

CLINICAL SCIENCE

Correlation between central corneal thickness and intraocular pressure peak and fluctuation during the water drinking test in glaucoma patients

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OBJECTIVE: To investigate the correlation between central corneal thickness and outflow facility assessed by intraocular pressure peak and fluctuation during the water drinking test.

METHODS: Fifty-five newly diagnosed primary open-angle glaucoma patients submitted to central corneal thickness measurements and water drinking test were enrolled in this retrospective study. Patients were divided into three groups according to their central corneal thickness. Pearson's Correlation test was performed in the groups with lower and higher pachymetric values.

RESULTS: The mean age was $65,65 \pm 28,28$ years; 63,63% were female and 52,72% were caucasian. The mean central corneal thickness was $544,32 \pm 36,86$ μm , and the mean baseline intraocular pressure was $23,36 \pm 6,26$ mmHg. During the water drinking test, the mean intraocular pressure peak and mean intraocular pressure fluctuation were $30,43 \pm 8,13$ mmHg and $31,46 \pm 18,46\%$, respectively. No relevant correlation was detected between the central corneal thickness and the intraocular pressure peak ($r^2=0,021$) or between the central corneal thickness and the intraocular pressure fluctuation ($r^2=0,011$). Group 1 presented a mean central corneal thickness of $505,81 \pm 13,86$ μm , and Group 3 was $583,55 \pm 27,87$ μm ($p=0,001$). The mean intraocular pressure peak was $31,05 \pm 9,05$ mmHg and $27,83 \pm 4,92$ mmHg in Group 1 and in Group 3, respectively ($p=0,193$). The difference of intraocular pressure fluctuation was not statistically significant between Group 1 (mean $28,47 \pm 16,25\%$) and Group 3 (mean $33,27 \pm 21,27\%$) ($p=0,43$).

CONCLUSION: In our case series, no correlation was found between central corneal thickness and water drinking test results.

KEYWORDS: Central Corneal Thickness; Intraocular Pressure; Primary Open-Angle Glaucoma; Stress Test; Water Drinking Test.

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INTRODUCTION

Glaucoma is a progressive optic neuropathy that leads to irreversible visual impairment if not properly treated. Intraocular pressure (IOP) is the main risk factor for glaucoma development and progression. However, despite IOP reduction to levels considered to be within normal limits, a significant group of patients still experience progression of glaucomatous optic neuropathy.¹⁻³ Recently, researchers have suggested that factors such as IOP peak and diurnal IOP variability may contribute to the worsening of glaucomatous damage.⁴⁻⁶

Some alternative methods to estimate the IOP profile have been described. A diurnal tension curve consisting of four to five measurements during office hours is routinely used. However, this test may miss up to 70% of IOP spikes since the highest IOP levels occur at around 6 and 8 a.m. in a supine position, which also compromises adequate evaluation of IOP fluctuation.^{4,7,8} The water drinking test (WDT) was demonstrated to be an important tool in the management of glaucoma and has been used to assess IOP peaks^{5,9,10} and the outflow system of the eye.¹¹

Central corneal thickness (CCT) was found to correlate positively with IOP,^{12,13} whereas thinner CCT was suggested to play a role in the development and progression of glaucoma.^{14,15} It was demonstrated that a diurnal range of CCT occurs, but such variation may not be enough to exert a significant influence on IOP values obtained by applanation tonometry, suggesting a single CCT measurement for assessment of glaucoma patients.¹⁶

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The aim of this study was to determine whether different corneal thicknesses may influence the IOP profile during WDT in primary open-angle glaucoma (POAG) subjects.

MATERIALS AND METHODS

In this case series, we reviewed the charts of fifty-five newly diagnosed POAG patients who were submitted, between January 2008 and April 2008, to the water drinking stress test and pachymetry. None of the patients was taking any ocular hypotensive medication during the study. Approval from the Institutional Review Board Ethics Committee was obtained for the study, which followed the principles of the Declaration of Helsinki.

Glaucoma diagnosis was based on changes in the neuroretinal rim of the optic nerve head and/or retinal nerve fiber layer and the appearance of VF defects.¹⁷ IOP values were taken into consideration, but they did not constitute an element of the diagnosis. At gonioscopy, all enrolled eyes presented open angle and no evidence of secondary glaucoma, such as pigment dispersion, pseudo-exfoliation material, or peripheral anterior synechiae.

Patients submitted to any surgical procedure or laser intervention before the investigation period, and patients with corneal or retinal diseases, non-glaucomatous optic neuropathy, or any other disease that could possibly interfere with the IOP or pachymetric measurements were excluded.

One eye of each patient was included in this study. If both eyes of the same patient were eligible, one was randomly selected.

Patients were submitted to WDT during the morning period. After baseline IOP measurement, they were asked to drink one liter of tap water within 5 minutes. Afterwards, IOP was measured three times at 15-minute intervals. The maximum value of the last three measurements during this stress test was considered to be the IOP peak. IOP fluctuation was considered to be the percentage of absolute fluctuation of IOP and was defined as the difference between the IOP peak and the baseline IOP divided by the baseline IOP (IOP peak – baseline IOP/baseline IOP).

IOP readings were obtained with a calibrated Goldmann applanation tonometer, and CCT was measured with a commercially available device (AL-3000 ultrasound Biometer/Pachymeter, CDB Ophthalmic/TOMEY, Phoenix, AZ, USA) by taking the average of 5 consecutive ultrasound pachymetry measurements in the elected eye of each subject.

To compare pachymetry with IOP peak and IOP fluctuation, patients were divided into three groups, according to percentiles 33,33 and 66,67. Thereafter, we compared data from Group 1 and Group 3 and excluded the intermediate pachymetry group (Group 2) from analysis to verify whether there is a correlation between CCT and the WDT results.

Statistical analysis was performed with commercial software (SPSS 15.0, SPSS Inc., Chicago, IL, USA). Analysis of variance and analysis of covariance were used to compare continuous data, and the chi-square test was used to analyze categorical demographic data between groups. The data included age, gender, ethnic group, CCT, and baseline IOP. Intraocular pressure peak and IOP fluctuation during the water drinking test were evaluated in each pachymetry group using the Student’s t-test. Pearson’s correlation was

employed to verify a possible association between pachymetry values and the WDT results.

RESULTS

Fifty-five eyes of 55 patients were included in this study. Twenty (36,36%) patients were male, and 35 (63,63%) female. The mean age of all participants was 65,65 ± 28,28 years (range 42–85). The majority of the patients (29 out of 55; 52,72%) were caucasian; 10 were Afro-Americans (18,18%), 1 was of Asian descent (1,81%), and 15 were mixed (27,27%). Demographic data are summarized in **Table 1**.

Central corneal thickness (CCT) measurements ranged from 477,5 to 670,2 µm, with a mean ± standard deviation of 544,32 ± 36,86 µm. The mean baseline IOP and the mean IOP peak were 23,36 ± 6,26 mmHg (range 14 – 40) and 30,43 ± 8,13 mmHg (range 20 – 58), respectively. The IOP fluctuation ranged from zero to 88,89%, where the mean IOP fluctuation was 31,46 ± 18,46%.

Mean CCT values in Groups 1 and 3 were 505,81 ± 13,86 µm and 583,55 ± 27,87µm, respectively (p<0,001). The mean IOP peak was 31,05 ± 9,05 mmHg in Group 1 and 27,83 ± 4,92 mmHg in Group 3 (p=0,193). The IOP fluctuation observed in Group 1 (mean 28,47 ± 16,25%) and in Group 3 (mean =33,27 ± 21,27%) also demonstrated no statistical significance (p=0,43). Those results are synthesized in **Table 2**.

No significant correlation was found between CCT and IOP peak (r²=0,021) (**Figure 1**) or between pachymetric values and IOP fluctuation (r²=0,011) (**Figure 2**) in the WDT.

Table 1 - Demographic data according to Central Corneal Thickness

	Group 1 (477–523,19µm)	Group 3 (559,43–671µm)	P Value
Number of Eyes	18	18	1,000 *
Mean Age (years)	65,50 ± 12,80	66,11 ± 7,38	0,870 *
Age Range (years)	43 – 85	44 – 76	
Gender (M/F)	7/11	6/12	0,248 †
Ethnicity			0,115 †
Caucasians	10	9	
Afro-Americans	5	2	
Asians	0	1	
Mixed	3	6	

*t test † Chi Square test SD = Standard Deviation

Table 2 - Results of Pachymetry and IOP measurements in Water Drinking Test

	Group 1 (477–523,19µm)	Group 3 (559,43–671µm)	P Value
Mean CCT (µm)	505,81 ± 13,86	583,55 ± 27,87	<0,001 *
Baseline IOP (mmHg)	24,67 ± 8,44	21,11 ± 3,74	0,073 *
IOP Peak (mmHg)	31,05 ± 9,05	27,83 ± 4,92	0,866 †
IOP Fluctuation (%)	28,47 ± 16,25	33,27 ± 21,27	0,913 †

*t test † ANCOVA IOP = Intraocular Pressure; CCT = Central Corneal Thickness

DISCUSSION

Glaucoma treatment is mainly based on IOP reduction, but there are some cases in which, even lowering IOP to what is considered adequate limits, progression still occurs.¹⁻³ In this study, we analyzed the relationship between IOP variability, which may be divided into IOP peak and IOP fluctuation, and CCT. Intraocular pressure peaks are not always obtained in office hours but are usually seen either in a 24-hour tension curve, as shown by Drance,⁷ or in the WDT, as demonstrated by other authors.^{5,18,19} This is the reason ophthalmologists should not perform just a single IOP measurement during office hours.

Moreover, CCT was found to be another important factor associated to glaucoma progression, once thinner corneas were observed to provide lower IOP readings compared to actual IOP, when assessed by applanation tonometers.¹⁵ Since Shah and coworkers showed that the diurnal variation of CCT is too small to have a significant influence on IOP measurement, obtention of a single CCT measurement is likely enough for the assessment of each glaucoma patient or glaucoma suspect.¹⁶ Based on such observation and associated to the fact that WDT is a stress test that offers a simplified method to assess the 24-hour IOP profile, in our paper CCT was obtained once. Further studies should evaluate the variation of CCT during the WDT.

In this stress test, the return to physiological IOP is dependent of the outflow facility, so, at least in part, the facility of outflow determines the IOP fluctuation observed in this exam. Additionally, Brubaker postulated that the WDT could be used as an indirect tool to measure outflow facility.¹¹ Indeed, the exact mechanism of the WDT over the IOP remains uncertain, but recently, De Moraes and colleagues demonstrated that there is an increase in choroidal thickness during WDT, what could, at least partially, contribute to the understanding of the WDT mechanism.²⁰

This study was designed to verify any correlation between CCT and trabecular meshwork outflow facility assessed by the WDT. Mosaed et al. demonstrated that the IOP fluctuation had no correlation with CCT obtained during office hours, what supported an independent role of CCT in glaucoma.²¹ On the other hand, after observing that ocular hypertensive patients with thinner corneas also had thinner nerve fiber layers, Henderson suggested that there may be some anatomic association between CCT and IOP.²² This could be a reasonable theory since the cornea and trabecular meshwork are derived from neural crest cells and, though, have the same embryonic origin.²³ However, our findings suggest that there is no relationship between CCT and trabecular meshwork tissues' resistance, at least when this last parameter is evaluated through the WDT.

Among our sample, a predominance of caucasians and females was observed, and our results showed a small difference of baseline IOP values between groups 1 and 3, but it was not statistically significant. Intending to eliminate any influence of IOP difference, we also performed comparisons regarding the IOP peak and IOP fluctuation using the ANCOVA test. The absence of data concerning the severity of the disease could be a limitation of our study, but, on the other hand, we studied glaucoma patients at the moment of diagnosis. Consequently, all enrolled patients' eyes were free of medication or drug side effects. This may be an advantage because it was shown that ocular hypotensive medications may alter CCT.²⁴

Some previous papers with cultured anterior segment tissues or living animals eyes were performed to assess factors that could be related to elevated trabecular meshwork resistance.^{25,26} However, such models do not represent the actual dynamics of living human eyes. The WDT offers clinicians a simple method to evaluate *in vivo* trabecular meshwork resistance through overcharged water ingestion. In our study, the WDT was used to evaluate patients with thicker and thinner corneas in order to verify one possible relationship between trabecular meshwork

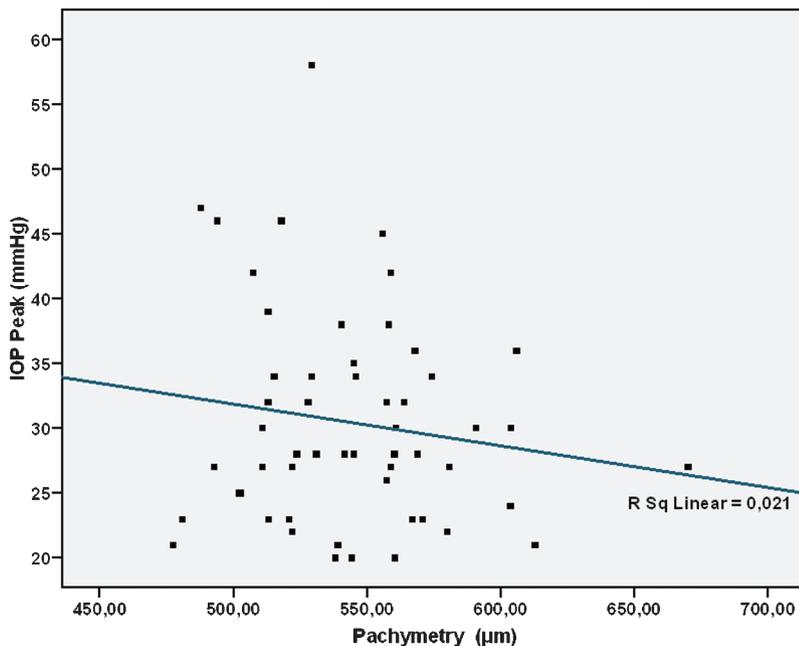


Figure 1 Correlation between Pachymetry and IOP peak in the Water Drinking Test.

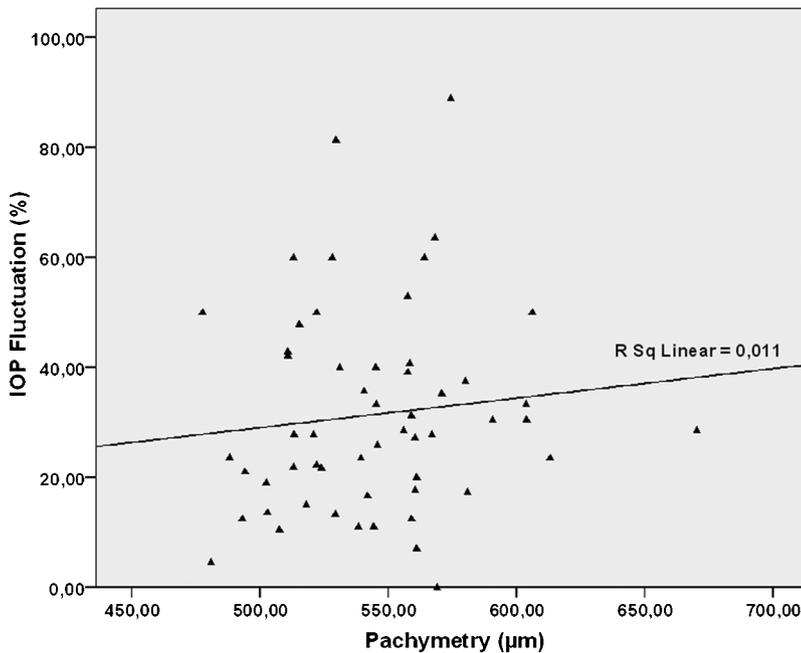


Figure 2 Correlation between Pachymetry and IOP fluctuation the Water Drinking Test.

function and CCT. We found no statistically significant evidence that a thin CCT is correlated with a different IOP peak or IOP fluctuation in the WDT than a thick CCT. This information encourages us to suppose that CCT does not influence the WDT performance and may not indicate eyes that have increased resistance of the outflow drainage pathway.

In summary, the current study showed that outflow facility assessed through WDT is not influenced by CCT in untreated glaucoma patients. Further studies should be conducted to investigate whether outflow facility is influenced by other corneal properties.

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