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The effect of moderate treadmill exercise on the resistive index of the medial long posterior ciliary artery in dogs

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Abstract: The resistive index (RI) is an indirect measurement of arterial resistance by means of a ratio between the peak systolic and end diastolic velocities recorded with a spectral Doppler device, especially used to evaluate the vascular damage in ocular diseases such as glaucoma. Some ocular variables such as the intraocular pressure (IOP), the choroidal thickness, the axial length and the ocular blood flow may be influenced by physical exercise. The purpose of this study was to evaluate the influence of the exercise on the RI of the medial long posterior ciliary artery in dogs, and correlate the data obtained with the IOP values. Ten clinically healthy dogs were subjected to moderate physical exercise on a canine motorised treadmill at different speeds for 45 minutes. A colour Doppler examination was performed and the RI values were calculated for the medial long posterior ciliary artery at rest, immediately after the exercise, and after 60 minutes at the end of the exercise. At the same times, the IOP was recorded by applanation tonometry. The data were analysed by a two-way repeated ANOVA measurement in order to compare the RI and the IOP. Wilcoxon's test was applied for the post hoc comparison. Spearman's rank correlation for non-normal distribution was used to determine a relationship between the RI and the IOP. The at rest RI was 0.722 +/–0.022, IOP 12.38 +/3.21 mm Hg. A significant decrease in the RI was observed immediately after the exercise (0.697 +/–0.035) and during the passive recovery phase (0.682 +/–0.042). A significant decrease in the IOP (11+/3.39 mmHg) was recorded after 60 min of the passive recovery phase; at the end of the exercise, a slight decrease (12.29+/4.26 mm Hg) mm Hg was detected. During the test, a linear correlation between the RI and the IOP was observed. Our results suggest that exercise induces the modification of the ophthalmic blood flow in dogs, presumably related to the compensatory neuro-hormonal mechanisms.

Keywords: physical exercise, ocular variables, ocular blood flow

Colour Doppler Imaging (CDI) is a valid method to study the ocular vascular flow velocity and characteristics. It permits one to have dynamic real-time anatomical vascular information; moreover, it allows one to evaluate the presence, the direction and the type of blood into a vessel (Szatmari et al. 2001). The internal and external ophthalmic artery, anterior ciliary artery, the short and long

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posterior ciliary arteries, primary retinal arteries are the ocular and orbital vessels most frequently imaged (Gelatt-Nicholson et al. 1999a). Using CDI, impedance indices such as the resistive index (RI), pulsatility index and systolic-to-diastolic peak velocity ratio characterising the resistance to flow in the vascular system may be calculated (Ferrandis et al. 2013).

The resistive index (RI) or Pourcelot ratio allows for the non-invasive assessment of the peripheral vascular resistance (Bude and Rubin 1999), vascular compliance, conductance and transmural pressure (Ostrowska et al. 2016). It is measured from the interpretation of the shape calculated by the spectral analysis of the vascular signals (Pozniak et al. 1988), as the ratio of the peak systolic velocity and the end diastolic velocity of the blood flow. An increase in the ophthalmic blood flow causes a decrease in the intraocular pressure (IOP) – according to the Goldman equation (Nassr et al. 2009). A high RI value is related to an increase in the distal vascular resistance and a decrease in the perfusion (Liu et al. 1997). In veterinary ophthalmology, normal RI values on the ocular and orbital vessels have been reported in healthy dogs (Gelatt-Nicholson et al. 1999a; Novellas et al. 2007); its use is especially interesting in animals suffering from diseases such as glaucoma, which helps determine a significant alteration of the ocular vascular pattern (Gelatt-Nicholson et al. 1999b; Lee et al. 2002). An increase in the RI on the medial long posterior ciliary artery was described in glaucomatous dogs treated with antihypertensive drugs, as a direct consequence of the intraocular pressure (IOP) decrease (Choi et al. 2011).

It has been reported that some ocular variables such as IOP (Gale et al. 2009), choroidal thickness (Sayin et al. 2015), axial length (Hong et al. 2014) and ocular blood flow (Beck et al. 1995; Kiss et al. 2001; Nemeth et al. 2002; Lovasik et al. 2003; Pournaras et al. 2004) may be influenced by physical exercise in humans. Data describing the effect of the physical exercise on the orbital and ocular blood velocity indicators, determined by Doppler imaging, have, to the best of author's knowledge, not been reported in the veterinary literature for dogs.

The aim of this study was to evaluate the effect of some moderate exercise on a treadmill on the RI of the medial long posterior ciliary artery (mLPCA) in dogs, correlating the variations in the RI with the changes in the IOP.

MATERIAL AND METHODS

The study was carried with the approval of the Ethical Committee of the Department of Veterinary Sciences, the University of Messina (Italy) (Protocol No.2017-11) in accordance with Italian and European regulations on animal welfare. Ten privately-owned dogs of both sexes (seven males and three females), belonging to different breeds (five cross-breed, three Hounds, one Beagle, one Cocker Spaniel), aged two to six years old (a mean of 3.8 ± 2.1 SD) whose body weight ranged between 12–20 kg (a mean of 14 ± 4.3 SD) were included. Written consent from each owner was obtained before the dog's enrolment in the study. All subjects were determined as healthy and normotensive on the basis of a thorough physical examination and an arterial blood pressure measurement. Furthermore, an ophthalmological examination, including a Schirmer tear test, fluorescein staining, slit-lamp biomicroscope, applanation tonometry, gonioscopy and a dilated fundus examination was performed in each dog. The dogs were not pre-trained to run on a treadmill, not familiar with the procedures and the equipment for RI and IOP evaluation. In order to acclimatise them to the procedures, the RI and IOP were evaluated once a day for five days in each dog. All dogs underwent a moderate exercise test on a motorised treadmill (Professional canine treadmill, Grillo®, Modena, Italy) for 45 min at different velocities: 2.5 km/h for 15 min, 5.0 km/h for 20 min, and 2.5 km/h for 10 min, once per day (at 08.00 h). The treadmill presented the following technical features: length 2.40 m (running surface 0.410 m), width 2.50 m (running surface 0.640 m), height 0.600 m, total weight 120 kg, speed 2.5–1.4 km/h. The environmental temperature was continuously recorded and maintained between 18–21 °C (64.40–69.80 °F), the relative humidity ranged between 50–60%. The RI and IOP were recorded at rest (T_0), immediately after the exercise (T_1) and after 16 min of passive recovery (T_2). One drop of a topical anaesthetic (Ossibuprocaine hydrochloride 0.4%, Novartis; Italy) was instilled in the conjunctival fornix of the left eye before being tested. The IOP was recorded by applanation tonometry (Tonopen-Vet, Medtronic, Solan, USA). CDI ultrasonography (MyLab40, Esaote, Italy) was performed using a 12–18 MHz probe. A coupling gel was applied from the dorsal region of the left zygomatic arch, positioning the transducer in a horizontal

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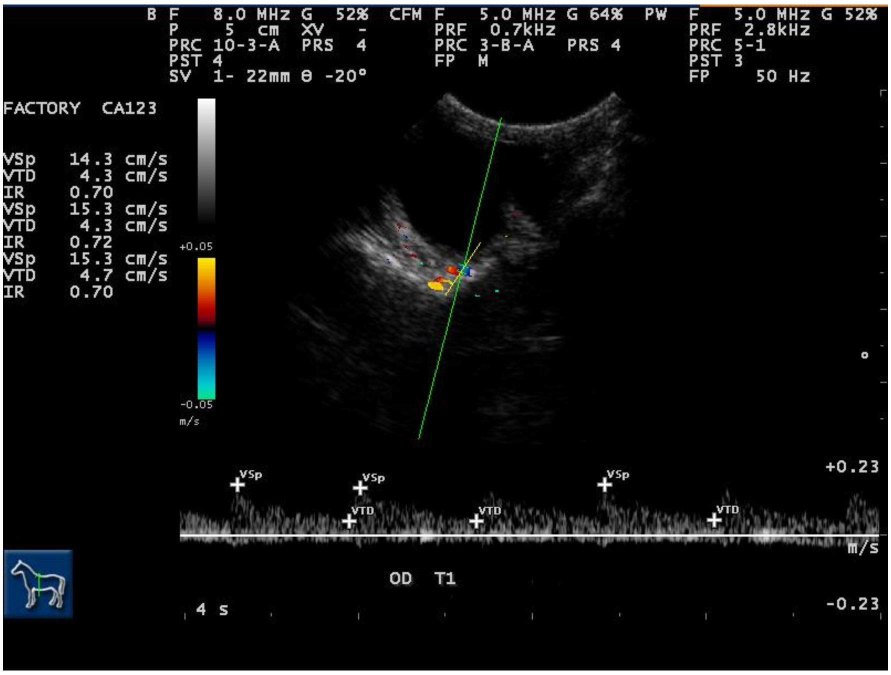

Figure 1. Pulsed Doppler ultrasonogram of the mLPCA in a dog. RI was calculated by the formula (PSV-EDV)/PSV

EDV = end diastolic velocity; mLPCA = medial long posterior ciliary artery; PSV = peak systolic velocity; RI = resistive index

plane. The identification of ocular vessel was obtained visualising the retro bulbar fat and the lateral wall of each eye (Lee et al. 2002). Once the mLPCA was localised, the Peak Systolic Velocity (PSV) and End Diastolic Velocity (EDV) were evaluated. The RI was calculated by the formula (PSV-EDV)/PSV (Macri et al. 2015) (Figure 1). At the end of the procedure, each eye was washed with a sterile physiological solution, in order to remove the ultrasound gel. The procedures were performed by the same examiners (respectively, M.R. for the IOP and F.M. for the RI) with the dogs restrained gently and placed in sternal recumbence. A mean value of the five measurements at each time point was used in the calculations for the IOP and RI. The mean values of the first measurement on each day were considered the baseline values.

Statistical analysis. The statistical analyses were performed using a software package (Version 17.0, SPSS, Inc., Chicago, USA). The data were expressed as mean ± standard deviation (SD) and analysed by two-way repeated ANOVA (analysis of variance) measurement in order to compare the RI and IOP before (T_0) and after the exercise (T_1, T_2). Where the ANOVA was showing an acceptable level of significance ($P \leq 0.05$), Wilcoxon's test was applied for the post hoc comparison. Spearman's correlation for non-normal distribution was used to determine the relationship between the RI and IOP. The statistical significance was defined as $P < 0.05$.

RESULTS

The effects of moderate physical exercise on the RI and IOP are summarised in Table 1. The values of the IOP and RI are expressed as a mean ± SD with their conventional units. The exercise induced

Table 1. The effects of the exercise on the PSV, ESV, RI of the medial long posterior ciliary artery and the IOP

	mLPCA PSV (cm/sec)	*mLPCA* EDV (cm/sec)	*mLPCA* RI	IOP (mmHg)
T_0	20+/–5.05[a]	5.81+/–1.53	0.722+/–0.022[a]	12.38+/3.21[a]
T_1	16.36+/–4.3[b]	5.27+/–0.74	0.697+/–0.035[b]	12.29+/4.26[ab]
T_2	16.18+/–4.16[b]	5.6+/–1.30	0.682+/–0.042[b]	11+/3.39[b]

EDV = end diastolic velocity; IOP = intraocular pressure; mLPCA = medial long posterior ciliary artery; PSV = peak systolic velocity; RI = resistive index

[a,b]A statistical significance between a and b within the columns ($P < 0.05$). All data represent the mean ± SD

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Table 2. Spearman´s rank correlation along a two-tailed *P* for each parameter observed

		PSV	EDV	RI	IOP
PSV	correlation coefficient	–	.033	.158	.267
	significance	–	.852	.505	.008
EDV	correlation coefficient	.033	–	.219	.286*
	significance	.852	–	.516	.004
RI	correlation coefficient	.158	.219	–	.425**
	significance	.505	.516	–	< 0.001
IOP	correlation coefficient	.267	.286*	.425**	–
	significance	.008	.004	< 0.001	–

EDV = end diastolic velocity; IOP = intraocular pressure; PSV = peak systolic velocity; RI = resistive index

*a significant difference between the measurements pre-exercise vs. post-exercise at the 5% significance level

**a significant difference between the measurements pre-exercise vs. post-exercise at the 1% significance level

a decrease in the RI and IOP immediately after the exercise, which was also maintained during the rest phase. Our results evidenced a significant variation in the RI values on the mLPCA between T_1 and T_0 ($P < 0.025$), and between T_2 and T_1 ($P < 0.021$). The IOP decreased significantly between T_2 and T_0 ($P < 0.001$). No significant differences between T_1 and T_2 were recorded. The IOP and RI appeared highly positively correlated ($P \leq 0.001$; R 0.425) (Table 2).

DISCUSSION

CDI is a useful method to investigate ocular and orbital blood flow characteristics (Aburn and Sergott 1993; Munk et al. 1993; Rojanapongpun and Drance 1993; Baxter et al. 1995; Dudea 2011) that has been successfully applied in clinical settings for the evaluation of the circulatory status in retinal vascular disorders and glaucoma (Williamson and Harris 1996; Rankin 1999; MacKinnon et al. 2000; Akal et al. 2014). The topography and direction of the blood flow in many ocular and retro-orbital vessels, such as the external and internal ophthalmic artery, anterior ciliary artery, short and long ciliary arteries and primary retinal artery, have been described clearly in dogs (Gelatt-Nicholson et al. 1999a; Lee et al. 2002; Novellas et al. 2007). Switching to the spectral Doppler mode, quantitative velocity measurements and the calculation of resistive indices may be evaluated. The resistive index has been used to assess the ocular vascular resistance in canine glaucoma and to monitor the hypotensive effect of a drug's administration (Gelatt-Nicholson et al. 1999b; Gelatt et al. 2003; Kallberg et al. 2003; Vrbovska et al. 2017). The present study has focused on assessing the effect of moderate exercise on the RI of the medial long posterior ciliary artery (mLPCA) using CDI, and to determine if the moderate exercise is effective in reducing the IOP, through adjustments of vasculature resistance. The mean values of the RI recorded in the dogs at T_0 differed from the data reported by Gelatt and Brooks (1999) in healthy non-conscious dogs (0.51 +/–0.08). In our opinion, this difference was attributable to the effect of the chemical sedation on the orbital tension and ophthalmic blood flow.

In humans, many investigators have demonstrated that physical exercise induces reductions in the arterial vascular resistance, apparently associated with an increase in ocular perfusion, suggesting that the ocular blood flow or microvascular pressures may be autoregulated by the vascular adjustment proximal to the orbit itself (Beck et al. 1995). The RI provides an indirect measurement of the arterial resistance by means of a ratio between the peak systolic, end diastolic and mean velocity of the spectral doppler waveform (Novellas et al. 2007). Our results showed that moderate physical exercise produces a decrease in the RI following on to a PSV and EDV decrease. Both a decrease in the blood flow and the vessel's narrowing may be involved in the indices of the blood flow velocity and resistance measured with the CDI (Roff et al. 1999). The constant level of blood circulation in the eyeball during the exercise is maintained by the local myogenic constriction of the smooth muscle cells in the arterial wall

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(Bayliss effect) and by the vasoconstriction induced by an increase in the sympathetic drive (Birch et al. 1995; Movaffaghy et al. 1998; Blum et al. 1999). Although changes in the dimensions of the arteries are considered an indirect indicator of the volume flow (Nemeth et al. 2002), the small vessel's diameter of the mLPCA was below the spatial resolution of the ultrasound biometric system so it was not possible to measure the vessels and the changes in the arterial dimension induced by the exercise.

A decreased blood flow in the mLPCA, extraocular branch of the ophthalmic artery, may be interpreted as a sign of autoregulation of the retinal circulation. The autoregulation represents the intrinsic ability of the vascular bed to maintain constant organ blood flow, through the increase of the vessel's tone despite changes in the perfusion pressure (Polska et al. 2007). In order to ensure an adequate supply of oxygen and nutrients to the retinal tissue, choroidal circulation is able to keep the perfusion relatively constant in spite of the changing intraocular pressure (Findl et al. 1997). Indeed, it has been reported a reduction in the blood flow in the ophthalmic artery and its branches after the exercise is associated with the unchanged blood flow velocities in the central retinal artery (Nemeth et al. 2002). Thus, our data suggested that the long posterior ciliary arteries may receive less blood during and after the dynamic exercise than in the rest condition (Nemeth et al. 2002). The decrease in the IOP after the moderate exercise observed in the present study, is consistent with the results of many earlier studies (Kiuchi et al. 1994; Martin et al. 1999; Albaugh et al. 2014; Wylegała 2016). Other authors have suggested that the decrease in the IOP during and after dynamic exercising avail it to maintain the constant blood flow in the central retinal artery by increasing the ocular perfusion pressure and moderating the changes in the resistivity indices caused by the exercise (Zhu et al. 2018). The highly significant positive correlation between the IOP and RI variations suggests that the IOP is also influenced by the cardiovascular and haematological adaptations necessary to guarantee the correct oxygen and blood-borne substrate supply to activate the muscles during exercise and the release of metabolites (Giudice et al. 2010).

In conclusion, as described in human patients, aerobic exercise could be the cause of significant changes in the IOP and in the RI, presumably related to compensative neuro-hormonal mechanisms.

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