

# The influence of central corneal thickness on progression of normotensive glaucoma

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**Objectives.** To verify whether there is a relation between central corneal thickness (CCT) and progression of normotensive glaucoma (NTG), to assess the impact of early changes in the visual field on their progression in time.

**Methods and Patients.** The sample consisted of two groups of patients with NTG. In the first group there were 50 eyes of 25 persons (15 females and 10 males) average age 63 years who had been treated with prostaglandins. The second group consisted of 50 eyes of 25 persons (16 females and 9 males) average age of 62 years who had had no local therapy. All patients were cardiologically compensated and had no other internal or neurological disease. Visual acuity was 1.0 with a possible correction (less than  $\pm 3$  dioptres) in all patients. The IOP ranged between 10-15 mmHg in all patients. If hypotensive ophthalmological therapy was initiated, it had been stable for the last five years. In all patients, we monitored CCT, excavation in the papilla (c/d), pattern defect (PD) and overall defect (OD) of the visual field. In 2013, changes in the visual fields were approximately the same in all patients. We compared the results of the visual fields after five years, i.e. the results were obtained in 2018. CCT was measured, using the ultrasound pachymeter Tomey SP-100. PD and OD of the visual field using the glaucoma fast threshold program with the MEDMONT M 700 device. For statistical comparison, we used the paired t test and correlation analysis.

**Results.** In both groups, we found progression of PD in time ( $P=0.0000$ ,  $P=0.0001$ , respectively). In the patients treated with prostaglandins, OD had not statistically significantly changed ( $P=0.49$ ) in contrast to the untreated patients ( $P=0.001$ ). There was no statistically significant relation between CCT and PD in any of the groups. It was similar between the CCT and OD. In the treated NTG patients, we found a weak correlation between the changes in PD in time ( $r=0.2846$ ,  $P=0.0438$ ) and moderately strong relation for OD ( $r=-0.63$ ). The finding was similar in untreated patients PD ( $r=-0.2$ ,  $P=0.162$ ) and OD ( $r=-0.443$ ,  $P=0.001$ ).

**Conclusion.** We found no relationship between progression of changes in the visual fields in CCT. Progression of changes in the visual fields was higher in patients who had more advanced changes at the beginning of observation. The untreated patients had progression of changes in the visual fields both in PD and OD in contrast to those who were taking prostaglandins and presented changes only in PD.

**Key words:** normotensive glaucoma, central corneal thickness, visual field, pattern defect, overall defect

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## INTRODUCTION

Normotensive glaucoma (NTG) is defined as progressive optic neuropathy with glaucomatous disc of the optic nerve and visual field in which IOP is equal to or lower than 21 mmHg (ref.<sup>1</sup>).

Differences compared to hypertensive glaucoma (HTG) were described in the previous paper<sup>2</sup>. In 2013, we referred to the effects of pharmacological therapy on the progression of changes in the visual fields in HTG. We found no differences between therapy with prostaglandins and beta blockers<sup>3</sup>. We found significant differences in the visual fields in time in NTG. The untreated patients or those treated with local prostaglandins had statistically significant changes in the perimeter compared

to those who were treated with beta-blockers. Therefore, the patients with NTG treated with beta-blockers were excluded<sup>4</sup>.

In another study on HTG, we found a correlation of progression of visual field changes with central corneal thickness (CCT) and the fact that progression was greater in patients who had greater changes at baseline<sup>5</sup>.

As for the CCT alone there was no statistically significant difference between patients with HTG and NTG (ref.<sup>6</sup>).

Since NTG is pathophysiologically a different disease than HTG, we wondered whether there is a similar relationship between CCT and progression of changes in visual fields over time and in NTG. This was the aim of our study.

## Group and methodology

Therefore, we included two groups of patients with NTG of approximately the same age in our group (0.58). First group consisted of 50 eyes of 25 persons (15 females and 10 males) of average age of 63 years who have been treated with prostaglandins. The second group consisted of 50 eyes of 25 persons (16 females and 9 males) of average age of 62 years who have had no local therapy. All patients were cardiologically compensated and had no other internal or neurological disease.

Visual acuity was 1.0 with a possible correction (less than  $\pm 3$  dioptres) in all patients. The IOP ranged between 10-15 mmHg in all patients. If hypotensive ophthalmological therapy was initiated, it had been stable for the last five years. In all patients, we monitored CCT, excavation in the papilla (c/d), pattern defect (PD) and overall defect (OD) of the visual field. In 2013, changes in the visual fields were approximately the same in all patients. We compared the results of the visual fields after five years, i.e. the results were found in 2018. Diagnosis of NTG was confirmed also using electrophysiological examination (pattern electroretinogram and pattern visual evoked potential).

CCT was measured, using the ultrasound pachymeter Tomey SP-100. PD and OD of the visual field using the glaucoma fast threshold program with the MEDMONT M 700 device. For statistical consideration, we used the paired t test and correlation analysis.

## RESULTS

The observed values and the results are shown in the Table 1 and 2.

**Table 1.** The observed values in patients treated with prostaglandins.

Patients treated with prostaglandins	
Number of patients	25
Mean age	63.16 $\pm$ 0.4
Lowest	36
Highest	76
Mean PD (2013)	2.85 $\pm$ 1.9
Mean PD (2018):	3.79 $\pm$ 2.6
<i>P</i>	0.0000
Mean OD (2013)	2.66 $\pm$ 1.66
Mean OD (2018):	2.79 $\pm$ 1.3
<i>P</i>	0.49
Dependence between CCT and progression of PD	$r = -0.205$ $P = 0.154$
Dependence between CCT and progression of OD	$r = 0.0412$ $P = 0.7765$
Dependence between PD 2013 and 2018	$r = 0.2846$ $P = 0.0438$
Dependence between OD 2013 and 2018	$r = -0.63$ $P = 0.000$

## DISCUSSION

Zeiter et al. and Araie et al. compared changes in visual fields in NTG and HTG and came to the conclusion that the changes were different in both groups. Changes in patients with NTG were predominantly localised closer to the centre<sup>7,8</sup>.

Caprioli and Spaeth showed that scotomas in NTG had a steeper slope, were significantly closer to fixation compared to HTG and exhibited greater depth<sup>9</sup>.

Thonginnetra et al. evaluated NTG and HTG patients using functional and structural tests and found functional differences between these two groups. The results had clinical implications for the evaluation of visual field defects in NTG and HTG eyes. Because a higher prevalence of visual field defects in the central region was found, they recommended that intensive testing of the central 10-degrees of the visual field (10-2 strategy) should be performed on patients with NTG (ref.<sup>10</sup>).

These conclusions have been confirmed also in our previous study in which the analysis showed that PD is statistically higher than OD ( $P=0.0001$ ) in patients with NTG. On the contrary, the patients with HTG had statistically higher values of OD compared to PD ( $P=0.002$ ) (ref.<sup>2</sup>).

The Medmont machine that we used to perform the visual field examinations works with the PD and OD indexes.

PD statistics are based on spatial correlation and are a measure of the clustering and depth of the defects. They are a scaled mean value of the product of a point's hill of vision (HoV) deviation and that of its neighbours. They are qualified by the extent to which the deviations are spatially correlated or clustered. For example, if deviations from the patient's HoV are distributed more or less

**Table 2.** The observed values in patients without local therapy.

Patients without therapy	
Number of patients	25
Mean age	61.8 $\pm$ 10.4
Lowest	36
Highest	74
Mean PD (2013)	2.18 $\pm$ 0.59
Mean PD (2018)	2.83 $\pm$ 1.44
<i>P</i>	0.0001
Mean OD (2013)	3.2 $\pm$ 1.07
Mean OD (2018)	3.61 $\pm$ 1.0
<i>P</i>	0.0001
Dependence between CCT and progression of PD	$r = -0.094$ $P = 0.519$
Dependence between CCT and progression of OD	$r = 0.1876$ $P = 0.192$
Dependence between PD 2013 and 2018	$r = -0.2$ $P = 0.162$
Dependence between OD 2013 and 2018	$r = -0.443$ $P = 0.001$

randomly throughout the field, then the PD will be small. As deviations tend to cluster, the index will increase, particularly in cases where both absolute deviations and clustering are high.

OD is the mean difference between the age-normal HoV and the mean deviation or patient-based HoV. This number is negative if the patient's HoV is less than the age-normal HoV. Up to three asterisks are appended to this number as a severity indication.

Since PD more closely describes the depth of defects with their aggregation, we used its values to assess changes in the visual fields also in this study.

The study on the relationship of CCT and progression of changes in the visual field in NTG is scarce in the available literature.

The effect of CCT on progression of HTG was investigated by Mokbel et al. and they found that patients with thinner CCT were likely to develop greater glaucomatous optic nerve and visual field damages than those with a thicker CCT (ref.<sup>11</sup>).

No relationship was found between CCT and visual field (VF) loss in treated patients with primary open-angle glaucoma or normal-tension glaucoma with asymmetrical CCT. Specifically, the thin eye did not have the more advanced VF loss or more rapid VF progression<sup>12</sup>. We might have received these results because they combined HTG and NTG in one group.

Jonas et al. investigated a relationship between CCT and progression of NTG. They found that CCT correlated significantly ( $P < 0.001$ ) and positively with the area of the neuroretinal rim and negatively with the loss of visual field<sup>13</sup>.

Other conclusions were reached by Lin et al. who revealed using the multivariate regression analysis an association between CCT and visual field defect in eyes with NTG but not in eyes with HTG (ref.<sup>14</sup>). Erdem et al. monitored 49 patients with NTG for 7-11 years. They found progression in 25 of them but it had not relation to CCT (ref.<sup>15</sup>). Choi et al. found that CCT was a significant factor in predicting the extent of localized RNFL defect at the initial examination of NTG patients<sup>16</sup>.

In our study, we did not assume a relationship between CCT and progression of changes in the visual field in NTG, at least in the early stages. We were prompted to this by other pathogenesis of changes in HTG compared to NTG. We also found no study in the literature comparing only NTG patients treated with prostaglandins or locally untreated.

We excluded the patients with NTG who have been treated with beta-blockers from our group. The reason was the outcome of our study, where we did not find a progression of changes in the visual field over five years<sup>4</sup>.

It is possible that the results of other authors are biased by not distinguishing the effect of treatment on NTG progression.

The results of this study confirmed our assumption. There was no relationship between progression of changes in the visual fields and CCT. We found that with the advancement of changes in the visual field, there is a greater progression of these changes. This is similar to HTG.

## CONCLUSION

We found no relationship between progression of changes in the visual fields and CCT. Untreated patients had progression of changes in the visual field in both PD and OD, unlike those who were treated with prostaglandins and had changes only in PD. Progression of visual field changes was greater in patients who had more advanced changes at the time of beginning of follow-up.

The study protocol was approved by the local Ethics Committee and the study was performed in accordance with Good Clinical Practice and the Declaration of Helsinki.

## ABBREVIATIONS

CCT, Central corneal thickness; HoV, Hill of vision; HTG, Hypertensive glaucoma; NTG, Normotensive glaucoma; PD, Pattern defect; OD, Overall defect; VF, Visual field.

**Author contributions:** JL: literature search and drafted the manuscript. All authors contributed equally to data collection, analysis, interpretation and correction of the final manuscript version.

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