Original Research Article

Role of central corneal thickness measurement in management of open angle glaucoma and glaucoma suspects in Calabar, Nigeria

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Abstract

Introduction: Central Corneal Thickness (CCT) is gaining increasing significance in the management of glaucoma patients due to the recognized relationship between CCT and intraocular pressure (IOP) levels. The Objective of this study was to evaluate to what extent CCT modified Goldmann Applanation Tonometry (GAT), and thus management decisions in the care of glaucoma patients and suspects in Calabar, Nigeria.

Materials and methods: All consenting patients seen from January to December 2015 in University of Calabar teaching Hospital (UCTH) eye clinic and Zerah Eye Hospital and Laser Center, Calabar who were diagnosed as Glaucoma suspects/patients were included. IOP was measured by Goldmann Applanation Tonometry (GAT), and CCT measured by handheld contact ultrasound pachymetry. Data entry and analysis was performed using STATA 12 software. Results were summarized in frequencies, percentages and means while comparison was done using 95% confidence interval.

Results: The study sample was 256 with 133(51%) females and 123(48%) males. The mean age was 45.52years ±17.82. The mean CCT was 530µm. An inverse relationship between CCT and age was seen; mean CCT of 518.29µm and 548.93µm for the oldest age and youngest age groups respectively. Increasing age is a known risk factor for glaucoma, but it remains to be elucidated if the progressive

thinning in CCT with age confers an independent risk factor. The mean IOP was 15.835 and CCT adjusted values for IOP varying from -7 to +7 mmHg with mean IOP adjustment of 0.84mmHg ± 2.66mmHg for right eye and mean IOP adjusted value of 0.98mmHg ± 2.69mmHg for the left eye. Over 50% had adjusted IOP values of ≥1.5mmHg, while 36% had adjusted values of ≥3mmHg.
Conclusion: Measurement of CCT was important for management decisions as 36% of study subject required IOP adjusted values of ≥3mmHg, thus affecting diagnostic criteria and modifying decisions on 'Target IOP' during management. Routine CCT measurement at diagnosis should be part of a minimum package of care even in low resource settings, for the glaucoma patients to avoid under-treatment/overtreatment from 'falsely' elevated or lowered IOPs.

Key words

Central corneal thickness, Glaucoma, Calabar, Nigeria.

Introduction

Central Corneal Thickness (CCT) is a measurement of the thickness of the central 3mm of the cornea [1]. Its measurement is important in corneal refractive surgeries, assessment of corneal endothelial function and the detection of corneal thinning conditions among other indications [2]. It is also gaining increased significance in the evaluation and management of glaucoma suspects and patients. This has resulted from the observed relationship between lower CCT, risk of glaucoma development and IOP levels, as reported in several studies [3-6].

Glaucoma is a leading cause of avoidable blindness in Calabar, Nigeria as indeed globally [7-9]. Determination of intraocular pressure (IOP) is important not only for the diagnosis and management of glaucoma but for almost all intra ocular surgical interventions. IOP is the most important modifiable risk factor for open angle glaucoma [1, 2]. The level of IOP is often used to decide when to commence treatment and for setting targets of IOP reductions to be achieved during treatment [1].

For about 50years, applanation tonometry using the Goldmann method has been the gold standard for measuring intraocular pressure [10, 11]. The Goldmann equation is derived from the Imbert-Fick principle which applies to an ideal dry, thin walled sphere [10]. The corneal surface deviates from this theoretical construct allowing intraocular pressure measured by the Goldmann applanation tonometer to be affected by Central corneal thickness [12, 13]. Ehler, et al. demonstrated the Goldmanns applanation tonometer (GAT) is most accurate with a CCT of 520 nm [14]. This is not always the case within and between populations. IOP measurement is said to correlate with CCT in a linear relationship [15].

African Americans were found to have on the average, thinner corneas than their Caucasian counterparts [16] and this may be related to why glaucoma appears to run a more aggressive course in the former population [7, 17, 17]. Shih and co-workers found that CCT measurement significantly contributed to modification of management strategies for 15% of glaucoma patients within their population [19]. Indeed reduced CCT is said to be an important independent risk factor in the development and severity of open angle glaucoma [20, 21].

Multicenter studies have demonstrated that CCT varies considerably among subjects even within the same country. The Ocular Hypertension Treatment Study reported a mean CCT of 573 (± 39.0)μm. The Rotterdam Study described a mean CCT of 537.4 (± 3.6) with a maximal difference between eyes of 42 μm. Subjects with primary open-angle glaucoma showed slightly thinner CCT than that of control subjects. People of Black African ancestry are believed to have thinner corneas and higher "corrected" IOPs than Caucasians or Asians. Normal-tension glaucoma

is reported to be associated with CCT in the low 500-µm range [2].

CCT ranges in Sub-saharan African countries including Nigeria are yet to be extensively evaluated. There are few studies on the subject in such settings [6, 22, 23]. Measurement of CCT, unlike IOP, gonioscopy and visual field assessments is yet to be included in the minimum requirement for the diagnosis and management of Open angle glaucoma in many centres in developing countries.

This is perhaps even more important for patients of African ancestry and in the subset of patients labeled as 'glaucoma suspects', who may be better served by routine pachymetry as thinner corneas may be responsible for their measured lower intraocular pressures using the Goldmann's technique. The purpose of the index study was to determine to what extent CCT affected IOP results and modify management decisions in the care of patients with open angle glaucoma and Glaucoma suspects within our population in Calabar, Nigeria. This to the best of our knowledge would be the first time this is being evaluated in that population.

Materials and methods

A cross sectional study design was chosen. The study was carried out in two centers; the eye clinic of the University of Calabar Teaching Hospital (UCTH) and Zerah International Eye Hospital and Laser Center Calabar. Ethical approval was obtained from the Hospital Research Ethics committee of UCTH. All consecutive patients seen in the two centers mentioned above who were diagnosed with Chronic open angle glaucoma or as Glaucoma suspects from January 2015 to December 2015, were included after an informed consent was obtained for the study. For the purpose of this study a glaucoma suspect is defined as a person who has one of the following findings in at least one eye:

- an optic nerve or nerve fiber layer defect suggestive of glaucoma (enlarged cup–disc ratio, asymmetric cup–disc ratio, notching or narrowing of the Neuro-retinal rim, a disc hemorrhage, or suspicious alteration in the nerve fiber layer)
- a visual field abnormality consistent with glaucoma
- an elevated IOP greater than 21 mm Hg

Where however two or more of these findings are present, the diagnosis of Primary Open Angle Glaucoma (POAG)) is supported, especially in the absence of a direct aetiologic factor and presence of other risk factors, such as age above 50 years, family history of glaucoma, and African ancestry. Diagnosis of a glaucoma suspect and POAG is also dependent on a normal open angle on gonioscopy [1]. When a patient presents with two of the above listed diagnostic features of glaucoma in the presence of normal intraocular pressures, a diagnosis of Normal Tension Glaucoma (NTG) was made.

Patients with corneal opacities, history of contact lens wear, dry eye syndrome and those who have had intraocular surgeries within six months of presentation were all excluded from the study. All patients had visual acuities recorded. IOP was measured by GAT after a drop of Proparacaine hydrochloride ophthalmic solution USP 0.5% was instilled in the conjunctival fornix along with Fluorescein. CCT was measured by handheld contact ultrasound pachymetry (Reichert iPac) by one person on all subjects. All patients had detailed eye examination to rule out other corneal pathologies, and confirm the diagnosis of Chronic open angle glaucoma. Every patient included in the study also had central visual field tested, FDT evaluation and OCT analysis of the Optic disc and nerve fiber layer.

During data entry, bio-data including age, sex, ethnic group and diagnosis were obtained and recorded in a record form. Data entry and analysis was performed using the STATA 12 software. Results were summarized in

frequencies, percentages and means while comparison was done using 95% confidence interval in differences of means.

Results

Demographics

The study sample was 256. The mean age was 45.52 years ±17.82. Age range was 7 to 89 years. Females were 133(51.95%) and males 123 (48.0%), as shown in **Table - 1**. The mean age for females was 42.65 ±18.06 while the mean age for males was 48.63 ±17.09.

CCT values for the right eye and left eye are shown in **Figures - 1 and 2** respectively. The mean CCT for the right eye for 254 samples was 532.48. SE 2.37, 95% CI (527.8039 - 537.1488) with a range of 439-649.

The mean CCT for the left eye for 255 samples was 531.26, SE 2.37 95% CI (526.5805 - 535.9293) range of 435-673. Mean CCT by age, gender, tribe, diagnosis was as per **Table – 2 to 5** respectively.

Table - 1: Age and sex distribution in the Study sample.

Age group (years)	Male	Female	Total
0-29	16(13.01%)	37(27.82%)	53(20.70%)
30-49	50 (40.65%)	46(34.59%)	96(37.50%)
50-69	40(32.52%)	44(33.08%)	84(32.81%)
70-100	17(13.82%)	6 (4.51%)	23(8.98%)
Total	123(100%)	133(100%)	256(100%)

Table - 2: Mean CCT by Age.

Age group(years)	Mean CCT OS(um)	Mean CCT OD(um)
0-29	548.55 +/- 39.63(53)	549.31 ± 41.04(52)
30-49	531.65+/-37.22 (96)	532.62 ± 35.45(96)
50-69	523.51+/-33.97(83)	525.55± 35.09(83)
70-100	517.74 ± 38.09(23)	518.83 ±38.45 (23)
Total	531.26± 37.90 (255)	532.48 ± 37.82 (254)

Right Eye Pearson chi^2 = 4.6522 Pr = 0.199

Left Eye -Pearson chi^2 = 4.7993 Pr = 0.187

Figure - 1: CCT for the left eye.

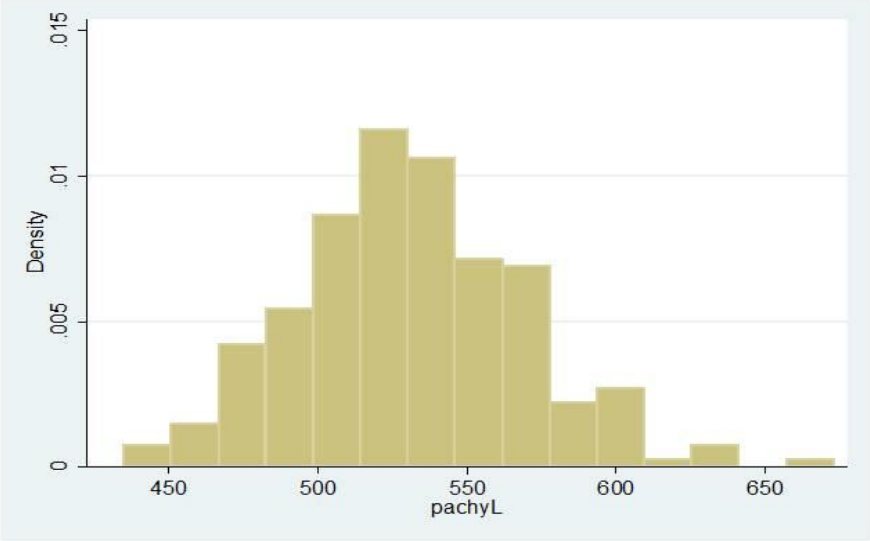

Figure - 2: CCT for the right Eye.

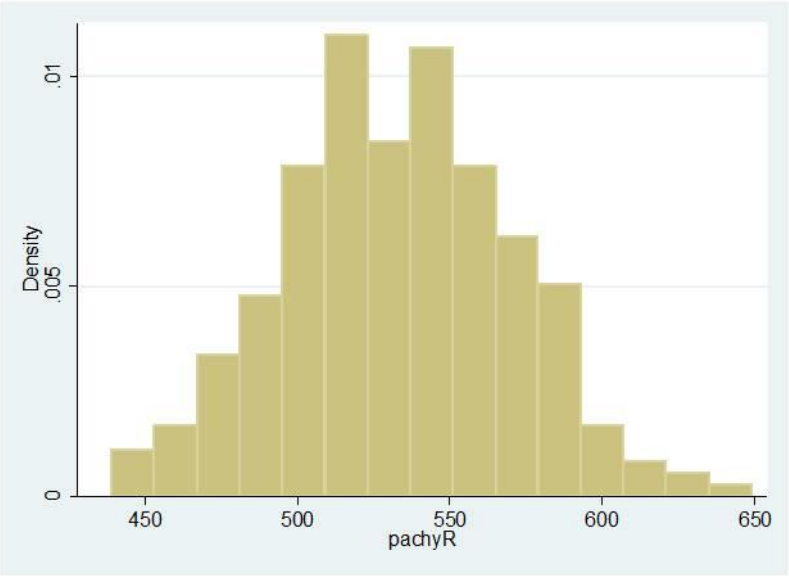

Table - 3: Mean CCT by Gender.

Mean CCT OD Male	Mean CCT OD Female	Total mean CCT OD	Mean CCT OS Male	Mean CCT OS Female	Total mean CCT OS
522.90 ±77.11 (123)	533.32 ±38.14 (133)	528.32 ±60.21 (256)	530.27 ±36.90 (123)	532.17 ±38.94 (132)	531.26 ±37.90 (255)

Left Eye - Pearson chi^2 = 0.4468 Pr = 0.504
Right Eye - Pearson chi^2 = 0.9475 Pr = 0.330

Table - 4: Mean CCT by Tribe.

Tribe	Frequency right eye	Mean CCT right eye	Frequency Left eye	Mean CCT left eye
Efik	41	520.88 +/41.61	42	524.60 ± 47.91
Northern CRS tribes	25	543 +/- 40.94	26	538.96 ± 42.71
Akwa-Ibom tribes	61	533.51+/-35.52	60	531.02 ±31.78
Others	127	533.65+/-36.52	127	531.99 ± 35.87
Total	254	532.48+/-37.81	255	531.26± 37.90

chi^2 = 1.8175 Prob>chi^2 = 0.611(right eye)
chi^2 = 9.9814 Prob>chi^2 = 0.019 (left eye)

Table - 5: Mean CCT by Diagnosis.

Diagnosis	Mean CCT OD	Mean CCT OS
POAG	528.07± 37.27 (123) 95% CI(521.41- 534.72)	526.85 ±36.40 (123) 95% CI(520.35 - 533.34)
Glaucoma suspect	536.62 ±37.99 (131) 95% CI (530.05-543.19)	535.36 ±38.94 (132) 95% CI(528.66 - 542.07)
Total	532.48 ±37.81 (254) 95% CI (527.80-537.15)	531.26 ±37.90 (255) 95% CI(526.58- 535.93)
P value	0.07	0.07

Table - 6: Corrected IOP.

Variable	mean	min	max	Total
Corrected IOP RE	0.84±2.66	-7	7	254
Corrected IOP LE	0.98±2.69	-7	7	255

Patients with IOP adjustment of more than ±1.5mmhg in the right eye (out of a total of 254) stood at 143(56.30%) with 92 (36.22%) having IOP adjustment +/- 3mmHg.
Patients with IOP adjustment of more than +/- 1.5mmHg in the left eye (out of a total of 255) stood at 136(52.81%) with 95 (36.73%) having IOP adjustment +/- 3mmHg.

Intraocular pressure
Mean IOP RE 15.88(252) ± 5.46
95%CI (15.20 -16.55) range 6 – 43
Mean IOP LE 15.89(252) ±4.89
95%CI (15.29- 16.50) range 6-42
Linear regression analysis of intra-ocular pressure with CCT for the right eye showed that intraocular pressure increase by 0.31um in for each 1mmHg increase in pressure with a p – value of <0.001. Corrected IOP was as per **Table – 6**.

Discussion

The mean central corneal thickness (CCT) of our study subjects was 530µm. This lends support to previous findings that Africans tend to have thinner corneas when compared with Caucasians. The Rotterdam study reported a mean CCT of 537 while The Ocular Hypertension treatment study reported a mean CCT of 573µm. No significant difference was found between male and female values. Mercieca, et al. in their study in South West Nigerian found significantly higher CCT values in men, and Egwuonwu in her study in Lagos, Nigeria found marginally higher CCT values in men [22, 23]. The Ocular Hypertension Treatment Study also reported a higher CCT thickness in men [3-6]. However, a number of other studies did not find any significant gender difference in CCT values.

The difference in CCT between right and left eyes was also found to be statistically not significant (see **Figures - 1 and 2**). CCT was seen to decrease steadily as age increases. This like most studies found an inverse relationship between age and CCT. Increasing age is a known risk factor for glaucoma, but it remains to be elucidated if this progressive thinning in CCT with age confers an independent risk in the development of glaucoma.

The mean IOP measurement in this study was 15.31mmHg for male and 16.355 for females. The CCT adjusted values for IOP varied from -7 to +7 mmHg, with mean IOP adjustment of 0.84mmHg ± 2.66mmHg for right eye and 0.98mmHg ± 2.69mmHg for the left eye. Over 50% had adjusted IOP values of ≥1.5mmHg, while 36% had adjusted values of ≥3mmHg. This is a significant adjustment in IOP values which is the major modifiable risk factor in the management of glaucomatous neuropathy. Some studies which used linear and mathematical (Orssengo-Pye) algorithms take adjustments in IOP of 1.5mmHg or greater as measurement-significant outcome which was the case for over 50% of patients in our cohort. IOP adjustments of 3mmHg or greater has been described as outcomes-significant results and this was the case for at least 36% of the patients in our study.

Conclusion

Since IOP is still the most important single modifiable risk factor for open angle glaucoma [1, 2, 9] and the level of IOP is often used to decide when to commence treatment, for setting targets of IOP reductions to be achieved during treatment [1], and for monitoring and follow-up during care, routine CCT measurement at diagnosis should be part of a minimum package of care for the management of glaucoma patients and suspects even in resource limited developing world settings. This would be even more important in patients of African ancestry, or with normal tension glaucoma where thinner central

corneas may consistently masquerade as lower IOP with the GAT.

Variations in the central corneal thickness in individuals lead to significant errors in the measurement of intraocular pressure. In the index study, IOP adjustments of 3mmHg or greater (outcomes-significant results) were recorded in at least 36% of the patients. This calls for routine CCT checks and adjustments where necessary to correct these errors caused by too thick or too thin corneas in order to avoid overtreatment or under-treatment accruing from falsely elevated or lowered IOPs within our setting where the risk is probably high.

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