THE EFFECT OF PHYSICAL ACTIVITY AND FITNESS LEVEL ON RETINAL MICROCIRCULATION

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Aim: To examine differences in retinal microcirculation between people with different degrees of physical fitness. *Methods:* The subjects were divided into athletes and non-athletes. Both groups took part in two examinations. The first examination was performed before short-term exercise and the second one immediately after it. First group consisted of 25 athletes (50 eyes), and the second group of 25 non-athletes (50 eyes) who were not previously exposed to acute physical stress. Athletes are defined as people who have been engaged in some form of regular physical activity for at least 5 years, and have met certain criteria according to the International Physical Activity Questionnaire (IPAQ). Non-athletes were those who were physically inactive or at least not regularly engaged in physical activity during the same period and did not meet the IPAQ criteria. The subjects were men and women between 18 and 26 years of age who did not have any cardiovascular disease, used drugs affecting the cardiovascular system, nor had an eye disease or a refractive error greater than spherical equivalent of +/-3 diopters. The examination consisted of optical coherence tomography angiography (OCT-A) imaging pre- and post-workout. The parameters taken into account were vascular density (VD) at three different macular areas according to the standard Early Treatment Diabetic Retinopathy Study (ETDRS) grid, i.e., central zone, inner zone and full area; perfusion density (PD), also at the three mentioned zones; and the area of foveal avascular zone (FAZ) in both eyes. The research also included a standardized survey on physical activity of the subjects (IPAQ), which was completed before the examination. The acute physical exercise consisted of the standardized incremental cycling ergometer test (ICET), which was performed on a stationary exercise bike for 5 minutes, at a given load of 12 degrees. On statistical processing of the data obtained, SPSS for Windows (version 13.0, SPSS Inc., Chicago, Illinois, USA) software was used. *Results:* Baseline measures of VD and PD were similar between the groups. FAZ surface was significantly increased in the athlete group compared with non-athletes both at baseline and after short-term exercise. VD was significantly higher in athletes post-exercise compared with the non-athlete group. Central PD was also significantly increased after exercise in the athlete group, and not in the non-athlete group. *Conclusion:* The results obtained in this study demonstrated that athletes exhibited a more intensive vascular reaction to exercise. The parameters in basal conditions did not show significant difference between the two groups, except for FAZ which was larger in athletes. Significant differences present post-workout in other measured values indicated a more dynamic vascular system in physically active individuals.

Key words: physical activity, retina, blood vessels, OCT-A, ICET

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INTRODUCTION

It is known that physical activity influences the cardiovascular system. Both acute and chronic physical activity have an impact on blood vessels, leading to structural and functional changes. Changes and adaptation depend on the level of physical load and can be modulated with oxidative stress and inflammation induced by exercise (1). With aging, our cardiovascular system reduces its compliance (2). This loss in compliance is caused by hypertrophy of the vascular smooth muscles, replacing smooth muscles with connective tissue, and gaining a higher level of cross-linking of the connective tissue. Physical activity has a protective effect on blood vessels through several mechanisms. First, there is an increase in blood pressure and in pulse, which leads to stretching of blood vessels that counteracts the formation of connective tissue cross-links. Second, during exercise, skeletal muscles have an impact on the vessels in a way that they cause vasodilatation that has a similar effect as mentioned previously. Third, physical activity leads to increase in the release and synthesis of nitric oxide that causes vasodilatation (3,4). These factors can have an antimitogenic effect that can in the end slow down or even stop the loss in the blood vessel compliance (5). Also, high levels of physical activity can improve retinal microcirculation both in children and adults. This happens because of the protective effect of exercise on small blood vessels (6). Some studies show that exercise causes changes in the optic nerve, macular perfusion, and there is an increase in the blood flow of the retina (7,8). All of these show how physical activity has a positive impact on the retina and that it may have a protective effect against diseases such as diabetic retinopathy and age related macular degeneration (9).

AIM

The aim of this research was to analyze differences in retinal microcirculation between subjects with different physical fitness levels.

METHODS

The subjects were divided into two groups, athletes and non-athletes. Study subjects underwent two sets of measurements. The first measurement was carried out before the acute physical exercise, and the second one immediately after it.

The mean age of athletes was 22.6±2.4 years; there were 32% of females. The mean age of non-athletes was 22.5±2.1 years of age, with 52% of females. In the first group of subjects there were 25 athletes (50 eyes), and in the second group 25 non-athletes (50 eyes) who were not previously exposed to acute physical stress. Athletes were defined as people who have been involved in some form of regular physical activity for at least 5 years in the form of training a sport, fitness, aerobic training, etc., and according to the Standardized International Physical Activity Questionnaire (IPAQ), they spent at least 3 days a week in intense physical activity (lifting weights, fast running/cycling, aerobics, etc.) or 7 days of combining intense and moderate physical activity and walking. Non-athletes were subjects who were physically inactive or at least not regularly engaged in exercise during the same period and did not meet the IPAQ criteria. The subjects were men and women between 18 and 26 years of age who did not have any cardiovascular disease, did not use drugs affecting the cardiovascular system, nor had an eye disease or a refractive error greater than spherical equivalent of +/- 3 diopters. The examination consisted of optical coherence tomography angiography (OCT-A) imaging pre- and post-workout using Zeiss Cirrus HD5000 device (Carl Zeiss Vision GmbH, Berlin, Germany). The parameters taken into account were vascular density (VD) at three different macular areas according to standard Early Treatment Diabetic Retinopathy Study (ETDRS) grid, i.e., central zone, inner zone and full area; perfusion density (PD), also at the three mentioned areas; and the area of foveal avascular zone (FAZ) in both eyes. The research also included a standardized IPAQ survey on physical activity of the subjects, which was completed before the examination. The acute physical exercise consisted of the standardized incremental cycling ergometer test (ICET), which was performed on a stationary exercise bike for 5 minutes, at a given load of 12 degrees. Subject pulse and oxygen saturation were measured using pulse oximeter (Pulse oximeter, model OXY 300, Beijing Choice Electronic Technology Co. Ltd., Beijing, China) pre- and post-workout. Numerical data were expressed as mean ± standard deviation (SD), and difference in numerical values between the groups was analyzed using Student's t-test. On statistical processing of the data obtained, SPSS for Windows (version 13.0, SPSS Inc. Chicago, Illinois, USA) software was used. The level of statistical significance was set at $p<0.05$.

RESULTS

Vascular density in basal conditions before acute exercise did not show statistically significant differences between the groups of athletes and non-athletes (Figure 1).

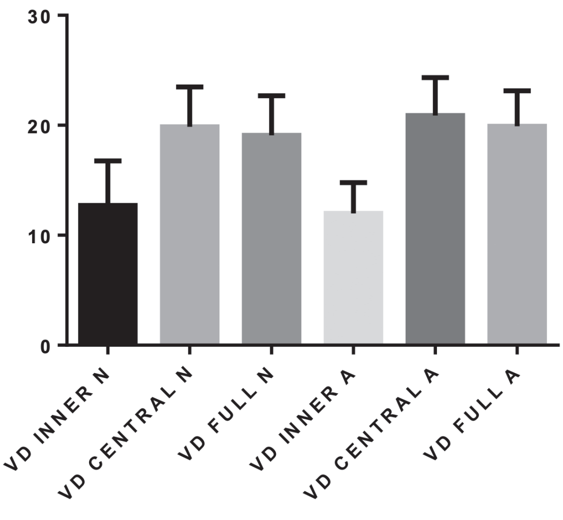

Figure 1. *Vascular density levels (arbitrary units) between the group of athletes (A) and the group of non-athletes (N) in basal conditions (pre-workout); VD INNER N – vascular density inner non-athletes, VD CENTRAL N – vascular density central non-athletes, VD FULL N – vascular density full non-athletes, VD INNER A – vascular density inner athletes, VD CENTRAL A – vascular density central athletes, VD FULL A – vascular density full athletes; data are expressed as mean ± standard deviation; n=50 per group, p>0.05, Student's t test.*

Perfusion density was similar between the groups at baseline measurements (Figure 2).

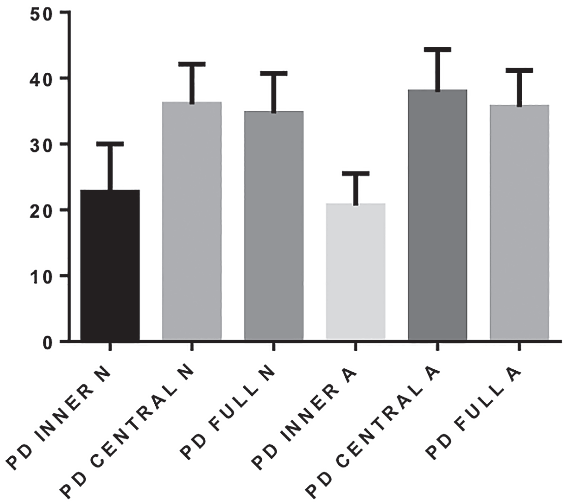

Figure 2. *Perfusion density levels (arbitrary units) between the group of athletes (A) and the group of non-athletes (N) in basal conditions (pre-workout); PD INNER N – vascular density inner non-athletes, PD CENTRAL N – vascular density central non-athletes, PD FULL N – vascular density full non-athletes, PD INNER A – vascular density inner athletes, PD CENTRAL A – vascular density central athletes, PD FULL A – vascular density full athletes. Data are expressed as mean ± standard deviation; n=50 per group, p>0.05, Student's t test.*

Athletes exhibited a larger surface of FAZ compared with non-athletes (0.17±0.01 mm^2*vs*. 0.21±0.01 mm^2, n=50 *per* group, p=0.008) (Figure 3).

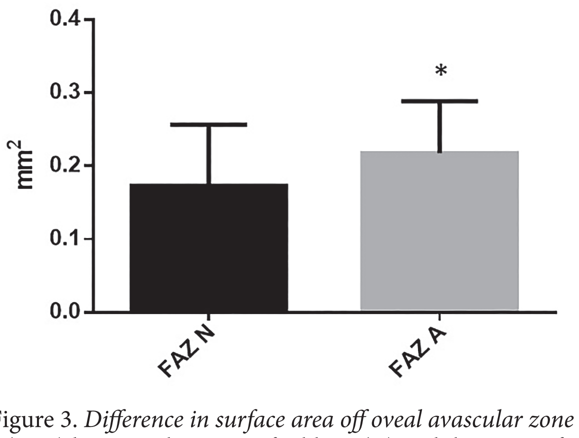

Figure 3. *Difference in surface area off oveal avascular zone (FAZ) between the group of athletes (A) and the group of non-athletes (N); data are expressed as mean ± standard deviation; n=50 per group, *p=0.008, Student's t-test.*

After exercise, non-athletes exhibited similar results as at baseline. Vascular density was significantly higher in athletes post-exercise at all measured areas, central, inner and full (11.99±0.39 *vs*. 17.55±0.92; 20.9±0.4 *vs*. 30.86±1.4; and 19.92±0.45 *vs*. 29.1±1.2, respectively, n=50 *per* group, p<0.001). Central PD was also significantly increased after exercise in the athlete group, and not in the non-athlete group (20.64±0.68 *vs*. 23.23±0.79, n=50 *per* group, p=0.01) (Figures 4 and 5).

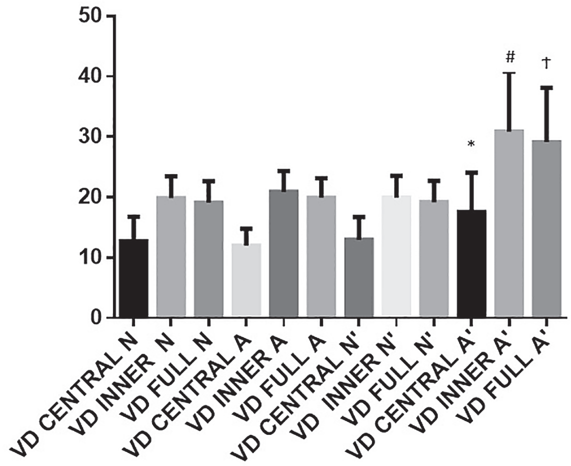

Figure 4. *Vascular density levels (arbitrary units) between the group of athletes (A) and the group of non-athletes(N) pre- and post-workout; VD INNER N – vascular density inner non-athletes, VD CENTRAL N – vascular density central non-athletes, VD FULL N – vascular density full non-athletes, PD INNER A – vascular density inner athletes, VD CENTRAL A – vascular density central athletes, VD FULL A – vascular density full athletes; post-workout marked with '; data are expressed as mean ± standard deviation; n=50 per group. *p<0.001 (VD CENTRAL A vs. VD CENTRAL A'), $^{\#}$p<0.001 (VD INNER A vs. VD INNER A'), $^{\#}$p<0.001 (VD FULL A v.s VD FULL A').*

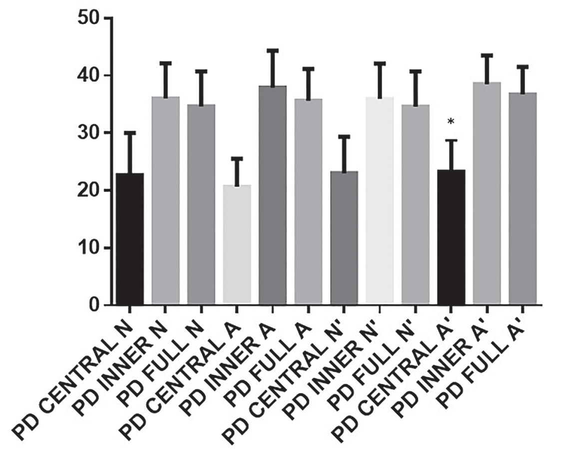

Figure 5. *Perfusion density levels (arbitrary units) between the group of athletes (A) and the group of non-athletes(N) pre- and post-workout; PD INNER N – perfusion density inner non-athletes, PD CENTRAL N – perfusion density central non-athletes, PD FULL N – perfusion density full non-athletes, PD INNER A – perfusion density inner athletes, PD CENTRAL A – perfusion density central athletes, PD FULL A – perfusion density full athletes; post-workout marked with '; data are expressed as mean ± standard deviation; n=50 per group, *p=0.01 (PD CENTRAL A vs. PD CENTRAL A').*

Foveal avascular zone demonstrated similar properties before and after exercise. The athlete group had a significantly larger surface of FAZ pre- and post-workout compared with the non-athlete group. The exercise itself did not affect FAZ surface in either group (0.17±0.01 mm^2 *vs.* 0.22±0.008 mm^2, n=50 *per* group, p=0.003) (Figure 6).

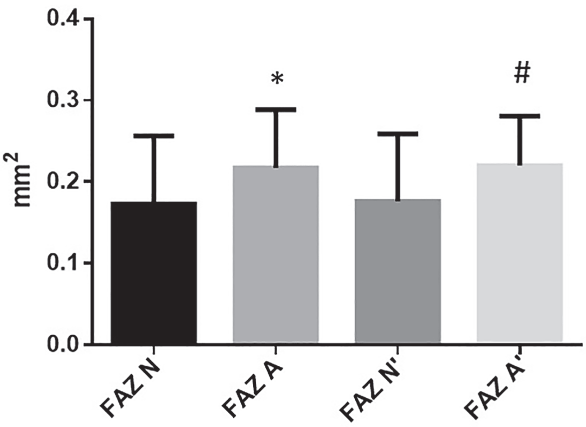

Figure 6. *Difference in surface area off oveal avascular zone (FAZ) between the group of athletes (A) and the group of non-athletes (N); post-workout marked with '; data are expressed as mean ± standard deviation; n=50 per group, *p=0.008 (FAZ N vs. FAZ A), #p=0.03 (FAZ N' vs. FAZ A').*

Athletes had a significantly lower pulse rate before and after exercise compared with non-athletes. There was no difference in the oxygen saturation rate (Table 1).

Table 1.*Pulse rate and oxygen saturation before and after acute exercise between athletes and non-athletes (n=50 per group, *Student's t-test)*

	Non-athletes		Athletes		p*
	X	SD	X	SD	
PULSE RATE	87.04	13.12	74.68	9.39	**<0.001**
Oxygen saturation	97.24	0.83	97.24	1.01	>0.999
PULSE RATE after exercise	136.76	16.38	101.24	11.37	**<0.001**
Oxygen saturation after exercise	96.96	1.14	97.16	1.14	0.538

DISCUSSION

The study included two groups according to their fitness level, athletes and non-athletes. The research was divided into two parts when the subjects underwent two measurements, i.e., before and after physical load, and the parameters were observed in those two measurements.

According to study results, there was no difference in the VD and PD parameters in basal conditions, which might mean that regular physical activity and fitness level did not affect density of retinal blood vessels or perfusion, but a difference was observed in the FAZ between the examined groups. During the study, the VD and PD parameters were observed in the surface layer of the retina. Although no difference was found in that layer, Kim *et al.* showed a reduction of VD in the surface layer in their research (10). Nelis *et al.* report that the main finding in OCT-A measurements was change in the size of the FAZ conditioned by greater physical fitness. They used multivariate regression analysis and found that running speed at individual lactate threshold, a marker strongly associated with aerobic performance capacity, significantly contributed to differences in the FAZ area. They conclude that smaller areas of FAZ were found in athletes (11). In the present study, we did not record such findings in young healthy adults. It is possible that differences in FAZ in the present study were due to acute vasoconstriction. Although certain trends were visible, it probably takes a longer period of different lifestyle to have an effect on FAZ that could be quantified by OCT-A.

This research showed significant differences in heart rate before and after exercise in athletes and non-athletes. Athletes had a lower heart rate than non-athletes in both measurements, which was expected, since the heart of athletes has a 40% higher stroke volume on average compared to physically inactive people (12). Concerning oxygen saturation, there were no statistically significant differences in relation to exercise, which is also consisted with previously reported data.

In the second set of experiments, after the respondents were subjected to a moderate form of physical activity, statistically significant increases in VD and PD were observed in the athlete group. The research conducted by Kim *et al.* showed no significant changes in retinal circulation before and after moderate physical activity, but there were significant changes in cardiovascular parameters, i.e., pulse and blood pressure (10). The study conducted by Nelis *et al.* determined that the only significant difference after physical activity in the two groups of subjects also was only recorded in FAZ, while other variables did not show statistically significant differences. Also, in this study, significant changes were recorded in heart rate. Among athletes, the expected values were significantly lower, and it was observed that these two variables are clearly related to regular physical activity (11). A major limitation of this study was that only young healthy adults were examined. Therefore, we could not observe long-term benefits of regular exercise and its effect on retinal circulation. Also, we did not separate different forms of regular exercise, and therefore could not establish specific benefits related to a certain sport or exercise form. Future studies are needed to further elucidate the effects of exercise on long-term retinal health.

CONCLUSIONS

In basal conditions, there was no statistically significant difference between athletes and non-athletes. People with increased physical fitness showed a larger area of FAZ in basal conditions and after exercise. Athletes demonstrated an increase in PD and VD parameters after physical activity. Significant differences in post-workout values indicate a more dynamic vascular system in physically active individuals.

REFERENCES

1. Green DJ, Smith KJ. Effects of exercise on vascular function, structure, and health in humans. Cold Spring Harb Perspect Med 2018;8(4):a029819.

2. Arnett DK, Evans GW, Riley WA. Arterial stiffness: a new cardiovascular risk factor? Am J Epidemiol 1994;140:669-82.

3. Segal SS, Kurjiaka DT. Coordination of blood flow control in the resistance vasculature of skeletal muscle. Med Sci Sports Exerc 1995;27:1158-64.

4. Rubanyi GM, Romero JC, Vanhoutte PM. Flow-induced release of endothelium-derived relaxing factor. Am J Physiol 1986;250:H1145-9.

5. Green DJ, Cable NT, Fox CH, Rankin JM, Taylor RR. Modification of forearm resistance vessels by exercise training in young men. J Appl Physiol 1994;77:1829-33.

6. Streese L, Guerini Ch, Bühlmayer L *et al*. Physical activity and exercise improve retinal microvascular health as a biomarker of cardiovascular risk: a systematic review. Atherosclerosis 2020;315:33-42.

7. Szalai I, Pálya F, Csorba A, Tóth M, Somfai GM. The effect of physical exercise on the retina and choroid. Klin Monbl Augenheilkd 2020;237:446-9.

8. Alnawaiseh M, Lahme L, Treder M, Rosentreter A, Eter N. Short-term effects of exercise on optic nerve and macular perfusion measured by optical coherent tomography angiography. Retina 2017;7:1642-6.

9. Okuno T, Sugiyama T, Kohyama M, Kojima S, Oku H, Ikeda T. Ocular blood flow changes after dynamic exercise in humans. Eye (Lond) 2006;20(7):796-800.

10. Kim SV, Semoun O, Pedinielli A, Jung C, Miere A, Souied EH. Optical coherence tomography angiography quantitative assessment of exercise-induced variations in retinal vascular plexa of healthy subjects. Invest Ophthalmol Vis Sci 2019;60:1412-9.

11. Nelis P, Schmitz B, Klose A *et al*. Correlation analysis of physical fitness and retinal microvasculature by OCT angiography in healthy adults. PLoS One 2019;14:e0225769.

12. Guyton A, Hall J. Medical physiology. Thirteenth edition. Zagreb: Medicinska naklada, 2016,1085-95.

SAŽETAK

UTJECAJ VJEŽBANJA I RAZINE OSPOSOBLJENOSTI NA MIKROCIRKULACIJU RETINE

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Cilj rada: Ispitati razlike u retinalnoj mikrocirkulaciji između osoba s višim i nižim stupnjem tjelesne osposobljenosti. *Postupci:* Ispitanici su bili podijeljeni na sportaše i nesportaše. Obje skupine pristupile su dvama odvojenim mjerenjima. Prvi pregled obavljen je prije fizičkog opterećenja, a drugi neposredno nakon njega. Prvu skupinu činilo je 25 sportaša (50 očiju), a drugu 25 nesportaša (50 očiju) koji prethodno nisu bili izloženi akutnom fizičkom stresu. Sportaše definiramo kao osobe koje se najmanje 5 godina bave nekim oblikom redovite tjelesne aktivnosti u obliku treniranja nekog sporta, fitnesa, aerobnog treninga i sl. te ispunjavaju određene uvjete prema međunarodnom upitniku o tjelesnoj aktivnosti *(International Physical Activity Questionnaire,* IPAQ). Neki sportaši nisu bili fizički aktivni ili barem ne redovito tijekom istog razdoblja i nisu ispunjavali navedene kriterije IPAQ. Ispitanici su bili muškarci i žene u dobi između 18 i 26 godina koji nisu imali nikakvu srčanožilnu bolest, nisu uzimali lijekove koji utječu na srčanožilni sustav niti su imali ikakvu bolest očiju ili refraktivnu grešku veću od sfernog ekvivalenta +/-3 dioptrije. Prikupljanje podataka provedeno je pomoću optičke koherentne tomografske angiografije (OCT-A). Analizirani su sljedeći parametri: vaskularna gustoća (VG) u tri različita područja makule prema mreži ETDRS *(Early Treatment Diabetic Retinopathy Study)*: središnja zona, unutarnja zona i puna zona; perfuzijska gustoća (PG), također u tri navedena područja; te površina fovealne avaskularne zone (FAZ). Istraživanje je uključivalo i standardiziranu anketu o tjelesnoj aktivnosti ispitanika (IPAQ) koja se ispunjavala prije samog pregleda. Fizičko opterećenje sastojalo se od standardiziranog testa ICET (incremental cycling ergometer test), koji se izvodio na stacionarnom sobnom biciklu u trajanju od 5 minuta pri zadanom opterećenju od 12 stupnjeva, nakon čega su ispitanicima izmjereni puls i saturacija. Također, prije same vježbe ispitanicima su izmjerene srčana frekvencija i saturacija u mirovanju. Za statističku obradu dobivenih podataka primijenjen je softverski sustav SPSS for Windows (verzija 13.0, SPSS Inc., Chicago, Illinois, SAD). *Rezultati:* Mjerenja u bazalnim uvjetima pokazala su slične vrijednosti VGi PG između skupina. Površina FAZ bila je statistički značajno veća u skupini sportaša u usporedbi s nesportašima i u bazalnim uvjetima i nakon tjelovježbe. Nakon tjelovježbe VG i središnji PG pokazali su statistički značajno povećanje u sportaša, dok u nesportaša nije bilo razlike prije i nakon tjelovježbe. *Zaključak:* Rezultati dobiveni u ovoj studiji pokazali su da sportaši imaju intenzivniju vaskularnu reakciju na vježbanje. Parametri u bazalnim uvjetima nisu pokazali značajnu razliku između dviju skupina osim za FAZ, koja je bila veća u sportaša. Značajne razlike bile su prisutne nakon treninga u drugim izmjerenim vrijednostima i ukazuju na dinamičniji vaskularni sustav u fizički aktivnih pojedinaca.

Ključne riječi: fizička aktivnost, retina, krvne žile, OCT-A, ICET