The Assessment of Retinal Nerve Fiber Layer Thickness Changing after Glaucoma Surgery by Optical Coherence Tomography, Phramongkutklao Hospial

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Objective: *To assess retinal nerve fiber (RNFL) thickness change in glaucoma patients after glaucoma surgery.*
Material and Method: *A prospective and cohort study of 19 patients who underwent trabeculectomy with mitomicin C or combined procedures or glaucoma drainage device surgery in Phramongkutklao Hospital were included. All subjects had obtained informed consents. Preoperative and 3 month-postoperative IOP and RNFL thickness were determined. Areas of peripapilllary RNFL thickness were evaluated by Stratus OCT scanning. The relationship between IOP reduction and RNFL thickness change after glaucoma surgery was analyzed.*
Results: *Postoperative RNFL thickness analysis found no significant increase in inferior, superior, nasal and temporal quadrants. The average of preoperative RNFL thickness was 59.58 $\pm$ 17.59 microns, whereas the average of postoperative RNFL thickness was 57.19 $\pm$ 14.97 microns ($p = 0.426$). Postoperative IOP was decreased significantly from 29.26 $\pm$ 8.58 mmHg to 12.11 $\pm$ 4.52 mmHq ($p < 0.001$). The mean of postoperative RNFL thickness was not significantly correlated with IOP reduction ($r = 0.306$, $p = 0.250$).*
Conclusion: *Post glaucoma surgery, RNFL thickness was not significantly increased although the IOP had significantly reduced. No correlation between IOP reduction and RNFL thickness was found.*

Keywords: *Optical coherence topography (OCT), Retinal nerve fiber layer thickness (RNFL), Intraocular pressure (IOP)*

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Glaucoma is a disease in which progressive loss of retinal ganglion cells (RGCs) results in thinning of retinal nerve fiber layer (RNFL) thickness and characteristic optic nerve damage. This process is irreversible and usually associated with increasing in intraocular pressure (IOP). Quigely HA studies show reversal optic disc cupping in early stage of primary congenital glaucoma following successful reduction of IOP[1], but the irreversible change of optic disc cupping was found in adults[2-4].

To estimate quantitative changes in optic nerve morphology and RNFL thickness, many studies used an imaging technique to assess structural changes in glaucoma. Studies using Heidelberg retina tomography (HRT) or confocal scanning laser ophthalmoscopy (CSLO) have shown that an optic nerve head can reversibly change in cup area, cup/disc area ratio, rim area, cup volume, rim volume, mean cup depth and maximum cup after significant reduction in IOP with medical or surgical treatment[5-7].

Optical coherence tomography (OCT), a new imaging technique can provide high-resolution cross-sectional imaging of eyes based on the principles of low-coherence interferometry. Therefore, peripapillary areas and RNFL thickness are able to be evaluated and quantified effectively[8,9]. These result in early diagnosis of glaucoma and precise monitoring progressive damaging in glaucoma.

Recent studies using OCT to evaluate a change of RNFL thickness before and after IOP reduction, different results were found. Aydin A ed al showed a significant increase in RNFL thickness in patients who underwent trabeculectomy[10], but Chang P showed no significant change[11].

To the authors' best knowledge there is no research about a change of RNFL thickness after IOP reduction in a Thai population. The purpose of the authors was to prospectively assess RNFL thickness

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change of Thai-glaucoma patients who had undergone successful glaucoma surgery by using Stratus OCT scanning and also the correlation between the IOP reduction and RNFL thickness.

Material and Method

The present prospective and cohort study was conducted in Phramongkutklao Hospital. The present study protocol was also approved by the Armed Forces Research Institute of Medical Sciences, Phramongkutklao Hospital.

Glaucoma patients, treated between October 2007 to October 2008 at Phramongkutklao Hospital, Thailand, were enrolled in the present study. Despite maximal medical treatment, all patients had uncontrolled glaucoma either progressive visual field loss or progressive optic neuropathy. All of them underwent glaucoma surgery. Informed consent was also obtained from all the patients.

All subjects underwent preoperative ophthalmologic evaluation. They consisted of the following: completely medical history taking, visual acuity testing, refraction, intraocular pressure (IOP) measurement using Goldman applanation tonometer, slit-lamp bio-microscopic examination, stereoscopic bio-microscopy of the optic nerve head (ONH) and RNFL using aspheric lens 90 D or 78 D or 60 D and indirect ophthalmoscope. Subjects also had SITA standard 30-2 of Humphrey visual field testing and stereoscopic optic disc photography under dilated pupil and Stratus OCT scanning of peripapillary RNFL thickness on the same day. Eyes with diabetic retinopathy, uveitis, post retinal surgery and other retinal disease were excluded from the present study.

Each eye of the preoperative patients was dilated with 10% phenylephrine and/or 1% tropicamide alone before recording the images. Then three circular scans around the center of the optic disc using a circle size of 3.4 mm, which have been shown to provide good reproducibility, was performed. The fast RNFL (3.4 mm) scanning of Stratus OCT was used for peripapillary RNFL thickness measurement. The averaged RNFL thickness measurements were obtained from the 3 circular scans and reported in the analysis printout. OCT scanning was performed by an experienced optometrist under dilated pupils and the highest quality image of the peripapillary RNFL, which signal strength was more than 6, was taken for each eye.

Furthermore the participants underwent conventional trabeculectomy with Mitomicin C or combined phacoemulsification with intraocular lens implantation and tabeculectomy with Mitomicin C or glaucoma drainage device implantation within 4 weeks after enrolling in the present study. OCT scanning of RNFL thickness was also obtained postoperatively at 3 months after successful surgery. The authors defined the successful glaucoma surgery if postoperative IOP was less than 18 mmHg with or without medication.

The differences between preoperative and postoperative RNFL thickness were analyzed for the whole group using paired t-test. Pearson's correlation was used to evaluate the associations between parameters. All analyses were performed with SPSS software (version 15: SPSS Inc) p-values less than 0.05 were considered to be statistically significant.

Results

Nineteen eyes of 19 patients satisfied all the inclusion criteria and were included for analysis. There were 11 (57.8%) men and 8 (42%) women with the mean age of 54.26 $\pm$ 17.14 years. Eleven eyes were right eyes and 8 were left eyes. Patient characteristics are presented in Table 1. Most common diagnosis was primary open angle glaucoma (8/19 eyes). Primary angle closure glaucoma was the second common diagnosis (6/19 eyes). Fourteen (73.7%) eyes underwent trabeculectomy with mitomycin C and 4 (21%) eyes underwent combined phacoemulsification with intraocular lens implantation and trabeculectomy with mitomycin C. In addition only one eye (5.3%) underwent glaucoma drainage device implantation. The majority of indications for glaucoma surgery were failure of control IOP regarding maximal tolerated medical

Table 1. patient characteristics (n = 19)

Age , years (mean $\pm$ SD)	54.28 $\pm$ 17.14
Gender (male, female)	11/8
Diagnosis	
Primary open angle glaucoma (POAG)	8
Juvenile open angle glaucoma (JOAG)	3
Primary angle closure glaucoma (PACG)	6
Secondary glaucoma	2
Type of surgery	
Trabeculectomy	14
Combined surgery	4
Glaucoma drainage device	1
Indication for surgery	
Failure of control IOP	15
Progressive optic neuropathy	4

IOP = Intraocular pressure

therapy.

The averaged pre-operative IOP was 29.26 ± 8.58 mmHg and the averaged postoperative IOP at 3-month-visit was 12.11 ± 4.52 mmHg. There was significant lowering in IOP following surgery (Table 2). The statistically significant difference between preoperative and postoperative IOP was -17.16 ± 8.76 mmHg (p-value < 0.001). However, cup to disc ratio of optic nerve head and visual acuity did not change significantly after surgery.

Preoperative and postoperative peripapillary RNFL thickness were obtained in 4 quadrants, such as inferior, superior, nasal and temporal. Mean peripapillary RNFL thickness measured by OCT is presented in Table 2. Following glaucoma surgery, there was a non-significant difference in all 4 quadrants of RNFL thickness. Preoperative overall RNFL thickness was 59.58 ± 17.59 microns, whereas postoperative overall RNFL thickness was 57.19 ± 14.97 microns (p-value = 0.426).

Table 3 summarizes the correlation between IOP reduction and RNFL thickness postoperative glaucoma surgery. The present study showed no statistically significant correlation between all parameters of RNFL thickness and lowering of IOP (r = 0.306, p-value = 0.250).

Discussion

Glaucoma is a disease or a group of diseases that usually causes a progressive structural and functional change. In terms of structural damage, it will cause retinal ganglion cell loss and also progressive thinning of RNFL and enlargement of cup to disc ratio. Multi-center clinical trials show that IOP is the major risk factor of glaucoma and a risk of glaucoma progression. This is the only risk factor that can be modified with medical treatment or surgery. If target IOP is achieved by lowering IOP, glaucoma progression would be halted or slowed. However, the damaged retinal ganglion cell and thinning of RNFL thickness are generally irreversible.

OCT has been shown to be an effective technique for glaucoma diagnosis. Many studies have used OCT to evaluate RNFL thickness[8,9]. Obtaining maximum possible signal strength is critical for reliable assessment of RNFL. The authors selected patients who had highly reliable signal strength (range 6-10) for statistical analysis.

The present study showed significantly IOP reduction over 30 % in each patient followed by filtrating surgery and also showed decreased RNFL thickness in 4 quadrants of peripapillary area after filtration

Table 3. The correlation between IOP reduction and RNFL thickness postoperative glaucoma surgery (n = 19)

OCT parameters	r	p-value
Max inferior	0.116	0.669
Avr inferior	0.244	0.363
Max superior	0.415	0.110
Avr superior	0.494	0.052
Nasal	0.074	0.786
Temporal	0.072	0.791
Over all	0.306	0.250

Table 2. Visual acuity, IOP and Mean peripapillary RNFL thickness measured by Stratus OCT between pre-operation and post-operation at 3 month-visit (n = 19)

	Preoperation	Postoperation	Differences	p-value
Visual acuity	0.36 ± 0.28	0.37 ± 0.29	0.01 ± 0.20	0.756
IOP	29.26 ± 8.58	12.11 ± 4.52	-17.16 ± 8.76	< 0.001
Cup to disc ratio	0.79 ± 0.12	0.79 ± 0.12		
OCT parameters:				
Maximum inferior	81.84 ± 31.84	79.21 ± 24.79	-2.63 ± 23.12	0.626
Average inferior	65.32 ± 27.48	61.00 ± 20.04	-4.32 ± 18.1	0.312
Maximum superior	83.58 ± 28.72	81.63 ± 28.11	-1.95 ± 23.79	0.725
Average superior	66.00 ± 22.30	64.11 ± 23.73	-1.89 ± 22.25	0.715
Nasal	56.59 ± 13.12	54.39 ± 16.18	-2.19 ± 13.17	0.478
Temporal	49.84 ± 15.43	49.04 ± 12.24	-0.80 ± 13.10	0.794
Over all	59.58 ± 17.59	57.19 ± 14.97	-2.38 ± 12.75	0.426
Signal strength	6.89 ± 1.70	7.00 ± 1.60	0.11 ± 1.52	0.767

IOP = Intraocular pressure, OCT = Optical coherence tomography

surgery. Duration of re-evaluate RNFL thickness was 3 months to reduce artifact from retinal edema after surgery. All OCT parameters showed no statistically significant change after glaucoma surgery. The authors also used Pearson's correlation to evaluate the corresponding between IOP reduction and RNFL thickness change. The present study found no significant correlation between IOP reduction and changes in RNFL thickness.

Several authors have experienced examining RNFL thickness pre and post reduction of IOP by using OCT. In 2003 Aydin A et al reported a statistically significant increase in overall RNFL thickness after IOP reduction by trabeculectomy. Preoperative RNFL thickness was 72 $\pm$ 20.5 and postoperative RNFL thickness was 81.7 $\pm$ 21.1 micron (p-value < 0.0001). They also found positive correlations between IOP reduction and RNFL thickness[10]. While Chang P et al had a different report. They showed RNLF thickness had no statistically significant change after IOP reduction (p-value = 0.303-0.655)[11].

There may be the majority of subjects in the present study had advanced stage of glaucoma. Each optic nerve cupping ratio was in range 0.9 to full cupping and some cases had pale disc. In advanced glaucoma, there are already small numbers of RNFL left to detect preoperatively. It might be difficult to demonstrate significant changes in these cases. The second reason is a possibility of no change in RNFL thickness after surgery or 3 months might be too early to detect a change. The similar result was also found by Chang P et al[11] with the same 3-month-visit. While a different result found by Aydin A et al had RNFL measurement at 8 months after surgery[10]. The RNFL thickness in the present study tend to be decreased in all quadrants after surgery. A minor trauma from sudden decreasing in IOP during surgery may be the cause of the damage. Finally the authors suggest to do further researches in these areas with a longer period of time and more enrolled participants to get more information.

Conclusion

Post glaucoma surgery, RNFL thickness was not significantly increased although the IOP had significantly reduced. No correlation between IOP reduction and RNFL thickness was found.

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Potential conflicts of interest

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การศึกษาการเปลี่ยนแปลงของความหนาของเส้นใยประสาทตาภายหลังการผ่าตัดต้อหินด้วยเครื่อง Optical Coherence Tomography ณ โรงพยาบาลพระมงกุฎเกล้า

สุทธินี มณีแสง, อรวสี จตุทอง, วัลลภ เอี่ยมสมบุญ

วัตถุประสงค์: *เพื่อวิเคราะห์การเปลี่ยนแปลงของเส้นใยประสาทตาหลังการผ่าตัดต้อหินโดยใช้เครื่อง Optical Coherence Tomography*

วัสดุและวิธีการ: *การศึกษาไปข้างหน้าของผู้ป่วยโรคต้อหินที่ได้รับการผ่าตัดต้อหิน หรือการผ่าตัดต้อกระจกร่วมกับการผ่าตัดต้อหิน หรือการฝังท่อเก็บกักน้ำเพื่อลดความดันตาที่โรงพยาบาลพระมงกุฎเกล้า จำนวน 19 คน ทำการวัดวิเคราะห์ความหนาของเส้นใยประสาทตาของผู้ป่วยต้อหินทั้งก่อนที่ได้รับการผ่าตัดต้อหิน หรือการผ่าตัดต้อกระจกร่วมกับการผ่าตัดต้อหิน หรือการฝังท่อเก็บกักน้ำเพื่อลดความดันตา และภายหลังการผ่าตัดดังกล่าวที่ระยะเวลา 3 เดือน ด้วยเครื่อง optical coherence tomography ตลอดจนการวัดความดันตาทั้งก่อนและหลังผ่าตัด นำค่าความหนาของเส้นใยประสาทตาที่เปลี่ยนแปลงและค่าความดันตามาวิเคราะห์หาความสัมพันธ์*

ผลการศึกษา: *ค่าความหนาของเส้นใยประสาทตาโดยรอบขั้วประสาทตาระหว่างก่อนผ่าตัดและภายหลังการผ่าตัดต้อหินไม่มีความแตกต่างอย่างมีนัยสำคัญทางสถิติ โดยเฉลี่ยค่าความหนาของเส้นใยประสาทตาก่อนผ่าตัดเท่ากับ 59.58 $\pm$ 17.59 ไมครอน ในขณะที่หลังผ่าตัดเท่ากับ57.19 $\pm$ 14.97 ไมครอน (ค่า p = 0.426) ค่าความดันตาก่อนผ่าตัดเท่ากับ 29.26 $\pm$ 8.58 มม.ปรอท แต่ค่าความดันตาหลังผ่าตัดลดลงเท่ากับ 12.11 $\pm$ 4.52 มม.ปรอท.(ค่า p<0.001) ค่าความหนาเฉลี่ยของเส้นใยประสาทตาหลังผ่าตัดไม่มีความสัมพันธ์อย่างมีนัยสำคัญทางสถิติกับค่าความดันตาที่ลดลง (r = 0.306, p = 0.250)*

สรุป: *ค่าความหนาของเส้นใยประสาทตาหลังผ่าตัดไม่มีการเปลี่ยนแปลงอย่างมีนัยสำคัญทางสถิติถึงแม้ว่าค่าความดันตาจะลดลงอย่างมีนัยสำคัญทางสถิติตรวจไม่พบความสัมพันธ์ระหว่างความดันตาที่ลดลงและค่าความหนาของเส้นใยประสาทตาหลังผ่าตัด*