Correlation of Central Corneal Thickness and Optic Disk Coherence Tomography in Patient with Open-Angle Glaucoma Secondary to Exfoliation Syndrome

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Abstract: Purpose and Background: Pseudo exfoliation syndrome (XFS) is considered to be the most common identifiable cause of open-angle glaucoma worldwide. Whereas the structural variation very soon display than functional variation, so this study designed to evaluate the correlation between structural variation in optic nerve and central cornel thickness (CCT) in patient with XFS and decide to quick diagnose and better elaborate treatment results. **Methods and Material:** 50 eye from 50 patient with definite exfoliation syndrome (XFS) evaluate under optic disc optical coherence tomography (OCT) and corneal Ultrasound pachymetry.Patıent dıvıded two subgroups: first group patıent wıth CCT>540 and secound groups wıth CCT≤540.Also 50 eye from 50normal groupapartıcıpıate ın thıs study wıth respect to ınclusıon and exclusion crıterıa. **Results:** Mean of CCT in XFS group was 504/5±4/6 µm and in control group was 526/3±2/8 µm compare the mean difference between two groups was statistically significant (P=0/032).However there was not any correlation between optic disc Stereo-metric OCT parameter and intraocular pressure with CCT in all parameter (P>0/05). **Conclusion:** Despite to thinner CCT in patient with XFS than to control group in this study، there was not any correlation between optic disc stereo-metric OCT parameter and intraocular pressure to CCT in XFS groups and divided subgroups according to CCT.
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1. Introduction

Pseudo exfoliation syndrome (PEX) is a common age-related disorder of the extracellular matrix that is frequently associated with severe chronic secondary open-angle glaucoma and cataract. PEX syndrome may affect up to 30% of people older than 60 in a worldwide distribution and is biomicroscopically diagnosed by abnormal fibrillar deposits on ocular structures that line the aqueous-bathed surfaces of the anterior segment. PEX syndrome is currently the most important and common single identifiable risk factor for open-angle glaucoma.

Most of the recent evidence presented suggests that PEX is in fact fibrillinopathy, however the exact pathogenesis of this syndrome is unknown. PEX Syndrome Occur in all geographic region worldwide with reported prevalence rates averaging approximately 10% to 20% of the general population over age 60.

Pex in female is common than male but the prevalence of glaucoma related to syndrome occur equally in two groups(Schlötzer-Schrehardt and Naumann, 2006).

Optical coherence tomography (OCT) is a high-resolution noncontact imaging modality. The ocular application of this technology provides quantitative measurements of the macular retinal thickness, peripapillary nerve fiber layer (NFL) thickness and topographical measurements of the optic nerve head (ONH). Cross-sectional studies have shown that measurements obtained from each of these regions can be used to differentiate between normal and glaucomatous eyes. Identification of structural optic nerve damage is important in the diagnosis and treatment of glaucoma and in monitoring its clinical course. Variability in the size and appearance of the optic disk of normal eyes complicates the detection of early glaucomatous optic nerve damage. Standard techniques to diagnose and monitor structural change in glaucoma have included serial stereoscopic photographs of the optic disk and monochromatic photographs of the RNFL. While these methods provide objective information for comparisons, the interpretation of photographs remains subjective, and variation in photographic assessment among even experienced observers is well documented.

Furthermore, qualitative assessment of photographs may not be sensitive to small changes over time. OCT can produce stereo-metric image of optic disk divided in two subgroups: Scan image and composite image. prameter related to scan image include: Rime area, average nerve width, cup diameter

and horizontal rim length. And the results related to composite image include consist of: Vertical and horizontal integrated rim area ، cup area, cup/disk area ratio, cup/disk horizontal area (Jaffe and Caprioli, 2004).

Recent studies on central corneal thickness (CCT) and its impact on applanation tonometry have shown that CCT does affect the accuracy of the IOP reading, with thinner corneas giving a falsely low reading, whereas thicker corneas yield a falsely high reading. This has prompted the development of correction factors and algorithms that attempt to adjust the applanation IOP based on deviation from a mean or normal CCT (Brandt, 2004).

According to the result of ocular hypertension treatment study(OHTS)subject with corneal thickness of 555μm or less had a threefold greater risk for development of primary open angle glaucoma (POAG)compare with participants who had a corneal thickness of more than 588 μm. whetear this increase risk of glaucoma due to underestimating actual IOP in patient with thinner corneas or whether thin cornea are a risk factor independent of IOP measurement has not been completely determined, but the OHTS found CCT to be a risk factor for progression independent of IOP level(Coleman, 2004).

Diagnosis of glaucoma on the basis of visual filed test may be associated with large ganglion cell death. Even if 50% of this cell death occurred but we don't any visual filed defect. However, assessment precocious disorders are very soon possible with respect new structural methods such as OCT (Kaushik, 2006; Sommer, 1991).

In overview of texts we didn't find any study to assessment correlation of central Corneal thickness in Patient with Open-Angle Glaucoma Secondary to Exfoliation Syndrome.

Hence to prevalence PEX glaucoma and ability of structural methods to early and meticulous evaluation of glaucoma and notability of CCT as a great risk factor we designed this study to further judgment this risk factor in commonest form of secondary open angle glaucoma. Affirm of this correlation can guide ophthalmologist to better diagnosis and lead us to precision evaluation of treatment result.

2. Material and Methods

According to the result of Sushmita and et al and with utilize this formula:

$$50 = n = \frac{4(Z_{1-\frac{\alpha}{2}} + Z_{1-\beta})^2}{(Ln\frac{1+r}{1-r} - Ln\frac{1+\rho}{1-\rho})^2} + 3$$

$Z_{1-\alpha/2}=1.96$
$Z_{1-\beta}=1.28$
$P=0.53$ $r= 0.15$

Fifty patients with medically controlled secondary open-angle glaucoma which attended the patients clinic of Tabriz, Nikookari Ophthalmic Center were included in this study. Patients with pseudoexfoliative glaucoma had gonioscopically open angle and fulfilled at least two of the following criteria: characteristic glaucomatous visual field defects, glaucomatous optic neuropathy, and /or IOP > 21 mmHg. The IOP measurement was > 21mmHg on at least three occasions. The selected patients were classified into:Group I: included with a thick CCT (≥ 540 μm); group II: included with a thin CCT (< 540 μm).

Each patient underwent a comprehensive ophthalmologic examination, including review of medical history, best-corrected visual acuity, slit-lamp biomicroscopy, IOP measurement using Goldmann applanation tonometry, gonioscopy, automated perimetry using Humphrey 24–2 visual field analyzer, CCT measurement using ultrasonic pachymetry, and optic nerve head OCT using Circus-SD OCT, Carl Zeiss Med Inc.Model 4000.

Inclusion criteria:

Inclusion criteria included age ≥ 40 years; best-corrected visual acuity not worse than log MAR 0.4, spherical refractive errors ≤ ±5.00 and cylinder ≤ ±3.00 diopters, reliable Humphrey visual fields, and good image quality with HRT.

Exclusion criteria:

Exclusion criteria were: concomitant corneal or retinal diseases, systemic diseases known to affect the visual field, contact lens wear (should not have been worn for at least 3 week before examination), history of intraocular surgery, others causes of glaucoma (including pigment dispersion glaucoma, iridocyclitis, and trauma), and retinal laser procedures (including panretinal photocoagulation).

We also select 50 normal eyes of 50 subjects with respect to all above criteria to compare of CCT measurement results.

Optic nerve head OCT evaluation:

Optic nerve head OCT was imaged with Circus-SD OCT. The tomography image was computed from the three dimensional image, then the contour line was drawn at the inner edge of the scleral ring. The reference plane was automatically determined parallel to the peripapillary retinal surface and located 50 μm under the retinal surface at the contour line and on the papillomacular bundle (350° to 356°). Patients whose

OCT images had a standard quality>5 were included for final analysis. The optic nerve head parameters measured by OCT and used in our study were rim are, cup area, inferior average of nerve fiber layer thickness, superior average of nerve fiber layer thickness and average of nerve fiber layer thickness.

Central corneal thickness evaluation:

Central corneal thickness (CCT) was measured with ultrasonic pachymetry (Sonoscan, model 4000 AP). The pachymetry measurement recorded for each eye separately was the mean of three measurements.

Statistical analysis:

This study was a cross-sectional study and values were recorded as mean±SD. This was done using SPSS program (standard version 16). Normalized distribution of values was determined using k-s test. stratified by CCT values and normal subjects. The Pearson's correlation coefficient was used to determine the correlation between CCT and RNFL measurements as well as CCT and ONH measurements in both groups of patients.

The results were considered significant at P <0.05.

3. Results

The study included 50 eyes of 50 patients with medically controlled SOAG(PEX Glaucoma). The range of age was more than 40 year old. Patients were divided to thick group or to thin group based on their median central corneal thickness (CCT). Data of 50 patients with XFG (Exfoliative glaucoma) and 50 normal controls were computed.

Table 1 shows the mean CCT in XFG (Exfoliative glaucoma) and normal subjects. The mean CCT of the OHT group was significantly lower than that of the normal group (P = 0.032)

Table 2:Correlation coefficients between CCT and optic nerve head parameters by OCT

Group	CCT (µm) Mean ±SD	Mean Difference XFG vs Normal's	P Value
XFG	504±4	504±11	0.032
Normal subject	526±2		

Table 2 shows the correlation coefficients regarding relationship to CCT. Regarding optic nerve head parameters by OCT, there was not statistically significant correlation between CCT and optic disk parameters.

Table 2: Correlation coefficients between CCT and optic nerve head parameters by OCT

OCT parameters	RFNL		CUP Area		Rim Area	
	P	r	P	r	P	R
CCT	0.44	0.1	0.6	0.06	0.8	0.02

RNFL= average of nerve fiber layer thickness, r=Pearson correlation coefficient, P=P Value

Table 3 shows mean and mean difference in XFG OCT parameters divided to thin and thick cornea there was also not statistically significant correlation between CCT and optic disk parameters in two subgroups.

Table3: OCT Parameter in XFG Stratified by Central Corneal Thickness (CCT)

OCT Parameter	CCT	Mean ±SD	Mean Difference ± SD	P
RNFL	≤540	69±22	1±7	0.8
	>540	67±20		
CUP Area	≤540	1.4±0.7	0.04±0.2	0.8
	>540	1.4±0.6		
Rim Area	≤540	1±0.6	0.05±0.1	0.7
	>540	0.9±0.5		

Table 4 shows mean and mean IOP difference in XFG divided to thin and thick cornea there also was not statistically significant correlation between IOP and CCT divided in two subgroups.

Table4: IOP average in XFG Stratified by Central Corneal Thickness (CCT)

	CCT	Mean ±SD	Mean Difference±SD	P Value
IOP average	≤540	185±29	3±11	0.7
	>540	154±51		

4. Discussions

Glaucoma is a progressive optic neuropathy in which morphological changes that occur at the optic nerve head and retinal nerve fiber layer are associated with functional deficit. Examining and monitoring the optic nerve head and the RNFL, structurally and functionally, is important for diagnosis and treatment. Apart from the topographical aspect, the relation between structural damage and functional damage also has a quantitative aspect (5).

The OCT measures the peripapillary RNFL thickness in many locations around the optic disk, but studies have demonstrated that the mean RNFL thickness, inferior RNFL thickness, followed by the superior RNFL thickness are the best discriminators for glaucoma in that order.(Sommer, 1991; Wollstein, 2005; Budenz, 2005; Leung, 2005).In this study we use mean RNFL thickness to measurement.

The ocular hypertension treatment study (OHTS) is multicenter randomized clinical trial to evaluate the safety and efficacy of topical ocular hypotensive medication in delaying or preventing the onset of visual

field loss and/or optic nerve damage in ocular hypertensive individuals at moderate risk for developing primary open-angle glaucoma. Baseline factors predictive of which OHTS participants developed POAG included CCT, cup/disk ratio, age, IOP, and pattern standard deviation. Central corneal thickness was a potent predictive factor for the development of POAG, with each 40μm reduction of CCT below the average of 572 μm conferring a 71% increased risk over a mean follow-up of 72 months. Although alternative hypotheses can be considered, we believe that much of the effect of CCT on glaucoma risk comes from its influence on Goldman applanation tonometry(Gordon, 2002).

In patients with thin central cornea, the vasculature has become more damaged due to repetitive movements of the more complaint lamina. Subsequently, it may be less able to respond to IOP reduction with a beneficial increase in blood flow. Laminar sheet compression is common in glaucoma. These suggest an interrelationship between the topographic and vascular properties of the optic nerve head(Herndon, 2004).

In addition, thin CCT was associated with increased cup/disc ratio. This finding in agreement with Herndon who found that, for an increase of 10 μm of CCT, the vertical cup-disc ratio decreased by 0.008, and the horizontal cup-disc ratio decreased by 0.007(Lesk, 2006).

In the present study, there was not a significant correlation between thin CCT and optic disc OCT parameters. However means CCT in-patient with XFG was thinner significantly than normal subject. This finding in agreement with this theory that CCT is an independent risk factor for glaucoma progression. In addition, we must be noted CCT mostly in evaluation of XFG. Low CCT in XFG patient especially has clinical as well as statistical significance, since a patient's glaucoma risk assessment may be directly affected by this decrease.

Unfortunately in the review of literature we didn't find any study to assessment CCT in XFG to compare result.

In a major review performed by Michal and classmate mean CCT was 534μm (Doughty and Zaman, 2004).this very similar to normal subject of our study and thicker than XFG in our study. In Barbados study the mean CCT was 545 μm (Nemesure, 2003).All of finding support that XFG patient has thin CCT and this is may be responsible for high prevalence of glaucoma in XFS. The main point we must be adjust IOP versus to CCT. The Early Manifest Glaucoma Trial demonstrated that glaucoma progression was lessened by 10% for every millimeter of mercury decrease in IOP, so adjusting IOP for decreased CCT may in fact alter glaucoma patient's risk profile for progression (Jonas, 2006).Thus, central corneal thickness was a strong predictive factor for the development of XFG, ever after adjusting for the effect of baseline age, IOP, cup/disc ratio, and visual field indices.

As noted above, we must be inclusive effect of CCT on measured IOP response to medication extends into the range of CCTs commonly encountered in clinical practice.

Using a biomechanical model of the cornea, the simulation results indicated that differences in corneal biomechanics across individuals may have greater impact on IOP measurement errors than CCT, and that if the material properties of the cornea were kept constant, variations in CCT would have the potential to produce errors of magnitudes of 2–3 mmHg from true IOP, while variations in biomechanical properties may result in IOP measurement errors up to 17 mmHg .In other words, it is likely that two eyes with the same true IOP and CCT but different corneal biomechanics (e.g. stiffness) give different IOP readings, and this is likely to represent one of the main reasons for which no linear correction formula is applicable if only CCT is introduced in the model to adjust the IOP reading(Liu and Roberts, 2005). This preface may be justify that why in our patient we can't establish significant correlation between IOP and CCT.IOP may be influenced under confounding factor such as corneal biomechanic.

Conclusion:

CCT is a significant predictor independent of glaucomatous damage and measuring CCT in glaucoma patients my help identify those patients who are at high risk for developing severe glaucomatous sequelae, thus enabling the ophthalmologist to treat their disease early.

It is important to understand how the information about CCT should be integrated in the clinical management of both ocular hypertension (OHT) and glaucoma and whether other ocular properties should be measured to better understand the individual risk profile.

We suggest further study to measurement of CCT with respect to biomechanical effect of cornea and adjusting IOP on CCT foundation.

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