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The Influence of Corneal Thickness on Progression of Hypertensive Glaucoma

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Abstract

Objectives: To verify whether there is dependence between corneal thickness and progression of glaucoma, to assess the impact of early changes in the visual field on their progression in time.

Methods and Patients: Findings of 132 eyes in 67 patients with primary hypertensive open-angle glaucoma, of 27 men and 40 women, mean age 66 years (28 - 84 years) were evaluated, retrospectively. Two women were included into the set with one eye (the other eye had the visual acuity below 0.1). All patients had compensated IOP after eventual correction to the corneal thickness below 18 mm Hg. None of the patients had been previously treated with brimonidine preparations or suffered from another eye disease.

Corneal pachymetry was performed on the ultrasound device SP-100 of Tomey Corporation.

The visual field was examined by static perimetry using MEDMONT M 700 device with a fast threshold glaucoma program. From two visual field tests during the past 5 years, pattern defects (PD) were evaluated.

Results: The obtained data were subjected to statistical analysis. The regression line showed a decreasing trend at the correlation coefficient r = -0.2675 (p = 0.0043). It is a statistically significant weak indirect dependence of progression of changes in the visual fields on the thickness of the cornea. Dependence of changes progression in visual fields on the initial values showed to be weak. The value of the correlation coefficient r = 0.290 (p = 0.0019).

Conclusion: The authors proved weak indirect dependence of progression of changes in visual fields in hypertensive glaucoma on the thickness of the cornea and a weak dependence of changes in the fields of vision on the initial values of the pattern defect.

Keywords: CCT; Hypertensive glaucoma; Changes in the visual field

Introduction

There are numerous studies in literature dealing with the influence of corneal thickness (CCT = Central Corneal Thickness) on visual function in hypertensive glaucoma. But the results are not unequivocal. Jonas et al. [1] showed a negative correlation between CCT and defects in the visual fields, but they have not observed the dependence on time (average 62 months). Chauhan et al. [2], who had been following 54 patients for 9.2 years, found no relationship between corneal thickness and progression of changes in visual fields either.

The recent studies of Lin et al. [3] have proven that eyes with incipient changes had greater CCT than the eyes with more advanced changes. They have found by regression analysis that in normotensive glaucoma there is a correlation between defects in the visual fields and corneal thickness but they have not proven this dependence in open-angle glaucoma. Mokhbela and Ghanem [4] demonstrated a correlation between CCT and perimetric changes. The study of Cao et al. [5] has not confirmed the relationship between CCT and changes in visual fields either.

In our previous study we demonstrated the possible difference of hypertensive glaucoma from normotensive ones [6].

Gordon et al. [7] conclude in their study that the corneal thickness is a strong predictive factor of open-angle glaucoma development. Patients with the cornea thinner than 555 μm were at three time's higher risk of glaucoma progression than patients with cornea thicker than 588 μm.

Therefore, we try in this work to give evidence about possible relationship between corneal thickness and progression of changes in visual fields in the hypertensive open-angle glaucoma group.

In our opinion, there are three possible answers to the question "Why the thinner cornea can lead to greater progression of changes in the visual field?"

First

During common ophthalmologic examination, with normal findings on the optic nerve discat "normal intraocular pressure" the eyes with thinner cornea may have already developed glaucoma. The experimental works of Naskar et al. [8] state that the changes at the level of ganglion cells occur earlier than the changes in their axons. Number of retinal ganglion cells in a rat model fell by 40% in 2.5 months, but the first changes at the optic nerve disc, in sense of origin of excavation, appeared in 2 months.

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Second

It can be assumed that in thinner corneas the lamina cribriformis is also thinner and thus, more elastic. Azuara-Blanco et al. [9], who measured the excavation of the disc in 10 emmetropic and 10 myopic patients (with normal IOP) using HRT, found that after the intraocular pressure had increased to 35.4, respectively to 34.4 mm Hg by means of a suction cup, the excavation at the disc enlarged as well. This leads to presumption that lamina cribriformis distortion in direction to the optic nerve may even cause the destruction of a part of axons in retinal ganglion cells.

Third

The loss of retinal ganglion cells involves a loss of their axons as well. This loss in pre- and retrolaminar area leads to the collapse of lamina cribriformis support and the excavation at the disc. So far, the description of the process in the Hayreh´s works [10].

The problem of sclera thickness after elevation of IOP was dealt with in experiment by Girardet al. [11]. Significant stiffening of the sclera follows the exposure to moderate IOP elevations in most eyes. Scleral hypercompliance may precede the stiffening or be a unique response to minimal chronic IOP elevation in some eyes. These biomechanical changes are likely to be the result of scleral extracellular matrix remodeling. Whether the stiffening thickening is permanent, and how the thinner sections coats will behave, is so far not known.

In our work, we wanted to verify, which of the above authors were right, i.e. whether, there is correlation between corneal thickness and progression of glaucoma. Further, we wanted to evaluate the influence of initial changes in the visual field on their progression over time.

Methods and Patients

The authors retrospectively evaluated the findings of 132 eyes, 67 patients with hypertensive primary open-angle glaucoma. These were 27 men and 40 women with a mean age of 66 years (28-84 years). Two women were included in the set with one eye (the other eye had visual acuity below 0.1).

Criteria for inclusion in the group were: IOP compensated by eventual correction for CCT below 18 mmHg, a minimum treatment period of at least five years prior to the first measurement of CCT and PD in the visual field (40% of eyes were treated with beta-blockers, 30% with prostaglandins, 10% with local blockers of carbonic anhydrase, and 20% with a fixed combination of beta-blockers with prostaglandins).

Factors that excluded the patients from our research study were: refraction higher than -6 diopters, other eye disease or a disease affecting the visual pathway, or previous therapy with brimonidine [12].

Corneal pachymetry (CCT) was carried out on the ultrasound device SP-100 Tomey (Tomey, Nagoya, Japan).

The value of CCT was examined in all eyes at visual field examination in 2006 in the morning hours in order to eliminate the change in corneal thickness during the day [13]. We have not counted with changes of CCT during the follow-ups [14].

The visual field was examined by static perimeter using fast threshold glaucoma program on the device MEDMONT M 700 (Medmont Pty Ltd, Australia). When necessary, correction was used for the distance of 30 cm. From the perimeter examinations we evaluated pattern defects (PD); the first results were collected from the period five years ago and the second ones from this year. The change in the results was the criterion of the glaucoma progression.

Results

Tables 1-3 show the corresponding values of PD (dB) five years ago and those at the last examination, in the value of CCT (μm). Values are sorted by the CCT values (μm) from the thinnest to the thickest.

The dependence of PD progression on its initial value and thickness of the cornea was tested using the linear regression and correlation. The correlation coefficient has always values in the range of -1 to 1. If the r is close to -1, it indicates an indirect relationship between the variables (the larger one variable, the lower is the other one). If the r is close to +1, it indicates a direct dependence (the larger one variable, the higher is also the other one). If the r is close to 0, it means that the variables are independent. One is not related to the other and vice versa. According to the correlation coefficient, it may be distinguished between weak ($|r|<0.3$), moderate ($0.3<|r|<0.8$) and strong ($|r|> 0.8$) dependence (correlation) (Figures 1-3).

CCT	Pattern Defect	
	0 year	5 years
467	5.10	8.19
468	4.84	5.61
481	1.58	1.27
482	1.76	2.18
484	6.82	9.31
489	8.23	10.63
490	3.57	3.61
490	2.52	2.97
496	9.24	14.32
500	6.48	8.47
500	3.75	7.3
501	12.90	13.02
505	3.26	4.08
509	1.90	1.70
511	2.10	2.28
512	2.87	3.70
512	1.94	1.69
512	1.85	2.93
513	5.71	14.41
514	2.14	1.54
515	2.89	3.21
516	1.72	2.06
516	1.55	2.90
516	2.06	1.83
517	3.14	5.07
517	1.63	2.97
517	2.36	2.56
519	2.57	3.40
519	1.95	2.81
520	2.16	2.58
522	14.61	20.89
523	2.09	2.11
525	1.93	1.83
525	11.37	13.81
525	4.46	5.03
527	6.90	11.87
527	2.06	2.23
529	2.20	1.80

Table 1

CCT	Pattern Defect	
	0 year	5 years
533	2.13	2.29
533	6.78	9.25
536	2.56	3.54
540	1.52	1.90
541	1.68	1.67
541	3.97	5.32
541	2.13	1.25
542	1.94	1.99
543	21.66	21.8
543	3.18	3.19
543	5.3	5.40
544	3.23	3.26
545	7.11	5.53
545	10.55	11.55
546	3.39	3.46
547	1.80	1.66
548	1.71	1.55
548	11.3	17.17
548	2.16	2.21
549	2.20	1.32
549	1.57	1.57
549	2.02	3.64
550	1.78	1.77
550	3.18	3.28
550	1.46	1.44
551	2.19	2.07
551	4.0	4.72
553	7.53	10.92
553	2.04	2.61
555	1.59	1.75
555	1.85	2.33
555	1.37	1.01
558	20.52	22.95
560	1.90	2.25
561	1.48	1.47
561	18.18	17.95
561	12.12	17.24

Table 2

Discussion

As mentioned in the introduction, we tried to verify in our work whether there is correlation between corneal thickness and progression of glaucoma. According to our results, the value of the correlation coefficient has a negative value r = -0.2675. Thus, it is statistically significant indirect dependence of glaucoma progression on the corneal thickness. However, the value shows rather weak dependence.

Another objective was to assess the influence of initial changes in the visual field on their progression over time. Our results show direct dependence of the progression on the initial value of PD. Thus, the higher the initial value of PD, the higher is the value of progression. The correlation coefficient r = 0.2901 shows, however, rather weak dependence. Similar data are not yet known from the literature.

The last figure 3 shows that the higher the initial PD, the faster progression of changes we can expect in the visual fields in thinner corneas compared to the eyes with thicker corneas. In the introduction, we dealt with possible causes of these changes.

Unlike the results of Jonas et al. [1], Lin et al. [3] and Cao et al. [5], already mentioned in the introduction that have not proved the dependence between changes in the fields of vision on the corneal thickness, our results are consistent with the OHTS study [7] and work of Mokhbel and Ghanem [4].

In the study of Chauhan et al. [2], who had been monitoring the nerve fiber layer by confocal scanning laser tomography and the visual field for 6 months, they conclude they have not found any relationship between these variables. Nevertheless, their negative result can be caused by the short follow-up period.

Some other studies, whose authors compared the corneal thickness with the findings in the layer of nerve fibers, on the disc of the optic nerve, are in accordance with our results as well. Henderson et al. [15] have proved the dependence of thin cornea on the thickness of the layer of nerve fibers (GD x VCC). Gunvant et al. [16] arrived at the same conclusion, too.

In our study, we have not dealt with the possible effect of topical medication on CCT and PD in hypertensive glaucoma. We wanted to select a group of patients with a minimum of variables. Therefore, we

CCT	Pattern Defect	
	0 year	5 years
562	2.02	2.04
563	1.58	1.95
566	2.59	2.46
568	2.01	1.1
568	1.91	1.02
570	1.97	2.13
573	1.77	2.35
575	1.80	1.61
575	2.78	5.64
577	3.65	3.45
578	1.15	1.38
579	1.8	1.72
580	1.9	1.31
581	1.2	2.27
581	0.2	0.3
582	11.12	4.76
584	3.54	4.03
585	1.74	4.23
585	3.08	3.08
589	1.31	1.72
589	2.32	2.24
589	12.6	10.86
590	7.32	6.30
590	3.73	4.20
591	1.28	1.77
592	2.26	2.49
594	2.02	2.41
595	3.61	5.00
597	4.07	6.20
603	1.99	2.39
605	8.33	11.05
605	2.30	2.50
610	1.99	2.28
615	2.18	1.08
618	1.18	1.35
629	2.53	1.56
646	2.53	2.38

Table 3

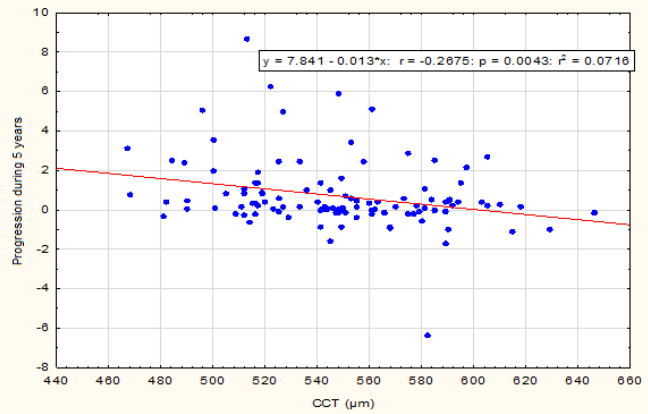

Figure 1: Testing the influence of the corneal thickness on the progression of corneal PD. Each point in the graph represents values of progression and corneal thickness in one patient. The regression line has a decreasing trend at the correlation coefficient r = -0.2675 (p = 0.0043). It is therefore, a statistically significant indirect dependence of the progression on the corneal thickness. Thus, the thicker the cornea, the smaller is the value of progression. The value of the correlation coefficient r = -0.2675 shows, however, rather weak dependence.

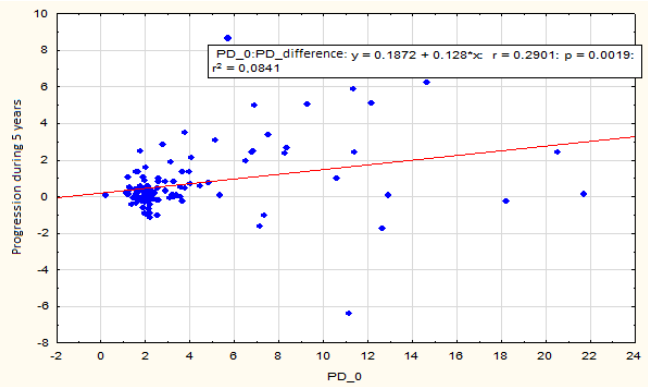

Figure 2: Testing the influence of initial value of PD on its progression. The regression line has a growing trend at the correlation coefficient r = 0.2901 (p = 0.0019). It is therefore, statistically significant direct dependence of the progression on the initial value of PD. Thus, the higher the initial PD, the greater is the value of progression. The value of the correlation coefficient r = 0.2901, however, shows rather weak dependence.

included in the study set the patients who received topical treatment at least five years before the first value of CCT and PD. Jonas et al. [1] have not proven any effect of beta blockers or topical carbonic anhydrase inhibitors on CCT. The CCT tended to be in the group of eyes that had received latanoprost [1]. Sen et al. [17] observed, unlike Jonas et al. [1], reduction of CCT during the two-year follow-up of topical treatment with l atanoprost and bimatoprost.

The question remains whether medicaments affect in a long term the CCT? This information is unavailable in the literature.

Why in some eyes of our sample an improvement of the PD occurred in the course of five years to, we do not know. We presume that the anti-glaucoma treatment may play a certain role.

Conclusion

The authors demonstrated weak indirect dependence of progression

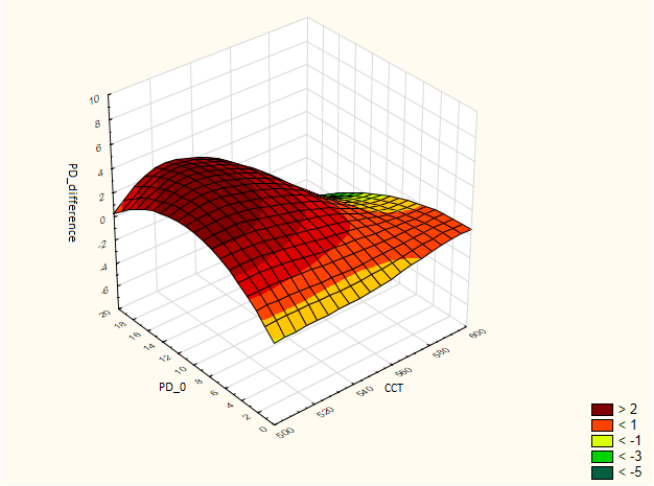

Figure 3: Graphical representation of the dependency using 3D xyz graph. In the 3D xyz graph on the vertical axis z, the PD variable (differences in values over time) is applied. The PD variables at time 0 and corneal thickness are represented graphically in the axes x and y at the base. From the shape of the graph, we can see that with decreasing thickness of the cornea and increased PD value at time 0, the rate of progression of PD increases. Conversely, with increasing thickness of the cornea and decreasing PD value at time 0, the rate of progression of PD decreases.

of changes in visual fields in hypertensive glaucoma on the corneal thickness as well as weak dependence of changes in the visual fields on the initial PD values.

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