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Evaluation of Resistive Index Using Color Doppler Imaging in Canine Ophthalmic Vasculature

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Abstract : Color Doppler imaging(CDI) was carried out to determine CDI-derived resistive index(RI) values of normal canine ophthalmic vasculature and its reproducibility. CDI was performed on 58 dogs, and normal ranges of RI value were calculated for the medial long posterior ciliary artery(mLPCA), ciliary artery(CA), and ophthalmic artery(OA). Ophthalmic vascular RI values of normal dogs were 0.67± 0.07, 0.70± 0.06, and 0.80± 0.04 in mLPCA, CA, and OA, respectively. Means of RI value of all vessel had no statistically significant difference by sex, fellow orbits, and skull type. The results suggest that color Doppler imaging is a noninvasive test which has the advantage of providing objective measurements of blood flow velocity parameter in the canine eye and orbit.

Key words **:** Color Doppler imaging, Resistive index, Ophthalmic vasculature, Dogs

Introduction

Many techniques have been devised to measure the ocular blood flow of the human and animal eye. For example, unlabelled or radioactively labelled microsphere method[9,17] and hydrogen clearance technique[22] were presented. But these methods were very invasive[20]. With technological advance, blood flow parameters of the orbital and ocular circulation can be assessed noninvasively using a variety of ultrasonic imaging techniques[10]. These modalities include transcranial Doppler ultrasonography[20], laser Doppler flowmetry[3,14,16], pulsed Doppler sonography[4,11,13,19], and most recently, color Doppler imaging(CDI)[2,5,10,12,15,21].

The introduction of color Doppler technology uses a combination of real-time imaging with superimposed color-coded vascular flow and thereby allows visualization of blood vessels below the resolution of real-time ultrasonography alone[2]. This technology, initially described in 1979, was not used for ophthalmic vascular investigation until 1989 in human medicine[10]. This is of particular benefit in the orbit, where the vessels are small and tortuous[2].

Both the resistive index(RI) and pulsatility index(PI) are been widely used in the clinical setting to quantify the relative pulsatility of the velocity waveform. Adamson *et al* found an excellent linear correlation between downstream microvascular resistance and these two indices, respectively[1].

In humans, numerous orbital and ocular vessels have been mapped and their blood velocity parameters and waveforms characterized using CDI[2,5,8,10,12,15,21]. A few veterinary report has evaluated CDI of the canine orbit and eye in a limited population of patients[6,7]. Furthermore, these studies were not conducted in conscious dogs. Specific normal orbital and ocular blood velocity parameters, as determined by Doppler imaging, have not been reported in the veterinary literature for the conscious dog, but are necessary for this diagnostic methodology to achieve its full potential.

This study was performed to assess the feasibility and reproducibility of CDI-derived RI measurement of the normal conscious canine ophthalmic vasculature

Materials and Methods

Experimental animals and preparation

All animal under study aged from 1 to 5years. Fifty eight clinically healthy dogs(116 eyes), weighing from 1.3 to 8.2 kg, were studied for normal RI value of ophthalmic artery(OA), ciliary artery(CA) and medial long posterior ciliary artery (mLPCA). The male : female ratio was 35 : 23. The brachycephalic breed were twenty two, the others were non-brachycephalic breed.

To determine the reproducibility of CDI-derived RI value measurement, eighteen dogs(18 Lt. eyes) were employed without distinction of sex and skull types.

A physical examination, CBC, and serum biochemical analysis were used to confirm the systemic health of each dog. Only dogs with test results within reference range limits were included in our study. The ophthalmic examination consisted of direct ophthalmoscopy, and tonometry. The IOP was 30 mmHg or less and the anterior segment and fundus examinations were normal. There was no evident signs of orbital disease or neuro-ophthalmologic disease. The dogs were housed in indoor cages and were fed standardized diet.

Color Doppler imaging technique

All CDI were performed using a Toshiba SSA-260A machine with a 7 MHz electronic sector probe. The same Doppler settings(pulse repetition frequency of 6000 MHz, medium gain setting, wall filtering of 100 MHz, and low to medium color Doppler flow setting) were utilized to minimize technical errors.

The eye and orbit were imaged with sitting position. Ani-

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mals remained in a sitting position throughout the trial period. Coupling gel was applied to the closed upper lid and the scan was performed. Horizontal scans was taken through the eye and orbit.

B-mode and CDI were performed initially to identify vessels of interest for subsequent spectral Doppler analysis. Spectral Doppler analysis of the ophthalmic artery was routinely performed retrobulbar region as it acompany with venous plexus. Ciliary artery was sampled an same manner of ophthalmic artery at roundly below optic nerve head.

Once a particular vessel was localized, interrogated using the Doppler gate to obtain a spectral waveform and thus quantitative information. The RI was determined by: RI = (PSV - EDV)/PSV where PSV was the peak systolic velocity, and EDV was end diastolic velocity.

The RI value was calculated for the vessel obtained from three similar-appearing Doppler waveforms to reduce the effects of physiologic variation. Furthermore, measurements were obtained three times for the vessel imaged in a sequence, and then an average value was used.

Reproducibility

CDI-derived RI measurements were performed 4 times, at 10days interval. Intraobserver variation was calculated based on the mean(and SD) of the differences in the results between two measurements and the coefficient of variation of the repeated measurements(COVr).

With regard to the mean of the differences, this involved first measurement and fourth measurement, calculation of the means and SD of these differences. The COVr was calculated from the follow formula: COVr = (SD of the mean differences/mean)°ø100%.

Statistical analysis

Statistical analysis was performed using the SPSS statistical computer program. According to property of sample, simple factorial ANOVA, paired sample t-test, or independent t-test were applied to data analysis.

Results

Color Doppler imaging of the eye

1) Normal range

The mean, standard deviation, and 95% confidence interval for the RI values were summarized in Table 1.

No differences were found in the RI values between sex, fellow orbits, and skull types(Table 2). Furthermore, the RI values[R square : mLPCA(0.16), CA(0.20), and OA(0.18)] were not correlated with age and body weight. For the instance of CA at orbital portion, differentiation between the short and long posterior ciliary arteries and distinction among them has so far not been possible.

Table 1. Resistive index in 58 normal dogs

Parameter		Range	Mean±SD	95% CI
RI	mLPCA	0.50~0.83	0.67~0.07	0.66 ; 0.69
	CA	0.56~0.83	0.70~0.06	0.69 ; 0.71
	OA	0.71~0.88	0.80~0.04	0.79 ; 0.81

SD: standard deviation, 95% CI : 95% confidence interval

Table 2. Simple factorial analysis of variance in the resistive index values among sex, fellow orbits, and skull types

Variable	Source of Variation	Degrees of Freedom	Mean Square	F value	
RI	mLPCA	Fellow orbits	1	2.809E-03	0.694(NS)
		Sex	1	3.116E-03	0.770(NS)
		Skull types	1	1.476E-02	3.633(NS)
		Interaction	4	8.328E-03	2.058(NS)
		Residual	108	4.047E-03	
		Total	115		
	OA	Fellow orbits	1	1.691E-03	1.573(NS)
		Sex	1	1.377E-03	1.281(NS)
		Skull types	1	3.251E-03	3.024(NS)
		Interaction	4	9.384E-03	0.873(NS)
		Residual	108	1.075E-03	
		Total	115		
	CA	Fellow orbits	1	2.603E-03	0.865(NS)
		Sex	1	5.303E-03	1.762(NS)
		Skull types	1	3.520E-04	0.117(NS)
		Interaction	4	5.080E-03	1.688(NS)
		Residual	108	3.009E-03	
		Total	115		

NS : not significant

Table 3. Reproducibility of resistive index values

Parameter		Mean	SD	Mean Difference			COVr(%)
				mdiff	SD	95% CI	
RI	mLPCA						
	first	0.68	0.08	-0.003	0.088	-0.047;0.041	12.9%
	fourth	0.68	0.03				
	CA						
	first	0.68	0.05	-0.021	0.054	-0.047;0.007	7.8%
	fourth	0.70	0.04				
	OA						
	first	0.80	0.03	-0.022	0.033	-0.037;-0.003	4.1%
	fourth	0.82	0.02				

first : first measurement, fourth : fourth measurement, mdiff : mean difference, 95% CI : 95% confidence interval,
COVr : coefficient of variation of repeated measurements

2) Reproducibility

With regard to intraobserver variation, the COVr(1st and 4th measurement) and mean difference between measurements for the RI values were summarized in Table 3.

Discussion

Gelatt *et al.*[7] reported evaluation of ophthalmic vessels using CDI in normal sedated dogs and glaucomatous dogs. But the ophthalmic vessel parameter measurement for the normal conscious dogs were not reported. Their report showed that the RI values were 0.58, 0.44, and 0.51 in the external ophthalmic artery, short posterior ciliary artery (SPCA), and long posterior ciliary artery, respectively. However, those were 0.80, 0.70, and 0.67 at the OA, CA, and mLPCA in this study. It was considered that these difference was due to their usage of analgesics or anesthetics which might influence orbital tension and ophthalmic blood flow, as they performed measurement under light sedation(butorphanol tartrate and acepromazine sulfate), lidocaine eye blocks, and corneal topical anesthesia(tetracaine HCl).

Greenfield *et al.*[10] and Lieb *et al.*[12] demonstrated, there were no significant differences in vascular resistance between right and left eyes or male and female subjects in human. Those results was corresponded to this study. As regards the differences of the RI value between skull type in this study, all parameters relatively increased in brachycephalic dogs than that of non-brachycephalic dogs, while the differences were insignificant. It was thought that many factors implicated in this subtle difference such as anatomical variation, surrounding tissue pressure, and restraint. Greenfield *et al.*[10] suggested that age might affect normal orbital blood flow and vascular resistance pattern. Baxter and Williamson[2] demonstrated that an increase in RI occurred with age in the central retinal artery and vein. In this study, no correlation was found between age and the RI values. This result might be ensued from age limitation(1-5years).

External pressure from the ultrasound probe may potentially result in an increase in IOP during the examination[21]. Ocular perfusion and the vascular resistance of the uveal and retinal vasculature may be altered by intraocular pressure[7]. It is important during Doppler imaging to minimize this external pressure so as to reduce any potential effect on blood flow[21]. In this study, external pressure of eyeball was applied during CA and OA RI measurement. Therefore, excessive pressure by the probe on the eyelid might have the potential to raise intraocular pressure and potentially alter intraocular hemodynamics. But external pressure was rarely applied during mLPCA RI measurement, because direct contact of eyeball was avoid.

In comparisons of the CDI blood velocity parameters among the different animal species, any anatomical differences of the ophthalmic vasculature must be considered[7]. Unlike in the primate system, there is no central retinal artery in a dog, therefore retinal vessels of dog arise from the ciliary system and penetrate the sclera in a circle around the optic disc[18]. To evaluate resistance of retinal blood flow, the RI of mLPCA was measured in replacement of central retinal artery in this study. Furthermore other arteries were located in orbital portion, while mLPCA was within eye. For this reason, mLPCA was useful indicator which represented retinal vascular resistance and direct compressive condition of eyeball, although mLPCA was minor artery which supplied blood for retina.

In human ophthalmology, CDI was commonly used to evaluate normal value and reproducibility of ophthalmic circulation on central retinal artery[2,5,10,12,19,21], central retinal vein[2,12], ophthalmic artery[2,4,10,11,12,15,21] and posterior ciliary artery[2,10,11,12,21]. The normal canine ophthalmic vessels identified in this study included the OA, CA and mLPCA. But CA was so difficult to visualize for its tortuosity. Futhermore, eyeball movement and blinking movement hindered the RI of CA measurement in conscious dogs. Lieb *et al.*[12] concluded that differentiation between the short and long posterior ciliary arteries and distinction among them has so far not been possible at the orbital region. In this study, CA means both short and long posterior ciliary arteries as its extraocular portion, differentiation of those vessels is very difficult with CDI. For this reason, the RI of CA is useless to objective blood flow parameter.

High reproducibility is critical for the CDI system, especially if this methodology is used to detect small differences in the blood velocity parameters that may occur in orbital and intraocular diseases, and in the evaluation and comparisons of various medical and/or surgical treatments. Past reports in humans using Doppler imaging of special normal blood vessels have yielded high reproducibility[2,11,15]. For example, reproducibility is estimated by ophthalmic artery, central retinal artery, and medial posterior ciliary artery, the RI values shown 4.8%, 6.4%, and 10.0% coefficient of variation of repeated measurements, respectively[2]. Previous animal study were similar results with humans[7]. In this study, very high reproducibility was demonstrated in selected ophthalmic blood vessels in normal conscious dogs. Therefore, these measurement, using the same experimental protocol, were highly reproducible, and might permit valid comparisons to the blood flow parameters of certain orbital and ocular diseases that possess vascular resistance changes.

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개의 안혈관에 대한 컬러도플러초음파를 사용한 저항지수의 평가

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요 약 : 개의 정상안혈관저항지수와 그 재현성을 측정하고자 컬러도플러 초음파를 이용하여 본 실험을 수행하였다. 내측 긴 후모양체 동맥, 모양체 동맥, 안동맥의 혈관저항지수의 정상범주를 측정하기 위하여 58두의 개에서 컬러도플러 초음파를 실시하였다. 정상견에서 내측 긴 후모양체동맥, 모양체동맥, 안동맥의 저항지수(%)를 측정한 결과, 그 수치는 각각 0.67±0.07, 0.70±0.06, 그리고 0.08±0.04이었으며, 모든 혈관의 저항지수는 좌우안구간에 차이가 없었으며, 성별이나 두개골 형태가 미치는 영향도 없는 것으로 판명되었다. 안혈관 저항지수의 반복측정에 따른 오차를 평가하기 위해서 4회 반복 측정한 결과, 안동맥저항지수의 반복측정변이계수가 4.1%로 가장 낮았으며 긴 후모양체동맥과 모양체동맥의 저항지수의 반복측정변이계수는 각각 12.9%와 7.8%로 모든 동맥에서 높은 재현성을 보였다. 이상의 결과로 보아, 컬러도플러 초음파가 개의 안구 및 안와의 혈순환에 대한 객관적인 측정자료를 제시하는데 매우 유용한 지표인 것으로 판단된다.

주요어 : 컬러도플러 초음파, 저항지수, 안혈관, 개