Choroidal thickness variation in highly myopic eyes during the water drinking test

Variação da espessura de coroide em olhos alto míopes durante o teste de sobrecarga hídrica

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ABSTRACT

Purpose: To evaluate variations in choroidal thickness (CT) during the water drinking test (WDT) in emmetropic eyes (EE) and highly myopic eyes (ME) using spectral-domain optical coherence tomography (SD-OCT).

Methods: Clinical trial performed at a tertiary care hospital comprising 30 randomly selected eyes. The WDT and SD-OCT macular scans were performed 10 and 45 min after water ingestion in 15 myopic and 15 EE of 15 healthy patients in each group. Primary study outcomes were average macular CT measured by SD-OCT and intraocular pressure (IOP) during the WDT.

Results: The mean spherical equivalent refraction was 0.15 ± 0.24 D in emmetropic and -7.1 ± 1.75 D in ME (p<0.001). No statistical differences between EE and ME were observed during the WDT response. EE had higher CT compared with ME at the fovea (361.4 ± 55.4 vs 257.9 ± 95.3; p<0.001), 3 mm nasal to the fovea (158.0 ± 71.8 vs 122.5 ± 54.5; p=0.047), and 3 mm temporally to the fovea (310.6 ± 52.4 vs 247.6 ± 90.1; p=0.05). Regarding CT variation, significant differences in foveal CT at 10 min after water ingestion were observed in both EE and ME, with no statistically significant difference observed between groups. A moderate correlation between IOP peak during the WDT and CT was demonstrated in ME (r=0.52; p=0.04).

Conclusions: No statistically significant differences in CT variation during the WDT were observed between EE and ME, indicating similar behavior of the choroidal bed during the WDT in both groups. Further, CT was thinner in highly ME, with CT variation unable to explain elevations in IOP observed during the WDT.

Keywords: Myopia; Choroid; Tomography; Optical coherence; Axial length; Eye; intraocular pressure; Water; drinking; Osmosis

RESUMO

Objetivo: *Avaliar a espessura de coroide (EC) e sua variação durante o teste de sobrecarga hídrica (TSH) em olhos emétropes (EE) e míopes (ME) utilizando a tomografia de coerência óptica Spectral-Domain (SD-OCT).*

Métodos: *Ensaio clinico realizado em um hospital terciário. 30 olhos selecionados randomizadamente, 15 míopes e 15 emétropes de 15 pacientes em cada grupo foram submetidos ao TSH e scans maculares com SD-OCT realizados 10 e 45 minutos após a ingestão de água. Os principais resultados avaliados foram média da EC na região macular pelo SD-OCT e pressão intraocular (PIO) durante o TSH.*

Resultados: *O equivalente esférico médio foi de 0.15 ± 0.24 dioptrias em emétropes e -7,1 ± 1,75 dioptrias nos olhos míopes (p<0,001). Não foram encontradas diferenças estatísticas durante a resposta ao TSH entre EE e ME. EE apresentaram maior EC em comparação com ME, tanto na região foveal (361,4 ± 55,4 vs 257,9 ± 95,3;* p<*0,001), 3 milímetros nasal à fóvea (158,0 ± 71,8 vs 122,5 ± 54,5;* p=*0,047) e 3 mm temporal à fóvea (310,6± 52.4 vs 247,6 ± 90,1;* p=*0,05). Em relação à variação da EC, diferenças estatisticamente significativas foram demonstrados na região foveal, 10 minutos após a ingestão de água em ambos EE e ME, sem diferenças entre os grupos. Moderada correlação entre pico de PIO durante o TSH e EC foi demonstrada em ME (r=0,52;* p=*0,04).*

Conclusão: *A diferença na variação da EC provocada pelo TSH não foi estatisticamente diferente entre olhos emétropes e míopes, o que sugere um comportamento semelhante da coroide nestes dois grupos quando submetidos ao TSH. Além disso, a EC é mais fina nos olhos alto míopes, e a variação na EC não explica o aumento da PIO durante o TSH.*

Descritores: *Miopia; Coroide; Tomografia de coerência óptica; Comprimento axial do olho; Pressão intraocular; Água; Ingestão de líquidos; Osmose*

INTRODUCTION

Myopia is typically classified into two groups: low-to-moderate myopia (-0.5 to -5.0 D) and high or pathological myopia (greater than -5.0 D)[1]. Pathological myopia is associated with several vision-threatening fundus complications such as macular atrophy, posterior staphyloma, lacquer cracks, choroidal neovascularization, macular hole, stretched vessels, patchy atrophy, tilting of the optic disc, and retinal detachment[2,3]. Such complications are typically caused by excessive elongation of the eyeball, which may also cause decreased choroidal thickness (CT) compared with emmetropic eyes (EE)[4,5].

Until recently, the utility of in vivo choroidal imaging was considered relatively poor. Methods such as indocyanine green angiography and ultrasonography have demonstrated utility in evaluating the choroid despite several limitations such as low-resolution images and possible operator-dependent variability[6,7]. The development of newer technologies such as spectral-domain optical coherence tomography (SD-OCT) has improved imaging visualization of deeper intraocular structures. However, effective measurement of OCT has only been possible since the development of enhanced depth imaging (EDI) technology by Spaide *et al.*[8] using the Heidelberg Spectralis (Heidelberg Engineering, Heidelberg, Germany) OCT instrument, with OCT measurements of the choroid shown to be reproducible[9].

Previously, the water drinking test (WDT) has predominantly been used as a diagnostic tool for glaucoma. However, the WDT was abandoned due to its poor diagnostic value[10,11] Recently, the WDT was revived as a tool to evaluate the outflow facility reserve of the eye[12]. The results of the WDT have been shown to correlate well with intraocular pressure (IOP) peaks occurring during daytime[13]. A correlation between WDT results and progression of glaucoma has also been demonstrated[14,15].

The choroid has been studied due to its potential role in the pathogenesis[16] of glaucoma, with several authors attempting to determine the relationship between glaucoma and CT[17-22]. De Moraes *et al.*[21] described an increase in CT during the WDT in a group of

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glaucomatous patients, which may partly explain observed increases in IOP following water ingestion. However, Arora *et al.*[22] found a significant increase in CT and a decrease in anterior chamber depth after WDT in angle closure eyes but not open angle eyes, indicating different behavior of the choroidal bed in these two conditions.

To the best of our knowledge, no previous studies have compared CT variation in response to the WDT between highly myopic eyes (ME) and EE. The purpose of the present study was to evaluate CT variation during the WDT in patients with ME compared with a control group of EE.

METHODS

All procedures of the present study followed the tenets of the Declaration of Helsinki and were approved by the Institutional Review Board/Committee of Ethics.

A total of 30 nonglaucomatous patients were recruited from the Department of Ophthalmology of the University of Sao Paulo School of Medicine and divided into the following two groups: 15 eyes chosen randomly from 15 consecutive patients with high myopia (>-5.0 D) and a control group of 15 eyes chosen randomly from 15 consecutive patients without myopia, with a spherical equivalent higher than 0.0 D and lower than +1.0 D. One eye per patient was included in the present study to avoid high intereye correlation in the analysis, as this has been known to falsely increase observed differences between groups[23]. Further, one eye per patient was randomly chosen for statistical analysis to avoid selection bias[24]. Each participant provided signed informed consent for participation in the present study.

To be included in the present study, all patients were required to have a normal optic disc appearance on fundus biomicroscopy and IOP lower than 21 mmHg on at least two measurements performed at two different days by the same examiner and with the same calibrated Goldmann tonometer (R900, Haag-Streit, Koeniz, Switzerland).

Exclusion criteria included conditions that may affect choroidal morphology and IOP outflow such as presence of any type of glaucoma, eyes with a history of retinal detachment, pars plana vitrectomy, scleral buckling or any intraocular surgery, antivascular endothelial growth factor therapy, diabetes, systemic arterial hypertension, use of any kind of eye drops, photodynamic therapy, foveoschisis, posterior uveitis, or macular hole.

Patients underwent refraction tests for classification into each of the two groups. Biometry was performed using an IOL Master 500 (Carl Zeiss Meditec Inc., Dublin, CA, USA), with a minimum of two consecutive measurements of axial length performed until two reliable readings were acquired with a signal-to-noise ratio greater than 2.0 for each measurement. Central corneal thickness was calculated using an ultrasound pachymeter as the mean value of five sequential measurements (Tomey Ultrasound Contact Pachymeter SP-3000, Tomey, Nagoya, Japan).

OCT measurements were obtained according to previously published methodology[20]. In brief, spectral domain OCT scans were performed in the macular region using a single, 30°, linear scan centered on the fovea. All images were obtained by EDI using a Heidelberg Spectralis OCT (Software version 6.3.4; Heidelberg Engineering, Heidelberg, Germany). The automatic real-time (100 frames) averaging mode was applied to ensure the quality of obtained images. All measurements were performed using a caliper available in the device software at 80% zoom. Scans were performed in a horizontal section in the subfoveal region, 3 mm temporally to the fovea and 3 mm nasally to the fovea at 500-µm intervals. SD-OCT macular scans were performed at baseline and at 10 and 45 min after water ingestion. CT was determined as the distance from the outer surface of the hyperreflective line, referred to as the "retinal pigment epithelium" layer, to the hyperreflective line of the inner sclera border. The same experienced nonmasked operator (RASG) performed two consecutive imaging scans per eye on all subjects with the same OCT instrument, with manual outlining of the CT. In cases where CT values differed between the two measures, a third scan was performed.

For the WDT, patients were asked not to drink any fluids for at least 2 h prior to the test. IOP was measured immediately prior to the ingestion of 1,000 mL of tap water in less than 5 min. IOP was measured again at 15, 30, and 45 min thereafter. The IOP peak was determined as the highest IOP measured during the WDT. The same calibrated Goldmann tonometer (Haag-Streit, Koeniz, Switzerland) was used for all IOP measurements. All measurements were performed by the same examiner who was blinded to the results of all previous examinations.

Pairwise comparisons between the two groups were performed using Student's *t*-test. *p*-Values less than 0.05 were considered statistically significant after correction using Bonferroni's test. Calculations of CT and IOP elevation during the WDT were based on percentage values and not on absolute values to decrease statistical errors associated with basal differences between CT values in ME and EE. The correlation between IOP peak during the WDT and foveal CT was evaluated using Pearson's correlation coefficient.

Statistical analyses were performed using SPSS 11.0 (SPSS Inc., Chicago, IL, USA).

RESULTS

Fifteen eyes from 15 myopic patients and 15 eyes from 15 emmetropic patients were included in the present study. The mean age was 23.1 ± 2.4 years (20-27) and 24.6 ± 2.7 years (21-29) in ME and EE (p=0.101, ns), respectively. In EE, the mean axial length was 23.21 ± 0.87 mm, and in ME was 26.38±0.97 mm (p<0.001). The mean central corneal thickness was 563.1±53.9 and 565.9 ± 39.8 µm (EE and ME, respectively; p=0.83, ns). The mean spherical equivalent refraction was 0.15 ± 0.24 in EE and -7.1 ± 1.75 D in ME (p<0.001).

Table 1 presents the results of WDT. Baseline IOP was 12.4 ± 2.7 mmHg in the emmetropic group and 12.4 ± 2.0 mmHg in the myopic group, with no statistical difference observed between groups. The IOP peak after water ingestion was 14.3 ± 2.7 and 14.2 ± 2.3 mmHg in EE and ME, respectively. No statistical difference in IOP peak during the WDT was observed between EE and ME, although a statistical significant increase in IOP during the WDT was observed in both groups, with a higher IOP peak observed at 15 min after water ingestion.

Table 2 presents baseline CT values and variations in both EE and ME groups during the WDT. The adjusted *p*-value for significance within each group was 0.008. Regarding baseline CT values, EE had greater CT compared with ME at the fovea (361.4 ± 55.4 vs. 257.9 ± 95.3; p<0.001), 3 mm nasal to the fovea (158.0 ± 71.8 vs, 122.5 ± 54.5; p=0.047), and 3 mm temporally to the fovea (310.6 ± 52.4 vs. 247.6 ± 90.5; p=0.05).

Regarding CT variation, statistically significant differences were in fovea CT at 10 and 45 min after water ingestion in both EE and ME. This increase in foveal CT was equivalent to 2.25% and 3.06% at 10

Table 1. Mean IOP in mmHg in EE versus ME at baseline and at 15, 30, and 45 min after the water drinking test (WDT). Data is presented as mean ± standard deviation

	Baseline	15 min	30 min	45 min	IOP peak*
EE group	12.4 ± 2.7	14.1 ± 2.6	12.8 ± 3.0	12.2 ± 2.7	14.3 ± 2.7
p value from baseline		<0.0001	0.395	0.709	<0.0001
ME group	12.4 ± 2.0	13.9 ± 2.3	13.4 ± 2.3	13.3 ± 2.2	14.2 ± 2.3
p value from baseline		<0.0030	0.051	0.043	<0.0020
p value between groups	0.947	0.8590	0.501	0.301	0.9010

*= IOP peak equals to maximum IOP identified after water ingestion; EE= emmetropic eyes; IOP= intraocular pressure; ME= myopic eyes.

Table 2. Choroidal thickness (µm) in EE and ME groups at baseline and 10 min and 45 min after the water drinking test (WDT). Data is presented as mean ± standard deviation (variation from baseline)

Interval	Nasal	Fovea	Temporal
		EE	
Baseline	158.0 ± 71.8	361.4 ± 55.4	310.6 ± 52.4
10 min	154.0 ± 77.1 (-2.53%)	369.8 ± 53.3 (2.25%)	309.8 ± 52.9 (-0.45%)
p value from baseline	0.599	0.002	0.531
45 min	152.0 ± 70.3 (-3.79%)	370.5 ± 56.3 (2.51%)	306.6 ± 57.0 (-1.28%)
p value from baseline	0.438	0.015	0.586
		ME	
Baseline	122.5 ± 54.5	257.9 ± 95.3	247.6 ± 90.5
10 min	125.6 ± 44.3 (2.53%)	265.8 ± 101.1 (3.06%)	253.1 ± 90.6 (2.2%)
p value from baseline	0.457	0.005	0.344
45 min	124.0 ± 48.6 (1.22%)	265.7 ± 100.3 (3.06%)	254.4 ± 89.6 (2.74%)
p value from baseline	0.755	0.024	0.026
p value between groups	0.047	<0.001	0.050

Adjusted *p*-value for significance within each group: $p<0.008$.

No statistical differences were observed in choroidal thickness variation during the WDT between EE and ME groups.

Nasal= 3 mm nasal to the fovea; Temporal= 3 mm temporal to the fovea; IOP= intraocular pressure; EE= emmetropic eyes; ME= myopic eye.

min and 2.51% and 3.05% at 45 min in EE and ME, respectively (no statistically significant difference was observed between groups). Further, a statistically significant increase in CT at 3 mm temporal to the foveal was observed at 45 min after water ingestion in ME.

No correlation was observed between IOP peak during the WDT and CT in EE (r=0.08; p=0.977). A moderate correlation between IOP peak during the WDT and CT was demonstrated in ME (r=0.52; p=0.04).

DISCUSSION

CT in ME was thinner than in EE in the present study, corroborating previous literature[25,26]. The nasal quadrant was thinner than the fovea and the temporal quadrant, which is in agreement with a previous report[25]. However, the mean subfoveal CT in ME was 257.9 ± 95.3 µm, thicker than the average thickness measured in other studies. Fujiwara *et al.*[26] reported a subfoveal CT of 93.2 µm (±62.5 µm) using the Spectralis with EDI, the same instrument using the present study. Further, Flores-Moreno *et al.*[27] reported a mean subfoveal CT of 166 ± 88.7 µm (13.5-486.5) using the Topcon 3 D-2000 OCT in a pattern that facilitates the visualization of deeper ocular structures, similar to the EDI in Spectralis. There may be at least two possible reasons for this difference. First, the mean age of the myopic group was 23.1 ± 2.4 years (20-27), significantly younger age compared with that in other studies[26,27]. Second, the mean spherical equivalent refraction was -7.1 ± 1.75 D in the myopic group, a smaller value than the -12.05 ± 5.02 D value reported by Flores-Moreno *et al.*[27] and -11.9 D (± 3.7 D) value reported by Fujiwara *et al.*[26]. CT is known to decrease with increasing age and degree of myopia. The results of a previously reported regression analysis indicated subfoveal CT decreases by 12.7 µm for each decade of life and by 8.7 µm for each diopter of myopia[26].

The exact mechanisms underlying the IOP elevation in response to the ingestion of 1 L of water are not completely understood[28]. This increase has been posited to be caused by an increase in aqueous humor production or a reduction in aqueous humor outflow. Brucculeri *et al.*[29] tested hypothesis that elevated IOP was determined by increased aqueous production resulting from a blood-ocular osmotic pressure gradient in 16 healthy volunteers. No variation in hematocrit, total plasma osmolality, or plasma colloid osmotic pressure was observed in this study, and the authors therefore concluded that neither vitreous hydration nor increased aqueous ultrafiltration was responsible for the increase in IOP. However, previous studies have indicated osmotic mechanisms may influence IOP during the ingestion of water[30-32]. Campbell *et al.*[30] analyzed blood sodium and diuresis in glaucomatous and nonglaucomatous patients and reported an initial fall in blood sodium after ingestion of water, which coinciding with the maximum rise in IOP but without a proportional relationship being observed. Spaeth [32] performed 234 WDT and demonstrated that osmotic changes contribute to the observed changes in IOP during the WDT but are unable to fully explain the rise in IOP following the ingestion of water.

In contrast, Brubaker[12] posited that the WDT may be a marker of the outflow facility of the eye. After drinking any hypotonic fluid such as water, there is an influx of volume into body tissues including the eye, thereby changing the episcleral venous pressure. Elevation of episcleral venous pressure may alter IOP by two mechanisms: increased resistance to aqueous outflow and engorgement of the choroidal vasculature and alteration of the trabecular outflow[28]. Thus, variations in the outflow facility of the eye may explain the variation in IOP during the WDT.

Previous studies have attempted to determine the correlation between the WDT and CT variation. De Moraes *et al.*[21] measured changes in CT after the WDT in a group of glaucomatous patients using ultrasonography. They reported a significant increase in CT after the WDT, associated with an IOP increase of 3.5 mmHg and a peak IOP at 30 min. They also demonstrated a moderate correlation between the CT peak and the ocular pulse amplitude peak, which the preceded IOP peak by 15 min. They concluded that acute water intake leads to a transient decrease in blood colloid osmotic pressure, which transfers fluid from the systemic circulation to the choroidal space due to the osmotic gradient, thereby increasing choroidal volume. This, in turn, would be transmitted to the anterior segment, causing fluid to exit in an amount dependent on outflow facility. Changes in IOP are therefore thought to depend on outflow facility[12].

Two recent studies evaluated CT changes during the WDT using OCT. Arora *et al.*[22] studied CT changes in a group of patients with open-angle and angle-closure glaucoma, where Mansouri *et al.*[33] evaluated CT changes after the WDT in healthy individuals. The first group[22] described a significant increase in CT and a decrease in anterior chamber depth after WDT only in angle closure eyes. According

to these authors, IOP increases without a commensurate CT increase in patients with open-angle glaucoma support the hypothesis that increased outflow resistance is the major mechanism underlying IOP elevations in response to WDT.

Mansouri *et al.*[33] demonstrated a statistically significant increase in macular CT after the WDT of a smaller magnitude, with an maximum increase of 4.3%. They observed no association between increased IOP and CT and concluded that choroidal changes did not fully explain WDT-related rises in IOP. We attempted to further investigate the findings of Mansouri *et al*.[33] by also evaluating healthy individuals without glaucoma. We divided individuals into two groups: highly ME and a control group of EE. As myopia is a risk factor for glaucoma development[34], and it is known that CT differs between EE and ME, we used macular OCT to evaluate the effects of the WDT over the choroid in these two groups of patients. The results of the present study corroborate the findings of Mansouri *et al*. We also found no statistically significant difference in mean central corneal thickness between the two groups, which may otherwise have interfered with IOP measurements.

Bonomi et al.[35] studied the outflow facility of 137 anisometropic subjects with unilateral high myopia and concluded that the outflow facility was higher on the myopic side, as the scleral rigidity was found to be lower as well. In the present study, considering that the WDT is a surrogate of the outflow facility, we were unable to demonstrate this difference. However, the present study was not designed to evaluate the outflow facility directly. It may be possible that, even with the outflow facility difference reported by Bonomi et al.,[35] the magnitude of such difference was not enough to be detected by the WDT.

Thinner CT is associated with poorer visual acuity in highly ME as shown by Flores-Moreno *et al.*[27]. They demonstrated that subfoveal CT, mean macular CT, and outer foveal thickness are the most important predictors of visual acuity in highly ME without macular pathology.

The present study has some limitations. CT was measured using EDI in spectral domain OCT, and the demarcation of CT was manually performed by the operator, which may have increased measurement variability. The same operator performed all CT demarcation in both ME and EE groups. However, the examiner was not blinded to measurement results.

We believe the present study to be the first in the literature designed to evaluate differences in CT elicited by the WDT between the EE and highly ME, which may reflect differences in the physiologic behavior of the choroid layer in both conditions. We observed greater CT in EE compared with ME. The identification of different choroidal responses to the WDT broadens our understanding of the mechanisms underlying increases in IOP during the WDT and the physiopathology of glaucoma development in ME. The importance of CT in higher myopics and its association with fundus changes in these eyes merits further investigation.

We were unable to find any statistical difference between these two groups of eyes during the WDT, indicating similar behavior of the choroidal bed in these two groups. Additionally, we observed a small increase in CT after water ingestion, indicating that CT variation alone is not enough to explain IOP elevations during the WDT.

REFERENCES

1. Jones D, Luensmann D. The prevalence and impact of high myopia. Eye Contact Lens. 2012;38(3):188-96.
2. Curtin B, Karlin D. Axial length measurements and fundus changes of the myopic eye. Am J Ophthalmol. 1971;71(1 Pt1):42-53.
3. Grossniklaus H, Green W. Pathologic findings in pathologic myopia. Retina. 1992;12(2): 127-33.
4. Takahashi A, Ito Y, Iguchi Y, Yasuma TR, Ishikawa K, Terasaki H. Axial length increases and related changes in highly myopic normal eyes with myopic complications in fellow eyes. Retina. 2012;32(1):127-33.
5. Flores-Moreno I, Lugo F, Duker JS, Ruiz-Moreno JM. The relationship between axial length and choroidal thickness in eyes with high myopia. Am J Ophthalmol. 2013;155(2): 314-9.
6. Guyer DR, Puliafito CA, Mones JM, Friedman E, Chang W, Verdooner SR. Digital indocyanine-green angiography in chorioretinal disorders. Ophthalmology. 1992;99(2): 287-91.
7. Coleman DJ, Silverman RH, Chabi A, Rondeau MJ, Shung KK, Cannata J, et al. High-resolution ultrasonic imaging of the posterior segment. Ophthalmology. 2004; 111(7):1344-51.
8. Spaide RF, Koizumi H, Pozzoni MC. Enhanced depth imaging spectral-domain optical coherence tomography. Am J Ophthalmol. 2008;146(4):496-500.
9. Branchini L, Regatieri CV, Flores-Moreno I, Baumann B, Fujimoto JG, Duker JS. Reproducibility of choroidal thickness measurements across three spectral domain optical coherence tomography systems. Ophthalmology. 2012;119(1):119-23.
10. Frankelson EN. The role of water test in evaluation of glaucoma control. Can J Ophthalmol. 1974;9(4):408-10.
11. Roth JA. Inadequate diagnostic value of the water-drinking test. Br J Ophthalmol. 1974; 58(1):55-61.
12. Brubaker RF. Importance of outflow facility. Int Glaucoma Rev. 2001;3:5.
13. Vasconcelos-Moraes CG, Susanna R Jr. Correlation between the water-drinking test and modified diurnal tension curve in untreated glaucomatous eyes. Clinics (São Paulo). 2008;63(4):433-6.
14. Susanna R Jr, Hatanaka M, Vessani RM, Pinheiro A, Morita C. Correlation of asymmetric glaucomatous visual field damage and water-drinking test response. Invest Ophthalmol Vis Sci. 2006;47(2):641-4.
15. Susanna R Jr, Vessani RM, Sakata L, Zacarias LC, Hatanaka M. The relation between intraocular pressure peak in the water drinking test and visual field progression in glaucoma. Br J Ophthalmol. 2005;89(10):1298-301.
16. Duijim HF, van den Berg TJ, Greve EL. A comparison of retinal and choroidal hemodynamics in patients with primary open-angle glaucoma and normal-pressure glaucoma. Am J Ophthalmol. 1997;123(5):644-56.
17. Cristini G, Cennamo G, Daponte P. Choroidal thickness in primary glaucoma. Ophthalmologica. 1991;202(2):81-5.
18. Spraul CW, Lang GE, Lang GK, Grossniklaus HE. Morphometric changes of the choriocapillaris and the choroidal vasculature in eyes with advanced glaucomatous changes. Vision Res. 2002;42(7):923-32.
19. Maul EA, Friedman DS, Chang DS, Boland MV, Ramulu PY, Jampel HD, et al. Choroidal thickness measured by spectral domain optical coherence tomography: factors affecting thickness in glaucoma patients. Ophthalmology. 2011;118(8):1571-9.
20. Mwanza JC, Hochberg JT, Banitt MR, Feuer WJ, Budenz DL. Lack of association between glaucoma and macular choroidal thickness measured with enhanced depth-imaging optical coherence tomography. Invest Ophthalmol Vis Sci. 2011;52(6):3430-5.
21. De Moraes CG, Reis AS, Cavalcante AF, Sano ME, Susanna R Jr. Choroidal expansion during the water drinking test. Graefes Arch Clin Exp Ophthalmol. 2009;247(3):385-9.
22. Arora KS, Jefferys JL, Maul EA, Quigley HA. Choroidal thickness change after water drinking is greater in angle closure than in open angle eyes. Invest Ophthalmol Vis Sci. 2012;53(1):6393-402.
23. Rosner B. Statistical methods in ophthalmology: an adjustment for the intraclass correlation between eyes. Biometrics 1982;38(1):105-14.
24. Murdoch IE, Morris SS, Cousens SN. People and eyes: statistical approaches in ophthalmology. Br J Ophthalmol. 1998;82(8):971-3.
25. Ikuno Y, Tano Y. Retinal and choroidal biometry in highly myopic eyes with spectral-domain optical coherence tomography. Invest Ophthalmol Vis Sci. 2009;50(8): 3876-80.
26. Fujiwara T, Imamura Y, Margolis R, Slakter JS, Spaide RF. Enhanced depth imaging optical coherence tomography of the choroid in highly myopic eyes. Am J Ophthalmol. 2009; 148(3):445-50.
27. Flores-Moreno I, Ruiz-Medrano J, Duker JS, Ruiz-Moreno JM. The relationship between retinal and choroidal thickness and visual acuity in highly myopic eyes. Br J Ophthalmol. 2013;97(8):1010-3. Comment in: Br J Ophthalmol. 2013;97(12):1613-4.
28. Danesh-Meyer HV. The water-drinking test: the elegance of simplicity. Clin Experiment Ophthalmol. 2008;36(4):301-3.
29. Brucculeri M, Hammel T, Harris A, Malinovsky V, Martin, B. Regulation of intraocular pressure after water drinking. J Glaucoma. 1999;8(2):111-6.
30. Campbell DA, Gloster J, Tonks EL. Some observations on the water-drinking test in glaucomatous and non-glaucomatous subjects. Br J Ophthalmol. 1955;39(4):193-203.
31. Galin MA, Mestre C, Nano H. The Water Provocative Test. Am J Ophthalmol. 1963;56: 554-61.
32. Spaeth GL. The water drinking test. indications that factors other than osmotic considerations are involved. Arch Ophthalmol. 1967;77(1):50-8.
33. Mansouri K, Medeiros FA, Marchase N, Tatham AJ, Auerbach D, Weinreb RN. Assessment of choroidal thickness and volume during the water drinking test by swept-source optical coherence tomography. Ophthalmology. 2013;120(12):2508-16.
34. Marcus MW, de Vries MM, Junoy Montolio FG, Jansonius NM. Myopia as a risk factor for open-angle glaucoma: a systematic review and meta-analysis. Ophthalmology. 2011;118(10):1989-94. Comment in: Ophthalmology. 2012;119(9):1941; author reply 1942.
35. Bonomi L, Mecca E, Massa F. Intraocular pressure in myopic anisometropia. Int Ophthalmol. 1982;5(3):145-8.