Med & Health 2011; 6(2): 107-113

ORIGINAL ARTICLE

Relationship between Central Corneal Thickness and Severity of Open Angle Glaucoma using Optical Coherence Tomography

Mushawiahti M[1], Syed Zulkifli SZ[2], Aida Zairani MZ[1], Faridah H[1]

[1]*Department of Ophthalmology, Faculty of Medicine, Universiti Kebangsaan Malaysia Medical Centre, Jalan Yaacob Latif, Bandar Tun Razak, 56000 Cheras, Kuala Lumpur*
[2]*Deans and Director's Office, Faculty of Medicine, Universiti Kebangsaan Malaysia Medical Centre*

ABSTRAK

Ketebalan kornea memainkan peranan penting dalam merawat pesakit glaukoma. Tujuan kajian in adalah untuk mengenalpasti hubungan di antara ketebalan tengah kornea dengan ukuran ketebalan lapisan saraf retina bagi pesakit glaukoma sudut terbuka (glaukoma bertekanan rendah dan glaukoma bertekanan tinggi). Ini adalah kajian pemerhatian dibuat ke atas pesakit di Pusat Perubatan Universiti Kebangsaan Malaysia dan melibatkan seramai 190 mata (190 pesakit). Pesakit adalah terdiri daripada 60 orang pesakit glaukoma bertekanan rendah, 61 pesakit glaukoma bertekanan tinggi dan seramai 69 pesakit normal yang digunakan sebagai kontrol. Pesakit-pesakit ini dikenalpasti berdasarkan kerosakan luas pandangan yang bercirikan glaukoma dan melalui catatan rekod tekanan mata sebelum rawatan dimulakan. Ketajaman penglihatan diuji. Ketebalan pusat kornea diukur menggunakan mikroskop spekular.Ukuran ketebalan lapisan saraf retina dibuat menggunakan 'optical coherence tomography. 'Keputusan kajian menunjukkan pesakit glaukoma bertekanan rendah didapati memiliki perbezaan ketebalan pusat kornea (503.07um±32.27) yang ketara, berbanding dengan kumpulan control, 517.45±31.74 (p=0.012). Manakala perbezaan ketebalan kornea adalah tidak ketara bagi pesakit glaucoma bertekanan rendah dibandingkan dengan pesakit glaukoma bertekanan tinggi.(p=0.386). Ukuran ketebalan lapisan saraf retina dan pengukuran urat mata menunjukkan perbezaan yang ketara diantara pesakit glaukoma susut terbuka dan kumpulan kontrol. Terdapat korelasi yang ketara di antara ketebalan purata lapisan saraf retina dan ketebalan saraf di bahagian atas dengan ketebalan pusat kornea bagi pesakit glaukoma bertekanan tinggi (r=0.251,0.401) tetapi tidak bagi pesakit glaukoma bertekanan rendah. Kesimpulan kajian ini menunjukkan korelasi ketara bagi ketebalan pusat kornea dengan purata ketebalan lapisan saraf retina dan ketebalan saraf di bahagian atas ('superior quadrant') bagi pesakit glaukoma bertekanan tinggi. Korelasi yang serupa tidak ditemui bagi pesakit glaukoma bertekanan rendah.

Kata kunci: glaukoma sudut terbuka, retina, kornea, optikal koheren tomografi

Address for correspondence and reprint requests: Dr Mushawiahti Mustapha, Department of Ophthalmology, Faculty of Medicine, Universiti Kebangsaan Malaysia Medical Centre, Jalan Yaacob Latif, Bandar Tun Razak, 56000 Cheras, Kuala Lumpur. Tel: +603-91455981 Fax: +60391737836 Email: drmusha@yahoo.com/ drmusha@gmail.com

ABSTRACT

Central corneal thickness plays a major role in the management of many types of glaucoma. Therefore, our aim is to determine the relationship between the severity of glaucoma measured by optical coherence tomography (OCT) and central corneal thickness (CCT) among normal tension and high tension glaucoma patients. This is an observational cross sectional study on 190 patients carried out in Universiti Kebangsaan Malaysia Medical Centre (UKMMC). Three groups of patients were identified; 60 normal tension glaucoma (NTG), 61 primary open angle glaucoma (POAG) and 69 control. Patients were identified based on the glaucomatous visual field changes and previous record of intraocular pressure before treatment. Visual acuity and intraocular pressure measurements were recorded. Specular microscope was used to measure the CCT and the severity of glaucoma was evaluated objectively based on the retinal nerve fibre layer (RNFL) thickness using optical coherence tomography. Results showed NTG patients had significantly thinner cornea, 503.07±32.27µm compared to the control group, 517.45±31.74 µm ($p=0.012$). However, there was no significant difference between the CCT of POAG and NTG groups ($p=0.386$).Retinal nerve fibre layer (RNFL) thickness was significantly different between the glaucoma and the control groups ($p<0.05$ in all quadrant). However, correlation between CCT and severity of RNFL thinning was only found for the POAG group but not for the NTG group. (mean RNFL and superior quadrant RNFL; $r=0.251,0.401$) . This study demonstrated the correlation between CCT and severity of glaucoma in POAG patients but not for the NTG group. Therefore, CCT is related to the severity of POAG-related visual loss.

Key words: open angle glaucoma, retina, cornea, optical coherence tomography

INTRODUCTION

Central corneal thickness plays a major role in the management of many types of glaucoma. Ocular hypertensive (OHT) studies (Kass et al. 2002, Gordon et al. 2002) has not only reported thin cornea as a predictor for the development of primary open angle glaucoma (POAG) but Copt et al (1999) has also reclassified more than 56% of OHT patients based on the corrected central corneal thickness (CCT). Additionally, Kim and Chen (2004) demonstrated progression of disease was more likely in POAG patients with thinner corneas, hence giving another insight in the role of CCT in managing glaucoma patients. Correlation between corneal thickness and the severity of the disease in the POAG group has been described by many authors using advanced glaucoma intervention study (AGIS) scoring (Kim & Chen 2004, Herndon et al. 2004). However, this relationship is not well described for the NTG group of patients.

Optical coherence tomography shows good topographic relationship between structural damage and functional loss (visual field loss) (Wollstein et al. 2004, Wollstein et al. 2005). The average RNFL thickness was found to have the strongest correlation with severity of the disease, followed by the inferior and superior quadrant measurements. The aim of this study was to investigate a possible correlation between the severity of glaucoma (based on RNFL thickness as

measured by OCT) and CCT among NTG and POAG group of patients.

MATERIALS AND METHODS

Patients

An observational study of patients who were treated for primary open angle and normotensive glaucoma was carried out at UKMMC, Kuala Lumpur from January 2006 to April 2007. This study was approved by the Medical Research and Ethics Committee UKM.

Design

Medical records of the patients were reviewed retrospectively for selection of cases. Sample size was calculated using the sample size calculation program version 2.1.30 February 2003. High tension glaucoma was diagnosed if the baseline IOP prior to treatment was more than 21mmHg with the presence of open angle on gonioscopy and glaucomatous optic disc changes. Those with baseline readings less than 21mmHg were classified as having normal tension glaucoma (NTG). All patients had glaucomatous visual field defects as confirmed by the Humphrey Visual Field test and only patients who were on medical treatment with no previous surgery were recruited for this study. Patients with significant anterior segment disease causing poor signal strength on the OCT were excluded from the study. Other exclusion criteria were those with diabetic retinopathy, contact lens user and high myopia of more than - 6 dioptre. The worse eye was chosen for the study.

Measurement of CCT was done using a specular microscope SP-3000P (Topcon Corporation, Tokyo). This method used a non contact technique to measure the corneal thickness, which was reported to have better repeatability compared to ultrasound pachymetry (Bovelle et al. 1999). Three readings with a standard deviation of less than 3µm were used, and the average was calculated for the analysis. Subsequently, measurement of RNFL was done by a single operator using the Stratus 3 OCT (Carl Zeiss Meditech, Dublin,CA) on well-dilated eyes. Good signal strength of 7 or more was included for analysis. Diagnosis was confirmed by looking at their previous record of baseline IOP before treatment and patients who were treated elsewhere with no known pretreatment IOP were excluded from the study. Purpose and details of the study were explained to the patient and informed consent was obtained. Demographic data, past medical history and ocular history were obtained from all patients.

The worse eye was chosen based on the humphrey visual field. Eyes with counting finger or worse vision were excluded. Visual acuity using the logMar chart was recorded and autorefraction was done to look at the level of refractive error. Anterior segment examination was performed and intraocular pressure was measured before gonioscopy was done. All patients were dilated and examination of the retina was performed to look for the presence of other ocular pathology which may affect the RNFL measurement. Optical coherence tomography was done for all patients with a dilated pupil and only those with a good signal strength were included in the study. Data was then collected and those with incomplete documentation were excluded. Data of the patients were then analyzed.

RESULTS

A total of 190 eyes from 190 patients were included in the study. There were 60 patients in the normal tension glaucoma (NTG) group, 61 patients for primary open angle glaucoma (POAG) group and 69 patients for the normal (control) group. Age for all the groups

were normally distributed (Shapiro-Wilk p > 0.05). Parametric statistical tests were used for the data analyses. All p-values were 2-sided and were considered statistically significant when the values were less than 0.05.

Mean age for the POAG group was 64.5±10.2 years, NTG group 65.0±7.6 years and the normal group 61.6±8.2 years old (One way ANOVA, p=0.195). Intraocular pressure was significantly different between the three groups (p<0.0001) (Table 1). Central corneal thickness of the NTG group was found to be thinnest among the three groups. Significant differences were noted between the CCT of the NTG patients compared to the control group (p < 0.05) (Table 1).

RNFL thickness was thinner in both glaucoma groups compared to the control group of patients (p<0.05) (Table 2). Both glaucoma groups had similar level of severity of disease based on RNFL (p >0.05).

A significant Pearson correlation coefficient was found in the POAG group between the CCT and RNFL in the superior quadrant and average thickness (r=0.265, p<0.05 and r=0.417, p<0.05 respectively). No significant correlation was found between the CCT and RNFL for the NTG group (Table 3, Figures 1, 2).

DISCUSSION

Normotensive glaucoma was long considered as a subset of POAG, sharing many similar characteristics except for the elevated IOP (Sowka 2005). In this study, mean CCT for NTG patients were found to be the thinnest compared to the POAG and the control groups. However, based on published calculations, (Doughty & Zaman 2000) the differences

Table 1. Intraocular Pressure and Central Corneal Thickness for the normal tension glaucoma, primary open angle glaucoma and control group.

	Normal Tension Glaucoma	**Primary Open Angle**	**Control**	**P value**
Intraocular Pressure(mmHg)	14.01(±2.4)	16.63(±2.9)	13.9 (±2.5)	**0.000**
Central Corneal Thickness (µm)	502.9 (±32.3)	508.3 (±34.7)	517.4(±31.5)	0.043

Table 2: Mean retinal nerve fiber layer thickness measurement in all quadrant

	Normal Tension Glaucoma	**Primary Open Angle**	**Control**	**P**
Mean RNFL	79.91(±20.04)	73.19(±18.23)	101.37(±12.32)	**0.000**
Superior Quadrant	98.67(±27.23)	91.97(±26.12)	128.83(±16.78)	**0.000**
Nasal Quadrant	65.97(±21.91)	57.36(±16.71)	75.62(±17.98)	**0.000**
Inferior Quadrant	94.27(±33.22)	83.16(±29.00)	126.10(19.29)	**0.000**
Temporal Quadrant	59.87(±15.92)	60.48(±19.65)	72.23(±13.99)	**0.000**

One way ANOVA

Table 3: Correlation between central corneal thickness and retinal nerve fibre layer

	Normal Tension Glaucoma		Primary Open Angle		Control	
	r	p	r	p	r	p
Mean RNFL (µm)	-0.058	0.657	0.265	**0.039**	-0.002	0.986
Superior Quadrant (µm)	-0.012	0.927	0.417	**0.001**	-0.101	0.410
Nasal Quadrant (µm)	-0.129	0.327	0.176	0.174	-0.054	0.657
Inferior Quadrant (µm)	-0.063	0.634	0.118	0.367	0.044	0.718
Temporal Quadrant (µm)	0.037	0.778	0.150	0.250	0.082	0.504

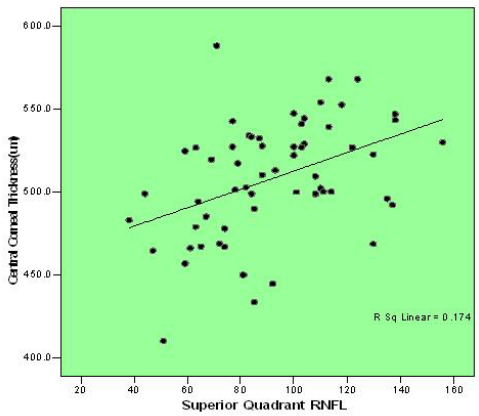

Figure 1. Correlation between the superior quadrant retinal nerve fibre layer (RNFL) and Central corneal thickness in Primary Open Angle Glaucoma

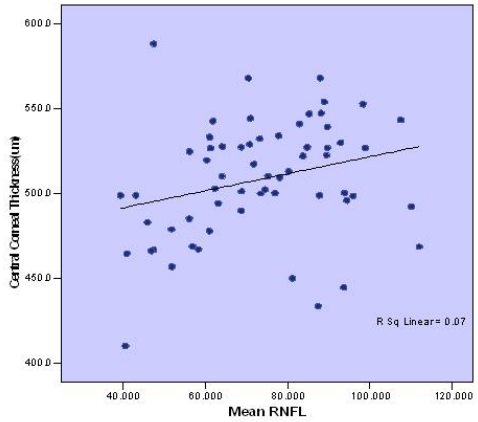

Figure 2. Correlation between the average(mean) retinal nerve fiber layer (RNFL) and Central corneal thickness in Primary Open Angle Glaucoma

were too small to influence the IOP measurement in a clinically meaningful way. Therefore the measured IOP achieved using the 'gold standard' technique of Goldmann tonometry may not differ significantly from the actual IOP in NTG patients. However, POAG patients were found to have relatively comparable corneal thickness with the normal population supporting the fact that the disease is truly an effect of an ageing trabecular meshwork. The value for CCT in this study however was slightly lower compared to other studies which mainly used ultrasound pachymetry to measure the CCT (Bechmann et al. 2000).

Significant correlation between the CCT and severity of RNFL was only found for the POAG group but not for the NTG group of patients. The results obtained were also comparable with a cross sectional study done using AGIS scoring which did not find any significant correlation between the corneal thickness and severity of the disease in NTG patients (Bechmann et al. 2000). The different

findings between these two groups of patients may implicate the possibility of different pathophysiology of the disease.

Cioffi and Liebman (2002) proposed possible relationship between a thin cornea and intracellular matrix changes at the level of lamina cribosa may predispose to glaucomatous changes. This idea would be an additional risk factor for this group of patients. Despite controlling the IOP, progression may seem to be inevitable in the presence of a thin cornea. However, this possibility may not be applicable to the NTG patients as similar correlation between the CCT and severity of the disease was not found. Therefore, consideration of NTG as a subset of POAG has to be evaluated with caution. Although clinically the appearance on gonioscopy may be similar, further evaluation at the cellular and genetic level may help to answer these questions. Other influential factors that may contribute to the severity of the disease for the NTG group were proposed by Doyle (Doyle et al. 2005). Higher association of systemic disease in the NTG group may affect the ocular perfusion indirectly leading to optic nerve damage in this group of patients (Doyle et al. 2005).

To date, there has been no study done to look at the association of CCT and severity of glaucoma in the NTG group using the OCT. However, this study was a cross sectional study and the stability of the disease was not analyzed. As such, the possibility of further RNFL progression was not taken into consideration. A prospective long term study may give a better understanding of the correlation between the corneal thickness and RNFL.

CONCLUSION

Significant correlation between the corneal thickness and severity of glaucoma is only present in POAG patients but not for NTG cases. Our results suggest that CCT is related to the severity of POAG-related visual loss thus measuring the corneal thickness in this group of patients may help to determine which patient would benefit from close monitoring. Furthermore, the old consideration of NTG as a subset of POAG may not be applicable with many studies showing dissimilar detail characteristics between those two groups.

ACKNOWLEDGEMENTS

The authors would like to express their greatest gratitude to the Department of Ophtalmology for the continous support throughout the study, Prof Dr Ropilah Abdul Rahman, Dr Fam Han Borr from Singapore National Eye Centre and Dr Nor Fariza Ngah from Hospital Selayang for their critical comments on this study.

REFERENCES

Bechmann, M., Thiel, M.J., Roesen, B., Ullrich, S., Ulbig, M.W. & Klause, L. 2000. Central corneal thickness determined with optical coherence tomography in various types of glaucoma. Br J Ophthalmol **84**(11): 1233-1237.

Bovelle, R., Kaufman, S., Thompson, H.W. & Hamano, H. 1999. Corneal thickness Measurements with Topscon SP-2000P specular microscope and ultrasound pachymeter. *Arch Ophthalmol* **117**(7): 868-870.

Cioffi, G.A. & Liebman, J.M. 2002. Translating the OHTS results into clinical practice. *J Glaucoma* **11**(5):375-377.

Copt, R.P., Thomas, R. & Mermoud, A. 1999. Corneal thickness in ocular hypertension, primary open angle glaucoma and normal tension glaucoma. *Arch Ophthalmol* **117**(1):14-16

Doyle, A., Bensaid, A. & Lachkar, Y. 2005. Central Corneal Thickness and Vascular Risk Factors in Normal Tension Glaucoma. *Acta Ophthalmol Scand* **83**(2):191-195

Doughty, M.J. & Zaman, M.L. 2000. Major review; Human Corneal Thickness and Its Impact on Intraocular Pressure Measures: a Review and Meta analysis Approach. *Surv Ophthalmol* **44**(5): 367-408

Herndon, L.W., Weizer, J.S. & Stinnet, S.S. 2004. Central corneal thickness as a risk factor for

advanced glaucoma damage. *Arch Ophthalmol* **122**(1): 17-21

Gordon, M.O., Beiser, J.A., Brandt, J.D., Heuer, D.K., Higginbotham, E.J., Johnson, C.A., Keltner, J.L., Miller, J.P., Parrish, R.K., Wilson, R. & Kass, M.A. 2002. The ocular hypertension treatment study, baseline factors that predict the onset of primary open angle glaucoma. *Arch Ophthalmol* **120**(6): 714-720

Kass, M.A., Heuer, D.K., Higginbotham, E.J., Johnson, C.A., Keltner, J.L., Miller, J.P., Parrish, R.K., Wilson, R. & Gorodn, M.O. 2002. The Ocular Hypertension Treatment Study: A Randomized Trial Determines That Topical Ocular Hypotensive Medication Delays or Prevents the Onset of Primary Open-Angle Glaucoma. *Arch Ophthalmol* **120**(6): 701- 712

Kim, J.W. & Chen, P.P. 2004. Central corneal pachymetry and visual field progression in patients with open angle glaucoma. *Ophthalmol* **111**(11): 2126- 2132

Sowka J. 2005. New Thoughts on Normal Tension Glaucoma. *Optometry* **76**(10): 600- 608

Wollstein, G., Schumann, J.S., Price, L.L. , Hydin, A., Beaton, S.A., Stark, P.C., Fujimoto, J.G. & Ishikawa, H. 2004. Optical Coherence Tomography macular and peripapillary retinal nerve fibre layer measurement and automated visual fields. *Am J Ophthalmol* **138**(2): 218-225

Wollstein, G., Ishikawa, H., Wang, J., Beaton, S.A. & Paunesan, L.A. 2005. Comparison of three optical coherence tomography scanning areas for detection of glaucomatous damage. *Am J Ophthalmol* **139**(1): 39-43.