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Comparison of choroidal thickness in normal eyes and different ocular pathologies in a Brazilian population

Comparação da espessura de coroide em olhos normais e diferentes patologias oculares em uma população brasileira

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Abstract

***Objective**: To evaluate the choroidal thickness (CT) in healthy Brazilian subjects using spectral-domain optical coherence tomography (SD-OCT) and to compare with choroidal thickness measured in Brazilian patients with diabetic macular edema (DME), neovascular age-related macular degeneration (AMD) and high myopia. **Methods**: A retrospective analysis of spectral domain optical coherence tomography (SD-OCT) images of 181 Brazilian subjects. A total of 74 eyes were included in the normal control group, 50 eyes in the nvAMD group, 44 eyes in the DME group and 13 eyes in the high myopia group. CT was measured from the posterior edge of the retinal pigment epithelium (RPE) to the choroid/sclera junction at the fovea and at 500 µm intervals temporal and nasal to the fovea. All measurements were performed by two independent observers and were averaged for analysis. The statistical analysis and comparison were performed using Mann Whitney (unpaired t-test). **Results**: Seventy-four eyes from 74 patients with a mean age of 51.4 years were analyzed in the normal group with a mean nasal, subfoveal and temporal choroidal thickness measurements were 301.30 ± 12.86 µm, 311.61 ± 12.62 µm and 309.28 ± 12.28 µm respectively. All groups with disease demonstrated a statistically significant choroidal thinning when compared with matched-aged normal eyes. The mean reduction in the nvAMD group compared to normal were 60.65 µm nasally, 59.77 µm temporally and 56.59 µm at subfoveal position. In the DME group, the subfoveal reduction was 51.10 µm, 63.03 µm and 46.30 µm, nasally and temporally. The patients with high myopia presented the greatest reduction in CT compared to normal eyes, with a mean reduction of 159.9 nasal, 159.98 subfoveal and 154.65 at temporal. **Conclusions**: The present study evaluated choroidal thickness in Brazilian subjects, with intense miscegenation. The results demonstrated a statistically significant decrease of the choroidal thickness in all subtypes of chorioretinal disease. The small sample size in this study was a limitation. Additional research with a larger study population to better understand these findings.*

***Keywords**: Choroid; Diabetic retinopathy; Macular degeneration; Myopia; Tomography, optical coherence*

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Resumo

Objetivo: Avaliar a espessura da coróide (EC) de indivíduos brasileiros saudáveis utilizando tomografia de coerência ótica do domínio espectral (TCO-DE) e compará-la à espessura da coroide de pacientes brasileiros com edema macular diabético (EMD), degeneração macular neovascular relacionada à idade (DMRI) e miopia alta. **Metodologia:** Análise retrospectiva de imagens de tomografia de coerência ótica de domínio espectral (TOC-DE) de 181 indivíduos brasileiros. Um total de 74 olhos foram incluídos no grupo controle normal; 50, no grupo DMRI; 44, no grupo EMD; e 13, no grupo com miopia alta. A EC foi medida a partir da borda posterior do epitélio pigmentar da retina (EPR) até a junção coróide/esclera na fóvea e de intervalos de 500 µm, temporal e nasal, à fóvea. Todas as medidas foram realizadas por dois observadores independentes e as médias foram calculadas para análise. A análise estatística e a comparação das ECs foram realizadas usando o teste Mann Whitney (teste t não pareado). **Resultados:** Setenta e quatro olhos de 74 pacientes com idade média de 51,4 anos foram analisados no grupo normal, o qual apresentou espessura coróide nasal, subfoveal e temporal média igual a 301,30 ± 12,86 µm, 311,61 ± 12,62 µm e 309,28 ± 12,28 µm, respectivamente. Todos os grupos com doença demonstraram afinamento de coroide estatisticamente significativo quando comparados a olhos normais pareados por idade. A redução média de EC no grupo DMRI em comparação ao normal foi de 60,65 µm por via nasal, 59,77 µm por via temporal e 56,59 µm na posição subfoveal. O grupo EMD apresentou redução de EC igual a 51,10 µm em posição subfoveal, 63,03 µm por via nasal e 46,30 µm por via temporal. Pacientes com miopia alta apresentaram a maior redução de EC em relação aos olhos normais; os valores de redução média obtidos foram 159,9 por via nasal, 159,98 em posição subfoveal e 154,65 por via temporal.**Conclusões:** O presente estudo avaliou a espessura da coróide de indivíduos brasileiros com intensa miscigenação. Os resultados demonstraram reducção estatisticamente significativa da espessura da coróide em todos os subtipos de doença coriorretiniana. O pequeno tamanho da amostra foi uma limitação deste estudo. Pesquisas adicionais com população maior de estudo deveriam ser realizadas para ajudar a entender melhor esses achados.

Descritores: Coróide; Retinopatia diabética; Degeneração macular; Miopia; Tomografia de coerência óptica

Introduction

The choroid, which is part of the posterior uvea, is a vascular structure that extends from the margins of the optic nerve to the pars plana, where it becomes the ciliary body. [1] It is the major blood supply for the outer retina, specifically the photoreceptors, and prelaminar portion of the optic nerve head. These structures are supplied with choroidal blood flow, which has a high oxygen tension with an arterial/venous difference of 3%, compared to a difference of 38% in the retinal circulation.[1-3] The consequences of abnormal choroidal blood volume and compromised flow on the photoreceptors are unknown, but it could result in dysfunction and consequent visual impairment.[4]

The analysis of the choroid was unreliable due to its posterior location and the retinal pigmented epithelium cells that attenuate the light.[5] Evaluation of in vivo and real time of the choroidal structure became acceptable after the introduction of the spectral domain optical coherence tomography (SD-OCT).[6] The SD-OCT can detect reflected signals at a higher quality than ultrasound which was the previous equipment used to evaluate the choroid inaccurately.[7] With this technology it is possible to move the zero-delay line to a deeper position; this improves the image averaging and enhances the visualization of the choroid-sclera interface.[8, 9]

Previous reports demonstrated that choroidal thickness is modified in several diseases, such as diabetes mellitus (DM), age related macular degeneration (AMD), high myopia and central serous chorioretinopathy.[8, 10-13] The causes for choroidal thinning are multifactorial and dependent on the disease. For example, in diabetic retinopathy a choroidal vasculopathy induces CT changes, while in myopic patients CT thinning is secondary to stretching of the choroid.[4, 14] DM, nvAMD and high myopia were selected, as they are some of the most common causes of visual impairment in working-aged adults and the elderly population.[15-17] Previous reports about CT were based in subjects with little miscegenation, and the applicability of the results in Brazilian subjects, known to have a high degree of miscegenation, may not be reliable.[18]

The present study was designed to evaluate the choroidal thickness using SD-OCT in normal subjects and compare this to the CT in patients with DME, nvAMD and high myopia in a Brazilian population.

Methods

This was a retrospective analysis, conducted at the Federal University of São Paulo (UNIFESP) and at a private retina clinic, Brazil, and approved by the UNIFESP Institutional Review Boards (CEP 1365/2015). The study adhered to the tenets of the Declaration of Helsinki and informed consent was obtained from the subjects after explanation of the nature of the study. The statistical analysis and comparison were performed using Mann Whitney (unpaired t-test).

Subjects

A retrospective analysis was performed in OCT images of 181 Brazilian subjects who underwent OCT examination between July and December 2013. A total of 74 eyes were included in normal group, 50 eyes in the nvAMD group, 44 eyes in the DME group without retinal neovascularization and 13 eyes in high myopia group (defined as higher than negative 6.0 diopters). Only one eye of each patient with the best reproducibility regarding the eye disease were chosen.

The diagnoses of retinal diseases were based on Early Treatment Diabetic Retinopathy Study protocol for diabetic retinopathy; AREDS for exudative AMD and -6.00D was adopted as cut-off for high myopia.[19-21] The inclusion criteria were patients with no systemic or retinal diseases at the time of examination for the normal group, without any previous eye surgery or procedure.

Major exclusion criteria included the following: another ocular or systemic disease that could cause changes in choroidal thickness, previous treatment for DME or AMD, retinal laser therapy and previous pars plana vitrectomy.

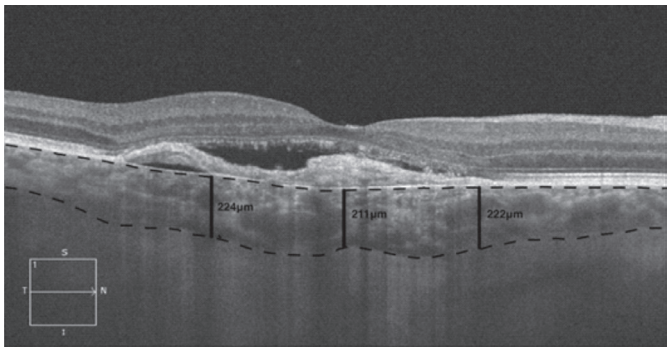


Figure 1: Spectral Domain OCT. Central choroidal thickness measurements from the outer edge of the hyperreflective retinal pigment epithelium (RPE) to the inner sclera at the fovea and at 500-µm intervals nasally and temporally

Choroidal Thickness Measurement

The SD-OCT scans were performed using HD-OCT (Cirrus™ HD-OCT, Carl Zeiss Meditec, Inc. Dublin CA, software version 5.2.1.12, model 4000). The scan pattern used on Cirrus HD-OCT was horizontal high-definition 5-line raster with 9 mm length and 0.25 mm distance between lines. To be included in this study, images had to be at least 6 out of 10 in intensity and taken as close to the fovea as possible. Using the Cirrus linear measurement tool, 2 independent observers measured CT perpendicularly from the outer edge of the hyperreflective retinal pigment epithelium (RPE) to the inner sclera at the fovea and 500 µm intervals temporal and nasal from the fovea (Figure 1).

Analysis

Data was expressed as means with the standard error of the mean. Statistical analyses were performed using Mann Whitney (unpaired t-test). A 95% confidence interval and a 5% level of significance were adopted. Therefore, the results with a P value < 0.05 were considered significant. All statistics were calculated using a paired t-test in Graph Pad Prism 5.0 software for Macintosh.

Results

A total of 181 eyes of 181 patients were included for analysis. The normal group included 74 eyes from 74 patients (46 female, 28 male) with a mean age of 51.4 years. The mean nasal, subfoveal and temporal choroidal thickness measurements were 301.30 ± 12.86 µm, 311.61 ± 12.62 µm and 309.28 ± 12.28 µm respectively.

The nvAMD included 50 eyes from 50 patients, with a mean age of 77.60 years (± 8.12), 72% of the sample were women (36 female, 14 male). The mean nasal, subfoveal and temporal choroidal thickness measurement were 192.30 µm (±10.28), 202.56 µm (±10.28), 204.12 µm (± 10.28) respectively. The nvAMD age matched randomized sample presented mean age of 72.85 years (± 7.07) and measures of 252.95 µm (±18.83) nasal, 259.15 µm (± 17.62) subfoveal and 263.89 µm (± 19.56) temporal. The mean difference between groups was 60.65 µm nasally, 59.77 µm temporally and 56.59 µm at subfoveal position with p <0,05 (Figure 3).

The DME group (44 eyes; 24 female and 20 male) had a mean age of 68.93 years (±10.99) against 65.02 years (± 9.39) of the randomized sample with normal eyes. Comparing the choroidal thickness, the subfoveal CT demonstrated a difference of 51.10 µm, with 230.45 µm (±11.37) in Group DME and 281.55 µm (±12.57) in the normal group. Nasal and temporal CT also presented differences, 63.03 µm and 46.30 µm respectively. All differences were statistically significant (p<0,05) (Figure 4).

In the high myopia group (13 eyes; 10 female and 3 male) the mean age was 53,15 years (±16,13), while randomized sample presented a mean age of 53,08 years (± 17,25). The OCT demonstrated CT measures of 140.61 µm (± 18.51), 150.69 µm (±17.63) and 157.46 µm (±19.46), nasal, subfoveal and temporal, respectively. The normal group presented CT 300.51µm (±12.92) nasal, 310.67 µm (±12.57) subfoveal and 312.10 µm (±12.82) temporal. The difference was statistically significant: 159.9 nasal, 159.98

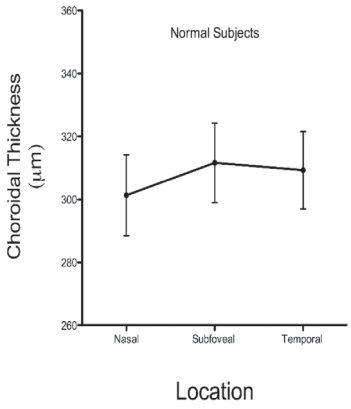


Figure 2. Graph of choroidal thickness in normal subjects. Mean choroidal thickness at the fovea and at 500-µm intervals nasally and temporally.

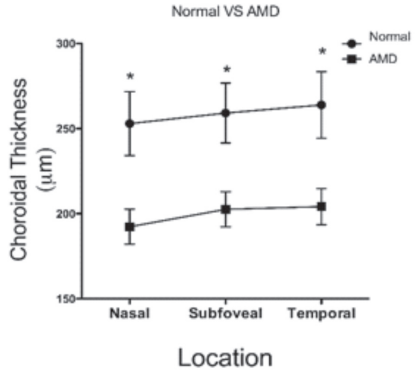
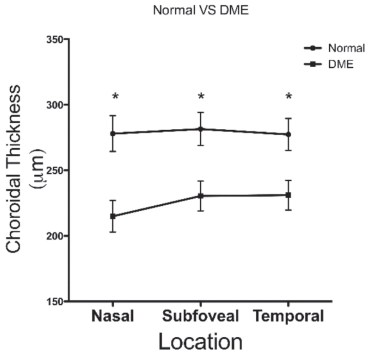


Figure 3: Graph of choroidal thickness in the neovascular age-related macular degeneration group compared to age matched normal eyes. Mean choroidal thickness at fovea and at 500-µm intervals nasally and temporally.

Figure 4: Graph of choroidal thickness in the diabetic macular edema group compared to age matched normal eyes. Mean choroidal thickness at fovea and at 500-µm intervals nasally and temporally.



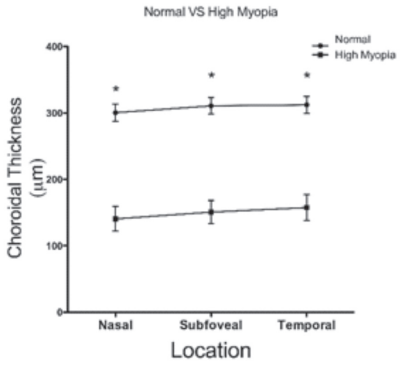


Figure 5: Graph of choroidal thickness in the high myopia group compared to age matched normal eyes. Mean choroidal thickness at fovea and 500-µm intervals nasally and temporally.

subfoveal and 154.65 temporal (Figure 5).

Discussion

Historically, choroidal analysis has been based on histological examinations and the ability to image and assess the choroid with SD-OCT became an exciting alternative.[9, 22] The choroid plays a vital role for eye physiology and provides metabolic support to the outer retina, including the photoreceptors and the prelaminar portion of the optic nerve head.[2, 3]

The Brazilian population sampled in this study is of great importance due to its intense ethnical miscegenation. (18). The results suggested a mean normal choroidal thickness of 301.30 ± 12.86 µm nasally, 311.61 ± 12.62 µm subfoveally and 309.28 ± 12.28 µm temporally for Brazilian subjects, which was similar to other studies in non-Brazilians.[9,23] In a Thailand study with 144 healthy patients, the mean foveal CT was 282.4 ± 13.8 µm, demonstrating that different nationality had a role in CT.[24]

It was well noted that choroidal thinning occurs as we age, there is approximate decrease in CT of 15-25 µm per decade. [23, 25, 26] The sex could also influence in the choroidal thickness, with age and axial length paired the subfoveal choroid was 99.16 µm thicker in men. [26] In this study the groups were not paired by age or sex, which could be a confounding factor to the measure.

AMD is the leading cause of blindness in elderly people (>60 years), becoming a public health problem since world is aging rapidly.(16) AMD manifests in early stages with drusen and pigmentary changes while severe cases manifest either as neovascularization (wet AMD) or geographic atrophy (dry AMD) and choroidal circulation have been hypothesized to contribute to the development of AMD.[8, 20, 27]

Choroidal thickness seems to be unaffected by the early AMD despite an inverse correlation between the drusen area and choroidal thickness, thinner choroid tended to have greater drusen load.[27,28]The present study demonstrated a choroidal thinning in subjects with neovascular AMD compared to age-matched control eyes in all measured points. This was consistent with findings from previous studies which demonstrated a choroidal thinning in patients with both advanced dry and wet AMD.[8, 13, 29-31]

Diabetic retinopathy (DR) affects more than 90.000.000 people worldwide and is the leading cause of vision loss and blindness in working-aged adults.[15] Choroidal vasculopathy is involved in the pathogenesis of DR. Pathologic findings in the choroid of diabetic patients demonstrated blood vessels tortuosity, focal vascular dilatation and narrowing, hypercellularity, vascular loops, microaneurysm formation, areas of nonperfusion and sinus like structure formation between the choroidal lobules.[32, 33] In our study, the choroid in the DME group was thinner compared to age-matched normal subjects. This supports previous reports and reinforces the hypothesis that there is an obstruction of the choriocapillaris, vascular degeneration and decreased choroidal blood flow due to diabetic choroidal vasculopathy. [11, 34-36] Other studies in different populations agrees with this finding.[26, 37]

Myopia is the most common refractive error of the eye and affects 1.5 billion people worldwide.[17] The prevalence is rising dramatically reaching almost 80% of East Asian population, while in United States prevalence of high myopia (defined as SE-6.00 or more) raised eight times in the last 30 years.[10, 17] High myopia is accompanied by pathological structural changes, such as axial elongation of the globe, thinning and stretching of retina and choroid.[8, 14] Previous reports demonstrated the association between decreased subfoveal CT and visual acuity impairment, which is justified by abnormal metabolic support to photoreceptors.[8, 10, 14] Another important cause of vision loss in myopic patients is choroidal neovascularization, which is strongly related to the thinner choroids.[14] Our results, demonstrated a thinner choroid in high myopia group when compared to normal eyes, confirming the structures changes and the risk of visual loss in those patients.

The subfoveal choroidal thickness in different ethnicities paired by age, refraction error and axial length is not significant. [7] This study had similar findings to others despite the different age and population, confirming the thinner choroid in these ocular diseases. [10, 13, 14, 27, 37]

In conclusion, this study reported the normal choroidal thickness in a Brazilian population, which can be used in future studies. Additionally, there was choroidal thinning in three important chorioretinal diseases: diabetic macular edema, neovascular age related macular degeneration and high myopia. The small sample size in this study was a limitation, although choroidal abnormality may play an important role in visual prognosis in these diseases; further studies will be necessary to differentiate between cause and consequence.

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