1997).

In human medicine RI has been proved to be of value in predicting reversibility of renal failure, being the RI significantly higher in patients with persistent renal dysfunction than in those with recovery of the function (Platt et

al., 1991). It has been also reported that higher RI and PI in humans are associated with a faster decline in renal function (Petersen et al., 1997).
Increased RI was reported to be associated with early hypertensive renal damage and also to correlate with systemic blood pressure in human patients (Pontremoli et al., 1999). Increased RI has been also reported to be related to increased blood pressure and to duration of the disease in patients with hypertension (Veglio et al., 1992).

In the studies in which RI was evaluated in dogs and cats with renal disease, systemic blood pressure was either no evaluated (Morrow et al., 1996) or within normal limits in all the animals in which was measured (6 dogs and 4 cats) (Rivers et al., 1997), and correlation between RI and systemic blood pressure was not assessed. It would be of interest to investigate if such a relation between blood pressure and renal RI and PI exists also in dogs and cats, and therefore if the indices may be used in the prognosis and follow up of canine and feline patients with renal disease and / or hypertension.

The aims of this study were (1) to assess renal vascular resistance in dogs with renal disease, (2) to investigate the possible relationship between renal RI and PI with systolic blood pressure in dogs and cats with renal disease and (3) to investigate the relationship of the RI and PI with the severity of the renal disease (evaluated as laboratorial findings).

Materials and methods

Fifty three dogs and 22 cats attending the Veterinary Teaching Hospital of the Autonomous University of Barcelona with renal disease were included in the study. The diagnosis was based on clinical, biochemical and diagnostic imaging findings. Blood pressure and renal indices values previously obtained from 27 mixed breed healthy dogs and 10 mixed breed healthy cats (Novellas et al., 2007) were used as normal values for comparison with animals with renal disease. Values were obtained using the same technique and by the same operators to avoid variation.

Physical examination, complete blood cell count, biochemical profile (including total bilirubin, calcium, cholesterol, creatinine, phosphate, glucose, total protein, urea, sodium chloride, alanine amino transferase (ALT), creatine kinase, alkaline phosphatase (ALKP), gamma glutamil transferase (GGT), and proteinogram), urinalyses and complete abdominal ultrasound were performed in the animals. When possible, biopsy or post-mortem examination was performed.

Systolic blood pressure was determined before other interventions and after 5 to 10 minutes for adaptation to the environment. Systolic blood pressure was measured with a Doppler device (Vet BP Doppler Ultrasound Blood Flow Detector, Sonomed Ltd, 8 MHz transducer). The measurement was done with the animals in left lateral recumbency and the cuff placed on the proximal aspect of the tarsus to compress the cranial tibial artery. Three measurements

were obtained in every animal, as previously described (Stepien and Rapoport, 1999), and the mean value computed.

Triplex Doppler ultrasonography was performed with an ultrasound device (Acuson Computed sonography 128/XP or an Acuson Aspen). Hair was clipped and acoustic gel (Polaris II ultrasonic gel, GE Medical Systems) was applied to the skin. The animals were placed in right or left lateral recumbency to scan the nondependent kidney. A sectorial multifrequency transducer operating at 6 or 7 MHz was used. Color Doppler was used to visualize the intrarenal vasculature. Subsequent pulsed Doppler interrogation from interlobar or arcuate arteries was obtained with a sample width of 1.5 to 2 mm and a frequency of 5 MHz. The smallest scale that displayed the flow without aliasing was selected. The mean RI and PI for each kidney was determined by averaging a total of 9 Doppler wave forms at three separate locations as previously described (Nyland et al., 1993; Pollard et al., 1999).

The RI and PI were calculated automatically by the software of the ultrasound machine, after manually delimitation of peak systolic velocity, end diastolic velocity and time average maximum velocity (TAMX), as follows:

RI = (peak systolic velocity) – (end diastolic velocity) / (peak systolic velocity)

PI = (peak systolic velocity) – (end diastolic velocity) / (TAMX)

Heart rate was also calculated from the renal pulsed Doppler wave forms by the software of the machine.

When possible, follow up values were recorded, repeating all the measurements detailed above.

Statistical analysis was performed with a Statistical Package for Social Sciences (SPSS computer package). The indices, heart rate, and arterial pressure were found to have a normal distribution in dogs, therefore parametric tests were applied. In cats, all these values were also normal except for the PI, therefore non-parametric test were applied for the PI. The values of RI and PI of the animals with renal disease were compared with the values of the normal dogs and cats group following a Student's *t* test or Man-Whitney U test. Pearson or Spearman correlation studies were applied to determine relation of RI or PI to blood pressure and biochemical parameters. Differences between RI and PI in the animals with increased and normal systolic blood pressure were also investigated using Student's *t* test or Man-Whitney U test.

Statistical significance was stated as $P < 0.05$. Results are given as mean ± standard deviation.

Results

Dogs

Thirty male and 23 female dogs presented with renal disease were included in the study. Mean age was 6.46 ± 3.78 years. Thirty six of the dogs were diagnosed as chronic renal failure (CRF), 4 as acute renal failure (ARF) and 13 as other renal or urologic diseases, including 5 hydronephrosis, 4 neoplasias, 2 dogs with renal cyst, 1 with a presumptive renal abscess in the left

kidney, and 1 with unilateral ectopic ureter. Histopathological results were available for 16 animals (Table 1). In the dog with ectopic ureter this abnormality was confirmed at surgery.

The cut off upper values for normal RI and PI were obtained from the healthy dogs (mean + 2 standard deviations) and stated as 0.72 for RI and 1.52 for PI. Based on these upper limits, 20 (38%) dogs had high mean RI and 23 (43%) had high mean PI. Number and percentage of increased RI and PI for the different groups are given in table 2.

No differences were found between right and left kidneys, therefore the mean value for both kidneys were used for comparison. Significant differences were found between RI ($P < 0.001$), PI ($P < 0.001$) (Figure 1), systolic blood pressure ($P < 0.001$) values of the healthy dogs and the renal disease group. No significant differences were found between the heart rate of the groups. If different groups were considered based on increased systolic blood pressure (systolic blood pressure > 150 mmHg considered as hypertension (Kraft and Egner, 2003)), no differences in RI and PI between the groups were found. Twenty eight (53 %) of the dogs presented an increased systolic blood pressure.

Significant low correlation was found between RI and red blood cell count ($r = -0.389$, $P = 0.008$) and packed cell volume ($r = -0.309$, $P = 0.036$) and between PI and serum creatinine concentration ($r = 0.294$, $P = 0.038$), but not correlation was found between systolic blood pressure and either of the indices.

Three out of four dogs with diagnosis of chronic interstitial nephritis, one of two with glomerulonephritis alone and the dog with both chronic interstitial nephritis and glomerulonephritis presented increased indices.

Cats

Seven male and fifteen female cats presented with renal disease were included in the study. Mean age was 6.8 ± 3.57 years. Fifteen of the animals were diagnosed as CRF, 2 as ARF and 5 as others, including 5 cats with polycystic kidney disease (PKD) without clinical signs or laboratorial changes consistent with renal failure. In 4 of the CRF cats histological diagnosis was obtained from post mortem evaluation, and included 1 animal with chronic interstitial nephritis, 1 with chronic interstitial nephritis and glomerulonephritis and 2 animals with neoplasia (1 renal carcinoma, 1 multiple myeloma).

The cut off upper values for normal RI and PI were also calculated from a group of normal cats as mean + 2 SD and stated as 0.70 for RI and 1.29 for PI. Based on these upper limits, 12 (54%) cats had high mean RI and 11 (50%) had high mean PI. Number and percentage of increased RI and PI for the different groups are given in table 3.

No differences were found between right and left kidneys, therefore the mean value for both kidneys were used for comparison. Significant differences were found between RI (P = 0.0003) and PI (P = 0.003) values of the healthy cats and the renal disease group (Figure 2). No significant differences were found between the systolic blood pressure and the heart rate of the groups. If

different groups were considered based on increased systolic blood pressure (systolic blood pressure > 150 mmHg considered as hypertension (Kraft and Egner, 2003)), no differences in RI and PI between the groups were found.

Significant correlation was found between RI and serum creatinine (r = 0.556, *P* = 0.025) and urea (r = 0.742, *P* = 0.002) and between PI and serum creatinine (r = 0.568, *P* = 0.022) and urea (r = 0.775, *P* = 0.001), but not correlation was found between systolic blood pressure and either of the indices. All of the animals in which histological diagnosis was available presented with increased RI and PI except for the cat with chronic interstitial nephritis.

Discussion

Proposed normal upper limit values for renal RI in dogs slightly differ between previous studies from 0.70 to 0.73 (Nyland et al., 1993; Morrow et al., 1996; Rivers et al., 1997). In the present study, values obtained under the same conditions and by the same authors in a group of healthy non sedated dogs and cats were used as upper normal limits for renal RI and PI (Novellas et al., 2007).

RI and PI are used in human and veterinary medicine as indicators of vascular resistance. When vascular resistance increases either due to obstruction or vasoconstriction, diastolic blood flow is reduced to a larger degree in comparison to systolic blood flow (Rifkin et al., 1987). This fact is reflected as a higher decrease in end diastolic velocity than in peak systolic velocity and, therefore, increased RI and PI.

In human medicine, RI and PI have been related with severity and progression of chronic renal failure (Petersen et al., 1997). A positive correlation of RI with end organ damage of the kidney has also been reported (Pontremoli et al., 1999). Increased RI was reported in dogs with ureteral obstruction (Nyland et al., 1993) and in cats with obstructive renal disease (Rivers et al., 1997). Other renal diseases including acute and chronic renal failure (Rivers et al., 1997), congenital dysplasia (Morrow et al., 1996), or acute tubular necrosis (Daley et al., 1994), were also related with increased RI in animals.

Increased renal RI and PI were found in the present study in the dogs with renal disease in comparison with healthy dogs. Values were increased in about 50% of the dogs with CRF, were less frequently increased in dogs with other pathologies and tend to be normal in dogs with ARF. This lack of increased indices in animals with ARF differ from previous descriptions were increased RI were reported in animals with ARF (Morrow et al., 1996; Rivers et al., 1997). This could be due to the small number of animals with ARF included in our study and to a different cause of ARF. In human patients, RI may be helpful in distinguishing acute tubular necrosis from prerenal azotemia; higher RI values were found in patients with acute tubular necrosis in comparison with patients with prerenal azotemia (Platt et al., 1991). Three of our dogs with ARF presented prerenal azotemia, and the fourth postrenal azotemia, while four out of ten animals in a previous study (Rivers et al., 1997) presented acute tubular necrosis. The cause of acute renal failure in the other study was not reported.

Some studies in both human patients (Platt et al., 1990) and dogs (Morrow et al., 1996) suggest that renal pathology limited essentially to the

glomeruli do not present increased RI. However in other studies increased RI where found in dogs with glomerular disease alone (Rivers et al., 1997). One of the two dogs in the present study with histopathological diagnosis of glomerulonephritis alone presented increased indices. Given the small number of available histopathological diagnosis, further conclusions can not be stated. However it should be take in to account that 19/36 dogs with CRF were patients with leishmaniasis. In dogs with leishmaniasis the initial renal lesion is due to immunocomplexes deposit causing glomerulonephritis. If dogs with leishmaniasis were segregated from other animals with CRF in our study, the dogs with leishmaniasis showed a tendency to have lower values (mean RI = 0.71 vs 0.73 and PI = 1.56 vs 1.74). No statistical differences between the groups were found and the mean values of the animals with leishmaniasis were still statistically higher compared with healthy animals. So it would show that increased RI was present among these animals with glomerular disease. However, as glomerular disease progresses, tubulointerstitial disease may also be present in renal disease caused by leishmaniasis, although it is less frequent (Costa et al., 2003; Cortadellas et al., 2006). Then without the histopathological characterization of the lesions of these animals with leishmaniasis it can not be stated that increased indices were found in all these animals with glomerulonephritis alone.

Congenital renal dysplasia has been also reported to increase renal RI (Morrow et al., 1996). Congenital renal disease was presumptively diagnosed in 3 of the animals with CRF. Two of them presented increased values for both RI and PI and the third dog presented a PI in the upper limit of the normal value.

Higher indices were also found in 4 dogs in the group with other renal diseases. One was one animal with renal cyst, one presented hydronephrosis and two were animals with neoplasia. Obstruction has been reported to increase RI in human (Platt, 1992) and dogs (Nyland et al., 1993; Choi et al., 2003). However, increased RI values do not permit consistently diagnose obstruction (Nyland et al., 1993). It has been suggested than a difference of 0.10 or more between the obstructed and the non-obstructed kidney in the same patient may be helpful to diagnose obstruction in spite of the fact that RI measurements are within normal limits (Platt, 1992). RI and PI were over the normal values in one of the dogs with bilateral hydronephrosis; in another dog the difference in the RI between the hydronephrotic and the normal kidney was 0.1 (although both were within normal limits); and both indices were normal in 1 dog with bilateral hydronephrosis and in two dogs with unilateral hydronephrosis.

Similarly to what found in one of the dogs with unilateral hydronephrosis, very different values of the RI and PI were found in the dog with unilateral ectopic ureter (a difference of 0.17 for the RI and 0.52 for the PI). These were higher in the affected kidney and, even no hydronephrosis or hydroureter were present, they could be reflecting some degree of obstruction.

One dog presented with a presumptive renal abscess. Indices values in the affected kidney were increased above the normal values, and decreased until normal values after the effective antibiotherapy. No reports could be found with comparable descriptions, but both the increased values in this animal and the increased values in animals with neoplasia seem to support that many renal lesions can cause increased vascular resistance.

Higher values were also found in cats with renal disease in comparison with healthy cats. Values beyond the upper limit for the RI and PI were found, respectively in 67 and 73 % of the cats with CRF, in 1/2 cats with ARF and in none of the cats classified as others. All five cats in the other group were animals with PKD. RI and PI were used to assess renal function in human patients with autosomal dominant polycystic kidney disease (Kondo et al., 2001), and were reported to be higher than in control patients (Brkljacic et al., 1997). The five cats in the study were young animals (mean age 2.6 years) and had no signs of renal failure. An elder cat (9 years) with PKD and renal failure was included in the CRF group and presented increased RI and PI. Therefore it is likely that the disease was not severe enough in the five cats to show changes in the indices.

A positive correlation of RI with systolic blood pressure has been reported in human patients (Pontremoli et al., 1999). Increased RI has been also reported to be related to increased blood pressure and to duration of the disease in patients with hypertension (Veglio et al., 1992). No correlation could be found between systolic blood pressure and either RI or PI in our study population.

Heart rate was also reported to show negative correlation with RI (Mostbeck et al., 1990). No similar correlation was found in this study. Differences were not found between the mean heart rate of the healthy animals and those with renal disease.

In human patients RI has been reported to correlate with renal function in patients with renal disease. In several reports, RI correlated with serum

creatinine (Ikee et al., 2005), creatinine clearance (Shimizu et al., 2001; Ikee et al., 2005), and blood urea nitrogen (Mostbeck et al., 1991; Shimizu et al., 2001). In the present study negative correlations were found between RI and both red blood cell count and packed cell volume in dogs, similarly to a previous study where a direct association between anaemia and elevated RI was found (Morrow et al., 1996). It was suggested that anaemia may induce a hypoxic state in the kidney which will cause constriction of the vessels resulting in increased vascular resistance and elevation of renal RI. In the present study correlations between PI and creatinine concentration in dogs, and between both RI and PI and serum creatinine and urea in cats were found, suggesting some relationship between renal function and the indices.

Conclusion

In conclusion, no relationship could be found between renal RI and PI and systolic blood pressure in dogs and cats with renal diseases. Increased RI and PI were found in animals with different renal pathologies, including CRF, ARF, hydronephrosis, renal neoplasia, and renal abscess. Correlation between RI and PI and parameters of renal function were also found. Therefore RI and PI may be used in the evaluation and follow up of many renal diseases.

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Tables

Table 1. Classification of renal diseases and histopathological diagnosis available for dogs.

Clinical diagnosis	N	Histopathology (n)
Chronic renal failure (CRF)	36	Chronic interstitial nephritis (CIN)(4) Glomerulonephritis (GN)(2) CIN+GN (1) Non-specific nephrosclerosis (1)
Acute renal failure (ARF)	4	
Other	13	
Hydronephrosis	5	Secondary to transitional cell carcinoma (2) Secondary to periurethral fibrous reaction (1) Secondary to granulomatous reaction (1)
Neoplasia	4	Lymphoma (1) Multiple renal adenoma (1) Metastatic prostatic carcinoma (1) Haemangiosarcoma (1)
Ectopic ureter	1	Confirmed at surgery
Renal cyst	2	
Renal abscess	1	
Total	53	

Table 2. Number and percentage of increased RI and PI in the groups of dogs with disease.

Dogs	CRF	ARF	Other
PI			
PI ≤ 1.52	18 (50%)	3 (75%)	9 (69%)
PI > 1.52	18 (50%)	1 (25%)	4 (31%)
RI			
RI ≤ 0.72	19 (53%)	4 (100%)	10 (77%)
RI > 0.72	17 (47%)	0 (0%)	3 (23%)

Table 3. Number and percentage of increased RI and PI in the groups of cats with disease.

Cats	CRF	ARF	Other
PI			
PI ≤ 1.29	5 (33%)	1 (50%)	5 (100%)
PI > 1.29	10 (67%)	1 (50%	0 (0%)
RI			
RI ≤ 0.70	4 (27%)	1 (50%)	5 (100%)
RI > 0.70	11 (73%)	1 (50%)	0 (0%)

Figures

Figure 1. Whisker–plot of the resistive (RI) and pulsatility (PI) indices distribution in healthy dogs and in dogs with disease.

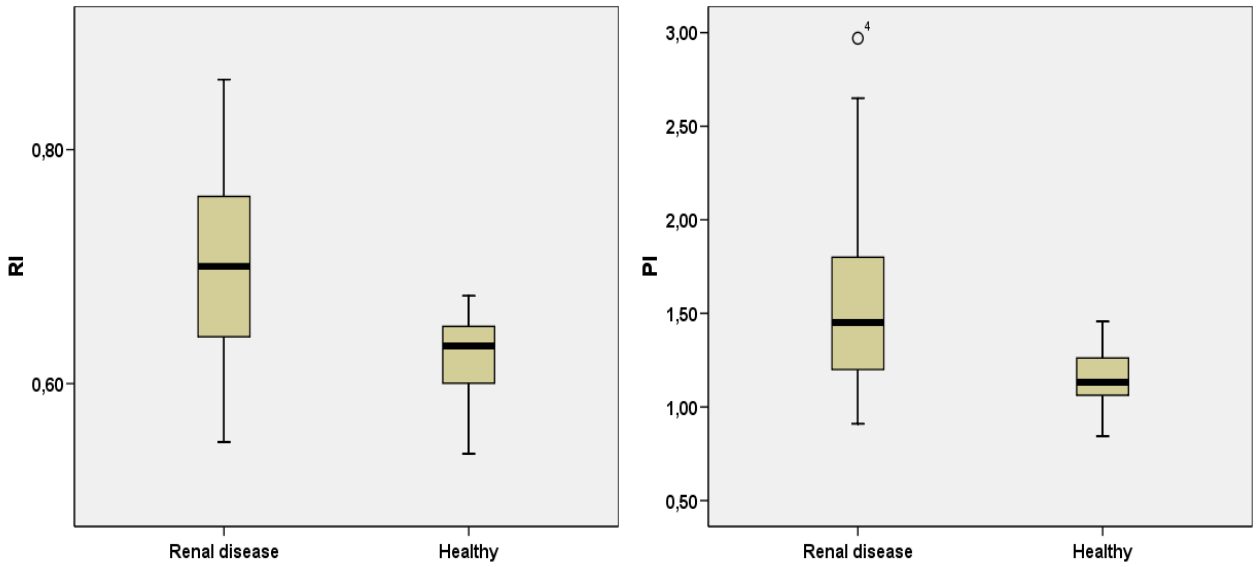
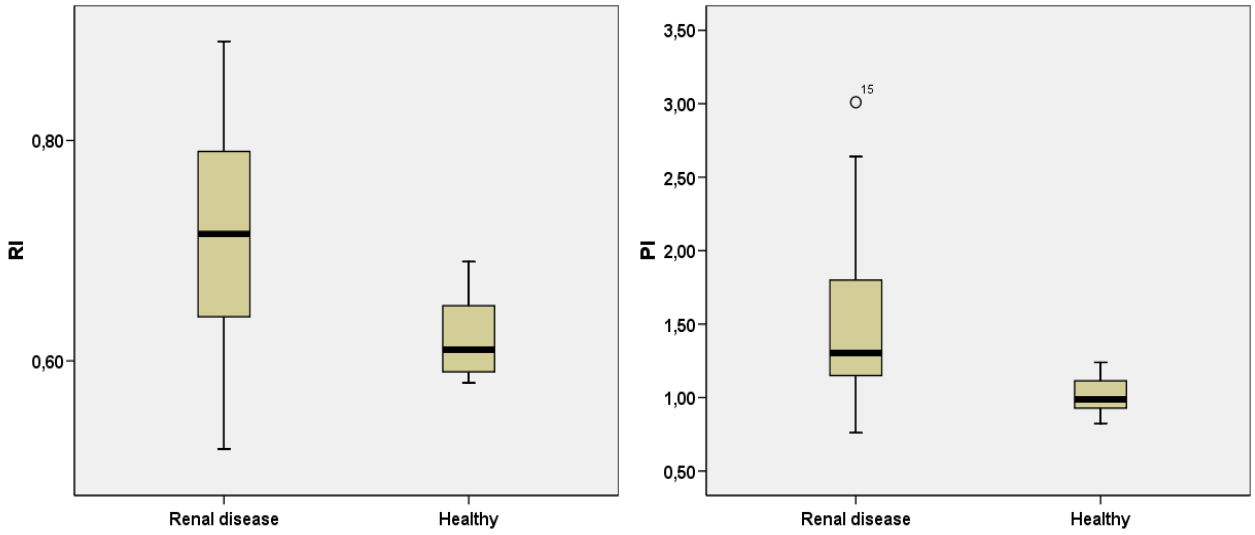


Figure 2. Whisker–plot of the resistive (RI) and pulsatility (PI) indices distribution in healthy cats and in cats with disease.



3. Determination of vascular resistance in the long posterior ciliary artery in dogs and cats with disease

Abstract

Hypertensive damage of the eye is documented in dogs and cats and is one of the most easily detected clinical consequences of systemic hypertension. Increased peripheral vascular resistance is found in human patients with systemic hypertension and it can be evaluated by means of RI and PI from pulsed Doppler waveforms. The aim of this study was to determine RI and PI in ocular vessels in dogs and cats with diseases that may be associated with hypertension and assess their relationship with systolic blood pressure. Systolic blood pressure, RI, and PI were measured in 31 dogs with diabetes mellitus (DM) and / or hyperadrenocorticism (HA), renal or hepatic disease and 4 cats with renal disease and compared with normal animals. No differences were found between the mean values of normal animals and animals with disease. Only 5 dogs and 1 cat presented indices values above the upper normal limits. Increased ocular RI and PI were not frequent in animals with these diseases.

Introduction

Hypertensive damage of the eye is documented in dogs and cats with hypertension[1-4] and is one of the most easily detected clinical consequences of systemic hypertension.

In human patients with hypertension blood flow velocity in ocular vessels is decreased due to increased peripheral vascular resistance [5, 6] and it can be evaluated by means of RI and PI from pulsed Doppler waveforms.

Doppler evaluation of the ocular and orbital vessels has been described in normal dogs. [7, 8] Increases in both RI and PI are described in Beagles with primary open angle glaucoma.[9] Systemically administration of amlodipine decreased RI and PI in normal dogs and mean systemic arterial blood pressure was significantly negatively associated with resistive index.[10]

However, evaluation of ocular RI or PI in animals with hypertension could not be found. The aim of this study was to determine RI and PI in ocular vessels in dogs and cats with diseases that may be associated with hypertension and assess their relationship with systolic blood pressure.

Materials and methods

Dogs diagnosed with diabetes mellitus, hyperadrenocorticism, renal or hepatic disease and cats with renal disease were included in the study.

Systolic blood pressure was determined before other interventions and after 5 to 10 minutes for adaptation to the environment. Systolic blood pressure was measured with a Doppler device (Vet BP Doppler Ultrasound Blood Flow Detector, Sonomed Ltd, 8 MHz transducer). The measurement was done with the animals in left lateral recumbency and the cuff placed on the proximal aspect of the tarsus to compress the cranial tibial artery. Three measurements were obtained in every animal, as previously described[11] and the mean value computed.

Previously to the examination, topical ocular anaesthesia -oxibuprocaine and tetracaine- (Colircusí anestésico doble. Alcon Cusí SA, Barcelona, Spain) was administered and sterile coupling gel (Ultrasound transmission gel, sterile R. Aquasonic 100. Parker Laboratories INC) was applied. A L10 lineal transducer operating at 11 MHz was used. Longitudinal dorsal plane of the eye was obtained with the animal in sternal recumbency and placing the probe directly on the cornea. Long ciliary posterior artery was visualized with colour Doppler in either the 9- or the 3-o'clock positions within the sclera. Then pulsed Doppler (7 MHz) was applied with a sample volume of 1.5 mm. When 3 similar appearance waveforms were obtained, calculation of the mean from 3 RI and PI for each eye was performed.

Blood pressure and ocular indices previously obtained from 27 mixed breed healthy dogs and 10 healthy cats[12] were used for comparison as a control group. Values were obtained using the same technique and by the same operators to avoid variation due to this factors.

Heart rate was calculated from the renal pulsed Doppler wave forms by the software of the machine. Abdominal ultrasound was performed in all the animals. Renal pulsed Doppler was performed and renal indices were calculated as previously described.[12]

Statistical analysis was performed with a Statistical Package for Social Sciences (SPSS computer package). The indices, heart rate, and arterial pressure were found to have a normal distribution using a Shapiro-Wilk test, therefore parametric tests were applied. The values of RI and PI of the animals with DM and/or HA were compared with the values of the healthy dogs group following a Student's *t* test. A Pearson correlation study was applied to determine relation of RI or PI to blood pressure and biochemical parameters. Statistical significance was stated as $P < 0.05$.

Results

Ocular RI and PI were determined from 19 dogs with renal disease, 3 dogs with hepatic disease, 9 dogs with diabetes mellitus and / or hyperadrenocorticism, and 4 cats with renal disease.

Obtaining pulsed wave Doppler spectra was difficult and time consuming in many animals with disease. Many animals were excluded because Doppler ultrasonography was impossible to perform due to poor cooperation. Patients

did not tolerate well the placement of the transducer on the cornea and it made studies impossible to perform in a clinical situation with limited time.

Mean RI and PI values for the different groups are given in Table 1. No statistically significant differences were found between the animals with disease and the normal animals (Figure 1). Considering upper limit values obtained from normal animals (Table 2), 2 animals with HA/DM presented increased RI (1 dog) or PI (2 dogs), 3 dogs with renal disease presented increased RI (1 dog) or PI (3 dogs), and none of the dogs with hepatic disease had increased indices. In cats, increased RI and PI were observed in 1 animal. Arterial blood pressure was higher than 150 in 3 of the dogs and normal in the remaining 2.

No correlation was found between any of the indices and the systolic blood pressure or the heart rate. Correlation was found between ocular indices and renal indices obtained in the same animals. Correlation coefficient was $r = 0.7$ ($p < 0.001$) between renal and ocular RI and $r = 0.66$ ($p < 0.001$) between renal and ocular PI.
The small number of cats included prevented further statistical analyses.

Discussion

Hypertensive damage of the eye is documented in dogs and cats with hypertension[1-4] and is one of the most easily detected clinical consequences of systemic hypertension.

Lesions associated with hypertension are typically a result from failure in vascular autoregulation of the retinal arteries. In response to increases in blood pressure, retinal arterioles undergo vasoconstriction. With chronic vasoconstriction, vascular smooth muscle cells have diminished contractile function and develop fibrous changes. Progressive degenerative changes in the vessel wall lead to rupture of the endothelial and muscle cells, with leakage of blood and serum into the retinal tissue and account for the effusive lesions characteristic of hypertensive retinopathy.[3]

In human beings decreased peak systolic and end diastolic velocities with increased extraocular RI are described in patients with systemic hypertension. These findings suggest that blood flow is decreased in these vessels because of the increased peripheral resistance in the small diameter vessels of the retina and optic nerve head.[5]

We evaluated RI and PI in animals with diseases related with hypertension. Doppler ultrasound examination probed to be challenging in our population due to poor cooperation. This fact reduced the number of patients in which the study could be performed. Then the number of animals studied is a clear limitation of the study.

No difference was found between the indices in the group of normal animals and the group with disease. Five animals with renal disease or DM/HA presented increased indices. Further, no correlation was found between any of the indices and blood pressure.

Conclusion

Obtaining RI and PI in non-sedated ill animals proved to be a difficult determination in our study. A sedation protocol which should not modify the indices should be considered to obtain these values. Increased RI and PI were not frequent in ill animals in the present study.

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Tables

Table 1. Mean (± SD) ocular RI and PI for dogs and cats with disease compared with healthy animals.

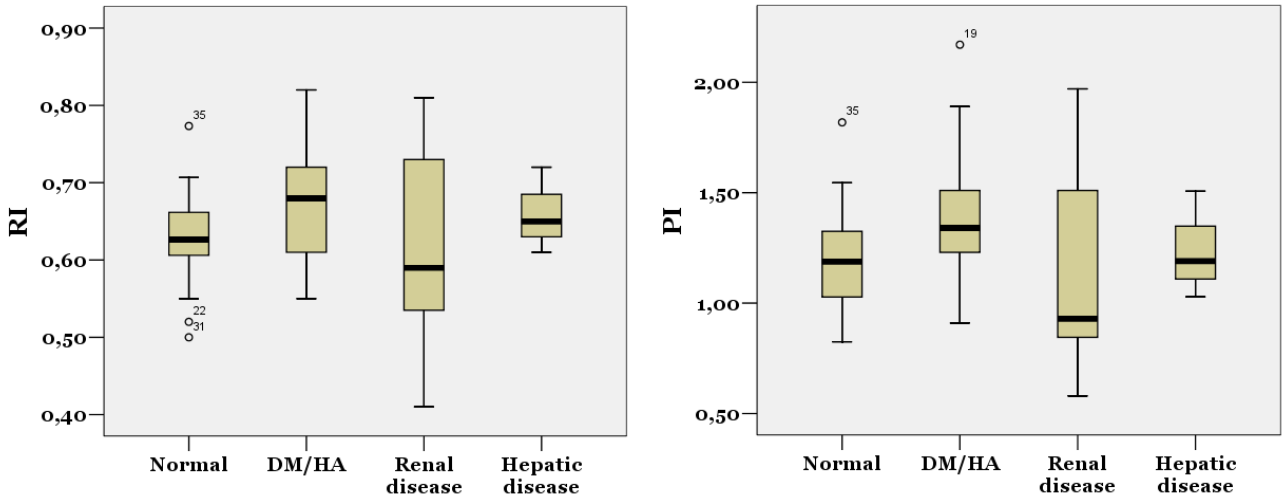
	Dogs				Cats	
	Healthy dogs	Hepatic disease	DM / HA	Renal disease	Healthy cats	Renal disease
RI	0.63 ± 0.06	0.66 ± 0.06	0.68 ± 0.08	0.61 ± 0.12	0.55 ± 0.05	0.58 ± 0.06
PI	1.15 ± 0.21	1.24 ± 0.24	1.41 ± 0.40	1.13 ± 0.43	0.79 ± 0.08	0.93 ± 0.11

Table 2. Upper limit values for ocular RI and PI in dogs and cats.

	Dogs	Cats
RI	0.76	0.72
PI	1.68	1.02

Figures

Figure 1. Boxplot of the ocular RI and PI for dogs with disease and normal animals. No statistically differences were found between the disease groups and the normal animals.



4. Annexed tables

To provide quick and easy comparison between different values and different groups of animals, some summary tables are provided.

Table 1. Values for renal and ocular RI and PI in healthy dogs and cats.

Group	Kidney		Eye	
	RI	PI	RI	PI
Dogs	0.62 ± 0.04	1.15 ± 0.15	0.63 ± 0.06	1.15 ± 0.21
Sedated dogs	0.73 ± 0. 03	1.56 ± 0.22	0.73 ± 0.05	1.60 ± 0.27
Cats	0.62 ± 0.04	1.02 ± 0.12	0.55 ± 0.05	0.79 ± 0.08

Table 2.Upper limit values for renal and ocular RI and PI in healthy dogs and cats.

Group	Kidney		Eye	
	RI	PI	RI	PI
Dogs	0.72	1.52	0.76	1.68
Sedated dogs	0.79	2.00	0.83	2.14
Cats	0.70	1.29	0.72	1.02

Table 3. Renal and ocular RI and PI in healthy dogs and groups with disease.

Group	Kidney		Eye	
	RI	PI	RI	PI
Healthy	0.62 ± 0.04	1.15 ± 0.15	0.63 ± 0.06	1.15 ± 0.21
Hepatic disease	0.70 ± 0.06*	1.53 ± 0.33*	0.66 ± 0.06	1.24 ± 0.24
DM / HA	0.68 ± 0.07*	1.37 ± 0.28*	0.68 ± 0.08	1.41 ± 0.40
Renal disease	0.70 ± 0.08*	1.56 ± 0.47*	0.61 ± 0.12	1.13 ± 0.43

*Statistically significant differences in comparison to healthy animals

Table 4. Renal and ocular RI and PI in healthy cats and cats with renal disease.

Group	Kidney		Eye	
	RI	PI	RI	PI
Healthy	0.62 ± 0.04	1.02 ± 0.12	0.55 ± 0.05	0.79 ± 0.08
Renal disease	0.72 ± 0.10*	1.53 ± 0.60*	0.58 ± 0.06	0.93 ± 0.11

*Statistically significant differences in comparison to healthy animals

Table 5. Systolic blood pressure, heart rate and age in healthy dogs and groups with disease.

Group	SBP (mmHg)	HR (bpm)	Age (years)
Healthy	126 ± 15	106 ± 24	4.31 ± 2.27
Hepatic disease	148 ± 25	118 ± 32	12.67 ± 3.78
DM / HA	171 ± 47	125 ± 37	11.05 ± 1.87
Renal disease	168 ± 41	115 ± 32	6.46 ± 3.78

Table 5. Systolic blood pressure, heart rate and age in healthy cats and cats with renal disease.

Group	SBP (mmHg)	HR (lpm)	Age (years)
Healthy	152 ± 25	190 ± 41	7.12 ± 3.19
Renal disease	137 ± 41	187 ± 35	6.80 ± 3.57

Discussion

RI and PI in normal dogs and cats

Non-sedated dogs and cats

Several studies have described RI and PI in normal dogs and cats.[15-20] Normal values slightly differ among the studies (Table 1).

Table 1. Comparison table for the normal RI values described in different studies

Dogs	Right kidney	Left kidney	Mean
Present study	0.62 ± 0.05	0.62 ± 0.04	
Nyland[18]	0.62 ± 0.05	0.63 ± 0.05	
Morrow[19]			0.61 ± 0.06
Choi[26]	0.64 ± 0.03	0.63 ± 0.04	0.64 ± 0.03
Cats			
Present study	0.62 ± 0.04	0.62 ± 0.04	
Rivers[16]	0.59 ± 0.05	0.56 ± 0.06	
Mitchell[17]			0.55 ± 0.07
Pollard[20]	0.58 ± 0.06	0.55 ± 0.03	

The upper limit value (mean + 2SD) beyond which RI is considered increased slightly vary among the studies. Some authors suggest an upper maximum value of 0.70 for both cats[16] and dogs[19], which is also the limit used in human medicine.[21] Others suggest an upper limit value of 0.73 for dogs[18, 22] and

of 0.71 for cats.[22] Renal PI values could not be found for non-sedated normal dogs. An upper value of 1.06 is obtained from a study in normal cats.[17]

Values obtained in our study suggested an upper limit values of 0.72 and 0.70 for renal RI in dogs and cats respectively and upper limit values of 1.52 and 1.29 for PI in dogs and cats respectively. Thus, renal RI limits obtained in the present study are similar to previously reported for both species. Renal PI for cats slightly differ from those previously reported.

Ocular RI for dogs also differs from a previous study.[44] Different approaches used in the studies may account for part of this variation.

Sedated dogs

Displacement of the examined vessel during Doppler ultrasonography due to breathing or movement of the patient makes obtaining good quality waveform difficult and time consuming, even in human patients.[29] In these instances, patient sedation facilitates ultrasound examination and may be useful to perform ultrasound guided fine needle aspirations or biopsies.

Some sedative and anaesthetics have been reported to alter renal vascular indices.[15, 17] In cats, a combination of atropine, acepromacine, and ketamine did not modify the indices significantly.[16]

The present study evaluated the effects of a sedative protocol that can be safety used in ill animals. This protocol was pretended to be used during ultrasound examination in dogs with disease, when required. We found that the

combination with midazolam and butorphanol produced significant increases in RI and PI. Decreased blood flow caused by midazolam administration could explain this increase in the indices.[57, 58] For six of the dogs at least one of the indices was increased beyond the upper limit and therefore presented as a pathologic value. Given that this fact could have made interpretation of values in animals with disease difficult, sedation was not used in the following studies.

RI and PI in dogs and cats with disease

In our studies increased renal RI and PI were found in animals with hepatic disease, renal disease and diabetes mellitus and hyperadrenocorticism as it is found in human beings.[29-31, 35] Then renal vascular resistance may be increased in some animals with these diseases and can be used as an indicator to evaluate for diagnosis and follow up of the disease.

RI and PI have been reported to correlate with a faster decline in renal function,[30] with some biochemical parameters, such as bilirubin, albumin, and creatinine levels and prothrombin time in patients with liver disease,[32] and with serum creatinine concentration, creatinine clearance rate, serum glucose concentration, cholesterol levels, presence of microalbuminuria, arterial blood pressure, patient age, and duration of the disease in patients with diabetes.[35-40]

We found correlation between several parameters and renal indices in our groups of dogs. In dogs with hepatic disease correlation was found between both indices and alkaline phosphatase; in the diabetic/hyperadrenocorticism group correlation was found between blood glucose and both indices; in dogs

with renal disease correlation was found between red blood cell count and RI and between serum creatinine and PI; and in cats with renal disease correlation was found between both indices and blood creatinine and urea levels.

PI is considered more accurate in differentiating abnormal waveforms because it incorporates mean velocity in its calculation. In human studies PI showed to correlate closer than the RI with some biochemical parameters and was therefore recommended to be used as an indicator for renal vascular resistance.[32] In the present studies, correlation between PI and blood parameters was higher than between RI and the same parameters for alkaline phosphatase in the hepatic disease group, for glucose in the diabetes / hyperadrenocorticism dogs, for the creatinine concentration in dogs with renal disease, and for serum creatinine and urea in cats with renal disease. These findings suggest that PI may be also more accurate than RI in dogs and cats as it is in humans.

For ocular indices no differences were found between the different groups of disease and the healthy animals nor were any correlations with biochemical parameters found. Examinations were often difficult and time consuming. However, correlation was found between ocular indices and renal indices obtained in the same animals.

Blood pressure

Increased RI has been related with early hypertensive renal damage and correlated with systemic blood pressure.[41, 42] No correlation could be found between the indices and systolic blood pressure in any of the groups.

Systolic blood pressure in dogs depends on age, breed, sex, temperament, exercise regime and diet.[52] Moreover, blood pressure is subject to fluctuations due to physiological variation and stress-related variation. White coat effect and stressful environment can raise the patient's blood pressure to values consistent with hypertension. To minimize these fluctuations and effects serial blood pressure measurements (3-5 separate reading) should be obtained after the patient has had some time to become acclimatized in a quite environment.[48]

Although these precautions were performed in our study, most Beagles were persistently stressed and presented high blood pressure. This effect can not be excluded also for some of the other animals. Ideally, to diagnose hypertension more than one high value has to be obtained in different occasions. Because the aim of the study was to compare blood pressure with the indices measured at the same time, repeated measures were not performed.

Conclusions

1. Resistive index and pulsatility index values obtained in the present study for healthy animals were similar to previously described.

2. Obtaining ocular RI and PI was difficult and time consuming in non-sedated animals.

3. Normal values proposed in this study for renal indices are RI ≤ 0.72 and PI ≤ 1.52 in dogs and RI ≤ 0.70 and PI ≤ 1.29 in cats.

4. Normal values proposed in this study for ocular indices are RI ≤ 0.76 and PI ≤ 1.68 in dogs and RI ≤ 0.72 and PI ≤ 1.02 in cats.

5. Renal and ocular RI and PI are increased in healthy dogs when a combination of midazolam and butorphanol is used.

6. Renal RI and PI may be increased in dogs with diabetes mellitus and hyperadrenocorticism, hepatic or renal disease and in cats with renal disease.

7. Ocular RI and PI were not increased in animals with any of the diseases compared to healthy animals.

8. Correlation exists between RI and PI and specific disease biochemical and haematological parameters.

9. No correlation was found between systolic blood pressure and renal or ocular RI or PI.

10. Renal vascular resistance may be used for the diagnosis and follow up of several diseases.

Resum

El ronyó i el globus ocular són òrgans sensibles a alteracions de pressió arterial. El ronyó participa en el control de la pressió arterial i les alteracions renals poden induir hipertensió arterial alhora que poden veure's agreujades per la hipertensió, entrant en un cercle viciós entre les dues alteracions. En pacients humans amb hipertensió s'ha observat un augment de la resistència vascular a nivell de les artèries renals i oculars. Aquest augment de resistència vascular es pot determinar mitjançant ecografia Doppler amb el càlcul dels índexs de resistència i pulsatilitat. S'han observat increments d'aquests índexs en vasos renals i oculars de pacients humans amb hipertensió, així com correlació entre els índexs i la pressió sistòlica i relació amb el dany hipertensiu. Els valors dels índexs en animals normals varien lleugerament segons els estudis. La tècnica, l'operador i l'administració de productes sedants o anestèsics poden ser factors de variació d'aquest índexs. Per aquest motiu és necessari obtenir els propis valors de referència.

L'objectiu del present estudi va ser valorar si en gossos i gats amb diferents malalties que poden causar hipertensió es pot observar també augment de resistència vascular renal i ocular, i si es relaciona amb la pressió arterial. Un cop obtinguts aquests valors en animals sans no sedats i valorat l'efecte d'un protocol de sedació adequat per utilitzar en animals malalts en cas necessari, es van obtenir els valors dels índexs renals i oculars i la pressió sistòlica en gossos i gats amb diferents patologies que s'associen a hipertensió, com ara les malalties renals, la *diabetis mellitus*, l'hiperadrenocorticisme i les malalties hepàtiques.

Es van observar augments significatius dels índexs renals en els diferents grups de malalties comparats amb els animals sans. També es van veure correlacions entre diferents paràmetres sanguinis i els índexs en les diferents malalties. En cap dels grups però es va observar correlació amb la pressió sistòlica. En conclusió, s'ha vist que s'observen augments de la resistència vascular perifèrica a nivell renal en aquestes malalties, així com cert grau de relació amb la gravetat de la mateixa (avaluada mitjançant paràmetres sanguinis) però no s'ha observat una correlació amb la pressió arterial.

Resumen

El riñón y el globo ocular son órganos sensibles a alteraciones de la presión arterial. El riñón participa en el control de la presión arterial y las alteraciones renales pueden inducir hipertensión arterial a la vez que pueden agravarse por la hipertensión, entrando en un círculo vicioso entre las dos alteraciones. En pacientes humanos con hipertensión se ha observado un aumento de la resistencia vascular en arterias renales y oculares. Este aumento de resistencia vascular se puede determinar mediante ecografía Doppler con el cálculo de los índices de resistencia y pulsatilidad. En pacientes humanos con hipertensión se han observado aumentos de los índices en vasos renales y oculares, así como una correlación entre los índices y la presión sistólica y una relación con la lesión inducida por la hipertensión. Los valores de los índices en animales normales varían ligeramente según los estudios. La técnica, el operador y la administración de productos sedantes o anestésicos pueden ser factores de variación de estos índices. Por esta razón uno de los primeros objetivos del estudio fue obtener los valores de referencia propios.

El objetivo del presente estudio es valorar si en perros y gatos con enfermedades que pueden causar hipertensión se puede observar un aumento de resistencia vascular y si éste se puede correlacionar con la presión arterial. Una vez obtenidos estos valores en animales sanos no sedados y valorado el efecto de un protocolo de sedación adecuado para utilizar en animales enfermos en caso necesario, se obtuvieron los valores de los índices renales y oculares y la presión sistólica en perros y gatos con diferentes enfermedades asociadas a hipertensión, como enfermedades renales, *diabetes mellitus*, hiperadrenocorticismo y enfermedades hepáticas.

Se observaron aumentos significativos de los índices renales en los diferentes grupos de enfermedades comparados con los animales sanos. También se vieron correlaciones entre diferentes parámetros sanguíneos y los índices en las diferentes enfermedades. En ninguno de los grupos se observó correlación con la presión sistólica. En conclusión, se ha visto que se observan aumentos de la resistencia vascular periférica a nivel renal en estas enfermedades, así como cierto grado de relación con la gravedad de la misma (evaluada mediante parámetros sanguíneos), pero no se ha observado correlación alguna con la presión arterial.

Summary

Summary

The kidneys and the eyes are sensitive to blood pressure changes. The kidney participates in blood pressure control and renal disease can cause arterial hypertension and be aggravated by hypertension, entering a vicious circle between both alterations. In human patients with hypertension, increased vascular resistance is observed in renal and ocular arteries. This increased vascular resistance can be measured with Doppler ultrasound by calculating resistive and pulsatility indices. Increased renal and ocular indices have been observed in human patients with hypertension, and a correlation between the indices and the systolic blood pressure and hypertensive damage has also been reported. The indices values in normal animals vary slightly among the studies and the technique, the operator and, the administration of sedative or anaesthetic drugs can cause variation of the indices. Then, obtaining your own reference values is necessary.

The aim of this study is to determine if increased vascular resistance is found in dogs and cats with diseases that can cause hypertension and whether they are related with arterial blood pressure. Values were obtained in non-sedated healthy animals and the effect of a sedative protocol appropriated to be used in ill animals, if necessary, was evaluated. Then renal and ocular resistive and pulsatility indices and systolic blood pressure were obtained in dogs and cats with diseases that can cause hypertension, such as renal disease, diabetes mellitus, hyperadrenocorticism, and hepatic disease.

Significant increased renal indices were found in the disease groups in comparison to healthy animals. Correlations with blood parameters and the indices were also found in different diseases. Correlation with blood pressure

was not found in any of the groups. In conclusion, increased peripheral vascular resistance was found in the kidney in animals with these diseases, as well as certain degree of relationship with the severity of the disease (evaluated by means of blood parameters). However, no correlation with systolic blood pressure was observed.

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