Saudi Journal of Ophthalmology (2016) 30, 9–13

Original Article

Choroidal thickness profile in Retinitis Pigmentosa – Correlation with outer retinal structures

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Abstract

Purpose: To compare the choroidal thickness (CT) of subjects with Retinitis Pigmentosa (RP) with age-matched healthy subjects and to correlate the visual acuity with retinal parameters including central macular thickness (CMT), inner segment/outer segment junction (IS/OS junction) integrity, external limiting membrane (ELM) integrity and choroidal thickness in subjects with RP.
Methods: Eighty-eight eyes (69 patients) with typical RP and 188 eyes of 104 healthy subjects were enrolled between September 2012 and January 2013.
All subjects underwent a comprehensive ocular examination including choroidal imaging using enhanced depth imaging with spectral domain optical coherence tomography. Outcome measures were CT difference between RP and age-matched healthy subjects; and correlation of various factors such CMT, IS/OS junction integrity, ELM integrity, and CT with visual acuity.
Results: Among RP subjects, mean age was 31.39 ± 13.4 years with a mean BCVA of 0.99 ± 0.94 logMAR. Mean spherical equivalent was −0.6 ± 1.6D. Mean CMT was 148.48 ± 119 μm. Mean subfoveal CT was 296.9 ± 72 μm. Mean IS/OS and ELM integrity was 42.2 ± 46.6% and 43.75 ± 45.7%, respectively. The mean age was 40.0 ± 13.5 years with a mean spherical equivalent of 0.18 ± 0.6D for the normal age-matched healthy group. Mean subfoveal CT was 283.1 ± 47.8 μm.
CT at various locations in patients of various ages in the RP group did not show any statistical significant difference ($P = \gg 0.05$) in comparison with age-matched healthy subjects. On multivariate regression, ELM percentage integrity had the strongest association with best corrected visual acuity, followed by IS/OS junction percentage integrity. Subfoveal choroidal thickness had very weak correlation with visual acuity as well other retinal parameters.
There was a significant difference in the outer retinal structure integrity ($p = 0.002$) and CMT ($p = 0.02$) between the eyes with good (⩾20/200) and poor vision (<20/200), but not in subfoveal choroidal thickness ($p = 0.3$).
Conclusions: Our study results did not show any significant difference in choroidal thickness between subjects with RP and age-matched healthy subjects. Choroidal thickness correlated better with the age but not with the vision or outer retinal structures in eyes with RP. Outer retinal structure integrity and CMT had a better correlation with visual acuity.

Keywords: Choroidal thickness, Retinitis Pigmentosa, RP, IS/OS junction, ELM junction

http://dx.doi.org/10.1016/j.sjopt.2015.09.003

Introduction

Retinitis Pigmentosa (RP) is the most common inherited retinal dystrophy. It starts with nyctalopia and progressively leads to profound visual field loss. The prevalence of RP is 1 in 3000–5000 individuals.[1,2] Sen et al. reported very high prevalence in India including approximately 1 in 930 persons in urban populations and 1 in 372 in rural areas.[3]

Received 10 November 2014; received in revised form 12 August 2015; accepted 14 September 2015; available online 25 September 2015.

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Peer review under responsibility of Saudi Ophthalmological Society, King Saud University

Production and hosting by Elsevier

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RP is characterized by degeneration of retinal pigment epithelium (RPE), attenuation of retinal vessels, loss of photoreceptors, sclerosis, and atrophy of the choriocapillaris, leading to localized areas of clinically visible chorioretinal atrophy and, consequently, a dramatic reduction in visual function.[4,5]

It has been hypothesized and partly proven that there is a primary vascular dysfunction and increased endothelin (ET-1) level in RP patients which ultimately leads to reduced choroidal as well as retinal blood flow.[6] Relative choroidal ischemia is increased in severely visually impaired eyes with RP.[7] Falsini et al. reported a relationship between the choroidal blood flow and reduced focal electroretinography responses.[8] Compromised choroidal circulation leads to choriocapillaris atrophy and eventually damage to photoreceptors.

Measurements of choroidal thickness in RP patients could be very useful for future therapies, such as suprachoroidal electrode arrays, to calculate the distance between the implant and the ganglion cell layer. Thus, a greater understanding of the choroid in diseased eyes is needed.[9]

Evaluation of the choroid is required to understand the pathogenesis of RP. With the help of enhanced depth imaging, changes in choroidal thickness have been reported in various retinal diseases. Previous studies on choroidal thickness have shown a decrease in choroidal thickness in eyes with RP and no correlation between the choroidal thickness and visual acuity in other inherited retinal dystrophies.[10,11] Correlation between visual acuity and photoreceptor damage has been shown in RP as well as various retinal dystrophies and retinal diseases.[12–16]

Dhoot et al. hypothesized that the poor choroidal blood flow leads to thinning of the choroid, which leads to photoreceptor damage.[10] Therefore, correlation between the photoreceptor status, visual acuity and choroidal thickness should be analyzed. Available literature on choroidal thickness in RP includes small case series with poor distribution of subjects in various age groups. None of the previous studies have correlated outer retinal structures status with choroidal thickness.

The aim of this study is to compare choroidal thickness between subjects with RP and age-matched healthy subjects and to correlate visual acuity with retinal parameters including central macular thickness (CMT), inner segment/outer segment junction (IS/OS junction) integrity, external limiting membrane (ELM) integrity and choroidal thickness in subjects with RP.

Methods

This prospective observational study was performed at the L.V. Prasad Eye Institute in India from September 2012 to January 2013. Prior approval from the Institutional Review Board was obtained and informed consent was obtained from each study subject. This study was conducted in accordance with the tenets of the Declaration of Helsinki.

Eighty-eight eyes (69 patients) with a diagnosis of typical RP were included in this study. All participants underwent a comprehensive ophthalmic examination including best-corrected visual acuity (BCVA) testing using early treatment diabetic retinopathy study (ETDRS) charts, slit-lamp biomicroscopy, intraocular pressure (IOP) measurement using Goldmann applanation tonometer and a dilated fundoscopic examination. All patients underwent electroretinography and Humphery visual field testing to confirm the diagnosis of RP. Typical RP was diagnosed as the presence of clinical findings such as arteriolar attenuation, midperipheral retinal hyperpigmentation (bone spicules), and atrophy of the RPE in the mid periphery of the retina.

Exclusion criteria included optic atrophy associated with RP, visually significant cataract, high myopia or hyperopia (greater than −6 or +3 diopters of refractive error), poor image quality, any other associated retinal pathology, or history of any intraocular surgery. Control group included healthy subjects with no ocular disease and without high refractive power (more than −6D or +3D).

Choroidal imaging

The spectral domain optical coherence tomography (SD-OCT) scans were obtained by using Cirrus HD-OCT (Carl Zeiss Meditec, Inc., Dublin, CA.) after dilatation of the pupil with 1% Tropicamide and 10% Phenylephrine eye drops. The scan used for imaging in this study is HD 1-line raster with enhanced depth imaging which is a 6-mm line consisting of 4096 A-scans, with an imaging speed of 27,000 A-scans per second, an axial resolution of 5 μm, a transverse resolution of 15 μm in tissue and an average of 20 frames (B-scans). Enhanced depth imaging, which automatically sets the choroid closer to the zero-delay line and thus theoretically provides better visualization of the choroidal/scleral interface, was used for all scans. Scans with a signal strength of greater or equal to 6 were used for analysis.

Image analysis

Choroidal thickness measurement: Using the Cirrus linear measurement tool, a single observer measured choroidal thickness perpendicularly from the outer portion of the hyperreflective line, corresponding to the retinal pigment epithelium, to the inner surface of the sclera at 500 μm intervals temporal and nasal from the fovea, up to 2500 μm as published in the literature.[17] Intraclass correlation coefficient for intra-observer reproducibility was 0.97.

Outer retinal structure analysis: For IS/OS and ELM integrity calculation, a previously described technique was used.[13] IS/OS and ELM integrity was calculated as the percentage integrity for the central 1000 μm (500 μm on both sides of the fovea) for both horizontal and vertical scans.[13] The average of both scans was considered for analysis.

Statistical analysis

Descriptive statistics included mean and standard deviation for continuous variables. As both eyes of most subjects were included for analysis, the correlation between the two eyes of the same subject was adjusted using generalized estimating equations (GEE) during the calculation of summary descriptive parameters. Multivariate models adjusted using GEE methods were fit to assess the effects of age, gender, spherical equivalent and macular thickness on the CT measurements. Statistical analyses were performed using MedCalc for Windows, version 12.5 (MedCalc Software, Ostend, Belgium). The alpha level (type I error) was set at 0.05. All the graphs were made using GraphPad Prism (GraphPad