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Assessing the alterations in retinal nerve fiber layer thickness before and following Glaucoma filtration surgery using optical coherence tomography: A clinical study

Dr. Sapna Raghuwanshi[1], Dr. Meemansha Patel[2], Dr. Kavisha Agarwal[3], Dr. Vaishali Ghanshyam Rai[4*]

[1]MBBS, MS, Associate Professor , Department of Ophthalmology, Atal Bihari Vajpayee Govt. Medical College Vidisha MP
[2]MBBS, 1st year PG, Department of Ophthalmology, Atal Bihari Vajpayee Govt. Medical College Vidisha MP
[3]MBBS, 1st year PG, Department of Ophthalmology, Atal Bihari Vajpayee Govt. Medical College Vidisha MP
[4]MBBS, DNB, Assistant Professor, Department of Ophthalmology, Atal Bihari Vajpayee Govt. Medical College Vidisha MP

Corresponding Author: Dr. Vaishali Ghanshyam Rai*
Email id: dr.vaishali.rai@gmail.com
Assistant Professor, Department of Ophthalmology, Atal Bihari Vajpayee Govt. Medical College Vidisha MP

Background: Retinal nerve fiber layer thickness is measured at a 3.5mm distance from the optic nerve head center. This thickness alteration is present even in absence of vision loss warranting continuous monitoring of the affected eyes. A high correlation is seen between alteration of retinal nerve fiber layer thickness and vision loss, allowing accurate assessment of progression of glaucoma.

Aims: the present study was conducted to assess the alterations in RNFL (Retinal Nerve Fiber Layer) thickness and intraocular pressure following glaucoma filtration surgery.

Materials and Methods: 36 subjects were evaluated from both genders and within the age range of 37-64 years and mean age of 53.82±12.94 years. For ocular examination, slit-lamp examination, tonometry, gonioscopy, and fundus examination were done. This was followed by the filtration surgery (trabeculectomy) where a tissue piece was removed in the drainage angle of the eye which made an opening at 0-4 months before and 2-4 months following Glaucoma filtration surgery along with intraocular pressure alteration. The collected data were subjected to the statistical evaluation

Results: Significant increase in RNFL thickness for overall quadrant and all individual quadrants ($p<0.05$). For the temporal quadrant, the RNFL thickness increased from 43.45±14.07 to 46.73±16.69 with p=0.067. In the inferior quadrant, it increased from 53.39±25.77 to 60.92±30.70 (p=0.002) and for the nasal quadrant, it was increased from 47.91±19.30 to 54.47±20.11 (p=0.007). For the overall quadrant, RNFL thickness increased from 52.58±17.38 to 58.50±20.18 with p=0.0001. For age >50 years and <50 years, RNFL

thickness increased significantly for all age groups and intraocular pressure decreased significantly. In the present study, RNFL thickness was increased for both females and males with reduced intraocular pressure significantly ($p<0.05$).

Conclusion: The present study concludes that RNFL thickness increase with a decrease in intraocular pressure following glaucoma filtration surgery. This increase in thickness was also seen with age and gender

Keywords: Glaucoma, Glaucomatous optic neuropathy, optic nerve head, optical coherence tomography, retinal nerve fiber layer thickness

Introduction

Glaucoma is one of the major leading causes of blindness in India with approximately 8% blindness seen secondary to glaucoma, whereas, the global incidence of blindness following glaucoma is 12% approximately. Glaucoma is optic neuropathy, which is progressive having peculiar visual field defect pattern and particular appearance of the optic disc. Glaucoma is frequently associated with increased intraocular pressure. Loss of vision associated with glaucoma is without symptoms, sustained, and silent, and hence, it remains not diagnosed and unnoticed in the majority of affected subjects.[1]

Generally, a bilateral disease pattern and adult disease onset are seen in primary open-angle glaucoma. It is also characterized by an open angle of normal appearance, greater than 21 mm of intraocular pressure, visual field loss, and glaucomatous optic nerve head changes. The risk factors for glaucoma are raised intraocular pressure, positive family history, corneal thickness, black race, myopia, and advanced age.[2] Glaucoma is characterized by retinal ganglion cell loss along with its axons. Approximately 6 years before any vision loss in glaucoma subjects is noticed, visual field damage and changes in the optic nerve head are seen in approximately 60% of eyes affected with glaucoma. Hence, for early detection and treatment of glaucoma, assessment of retinal nerve fiber layer damage and optic nerve head alterations are vital.[3]

These retinal nerve fiber layer damage and optic nerve head alterations are commonly and non-invasively detected using optical coherence tomography in glaucoma subjects. This helps in differentiating diseased subjects from healthy subjects without glaucoma. Retinal nerve fiber layer thickness is measured at a 3.5mm distance from the optic nerve head center. This thickness alteration is present even in absence of vision loss warranting continuous monitoring of the affected eyes. A high correlation is seen between alteration of retinal nerve fiber layer thickness and vision loss, allowing accurate assessment of progression of glaucoma.[4]

Such alterations can be limited using surgeries to decrease intraocular pressure with improvement in vision. One such acceptable surgery is filtration surgery, dependent on disease severity. Of other parameters detecting glaucoma progression, retinal nerve fiber thickness seems to be reliable and stable in a long duration.[5] However, the data depicting the reliability of alterations in retinal nerve fiber thickness before and after glaucoma filtration surgery as assessed on optical coherence tomography is limited in the literature. Hence, the

present study was conducted to assess the alterations in RNFL (Retinal Nerve Fiber Layer) thickness and intraocular pressure following glaucoma filtration surgery.

Materials and Methods

The present prospective clinical study was conducted to assess the alterations in RNFL (Retinal Nerve Fiber Layer) thickness and intraocular pressure following glaucoma filtration surgery at…….from……to……after obtaining clearance from the concerned Ethical committee. The study population was comprised of the subjects visiting the Department of Ophthalmology of the institute. Before enrolment, a detailed study design was explained to all the subjects. A total of 36 subjects were evaluated from both genders and within the age range of 37-64 years and mean age of 53.82±12.94 years.

Complete history and interviews were conducted before the ocular examination to assess associated risk factors, medical history, and family history. The inclusion criteria for study subjects were patients with a confirmed diagnosis of glaucoma who underwent glaucoma filtration surgery, subjects willing to participate in the study, fit for surgery, and subjects who underwent full ophthalmologic evaluation. The exclusion criteria were patients not willing to participate in the study, end-stage diseases subjects, macular dystrophy, cystoid macular edema, diabetic retinopathy, advanced cataract, and ocular pathology. Glaucoma was diagnosed by optic nerve head abnormality and visual field loss. Optical Coherence Tomography was conducted 0-4 months before and 2-4 months following Glaucoma filtration surgery.

For ocular examination, slit-lamp examination, tonometry, gonioscopy, and fundus examination were done. This was followed by the filtration surgery (trabeculectomy) where a tissue piece was removed in the drainage angle of the eye which made an opening. Visual field examination was warranted in cases with intraocular pressure of more than 21mm Hg, VCDR difference of >0.2 between two eyes, and ≥0.7 in any eye. The macular program was used in cases with advanced defects. Optical coherence tomography was done to assess retinal nerve fiber thickness.

The variables assessed in the surgery were visual field, intraocular pressure before and after surgery, and retinal nerve fiber layer thickness 0-4 months before and 2-4 months following Glaucoma filtration surgery along with intraocular pressure alteration.

The collected data were subjected to the statistical evaluation using SPSS software version 21 (Chicago, IL, USA) and paired t-test. The data were expressed in percentage and number, and mean with standard deviations. The level of significance was kept at $p<0.05$.

Results

The present study was conducted to assess the alterations in RNFL (Retinal Nerve Fiber Layer) thickness and intraocular pressure following glaucoma filtration surgery and assessed 36 subjects and 44 eyes. The subjects were evaluated from both genders and within the age range of 37-64 years and mean age of 53.82±12.94 years. There were 54% (n=19) females

and 46% (n=17) males in the present study. The present study showed that in early glaucoma only arcuate nerve fibers are damaged, whereas, in advanced glaucoma nerve fibers from all quadrants are damaged. Postoperatively, the retinal nerve fiber layer thickness increased significantly from 52.58±17.38 to 58.46±20.22.

On assessing the change in retinal nerve fiber layer (RNFL) thickness in quadrants following glaucoma filtration surgery, it was seen that there was a significant increase in RNFL thickness for the overall quadrant and all individual quadrants ($p<0.05$) (Table 1). For the temporal quadrant, the RNFL thickness increased from 43.45±14.07 to 46.73±16.69 with p=0.067. In the inferior quadrant, it increased from 53.39±25.77 to 60.92±30.70 (p=0.002) and for the nasal quadrant, it was increased from 47.91±19.30 to 54.47±20.11 (p=0.007). For the superior quadrant, RNFL thickness increased from 65.71±27.76 to 70.16±29.06, whereas for the overall quadrant RNFL thickness increased from 52.58±17.38 to 58.50±20.18 with p=0.0001.

The present study also evaluated age-related alteration in RNFL thickness (Table 2). The study results showed that for age >50 years, visual field (dB) was decreased significantly from 7.21±2.33 to 6.76±2.29 (p< 0.0001), cusp disc ratio decreased significantly from 0.85±0.11 to 0.79±0.12 (p=0.0006), average RNFL increased from 55.72±19.62 to 63.53±20.85 ((p< 0.0001), and intraocular pressure also decreased from 25.85±6.51 to 10.78±3.21 (p=0.053). For age >50 years, visual field (dB) was decreased from 6.91±3.61 to 6.44±3.12 non-significantly (p< 0.312), cusp disc ratio decreased significantly from 0.87±0.12 to 0.83±0.17 (p=0.03), average RNFL increased from 49.98±15.19 to 53.37±19.01 ((p=0.023), and intraocular pressure also decreased from 27.81±4.22 to 14.52±5.71 (p< 0.0001). The RNFL thickness increased significantly for all age groups and intraocular pressure decreased significantly.

In the present study, RNFL thickness was increased significantly for both females and males with reduced intraocular pressure. Based on genders, for females, the visual field increased from 6.89±3.26 to 7.03±2.59 non-significantly (p=0.8407) and the cusp disc ratio decreased from 0.86±0.12 to 0.82±0.14 non-significantly (p=0.0948). Average RNFL increased from 49.53±14.71 µm to 54.23±17.15 µm (p=0.0052) and intraocular pressure decreased from 27.27±6.88 to 14.19±6.11 mm Hg significantly (p< 0.0001). For males, the visual field decreased significantly from 7.19±2.92 to 6.25±2.85 (p=0.01), cusp field ratio also decreased significantly from 0.86±0.11 to 0.78±0.16 (p< 0.0001). Average RNFL increased from 52.29±19.33µm to 62.31±22.17µm significantly (p=0.001) and intraocular pressure decreased from 26.61±5.98 to 11.65±3.62 mm Hg significantly (p< 0.0001) as shown in Table 3.

Discussion

The results of the present study showed that the change in retinal nerve fiber layer (RNFL) thickness in quadrants following glaucoma filtration surgery, it was seen that there was a significant increase in RNFL thickness for the overall quadrant and all individual quadrants

(p<0.05). For the temporal quadrant, the RNFL thickness increased from 43.45±14.07 to 46.73±16.69 with p=0.067. In the inferior quadrant, it increased from 53.39±25.77 to 60.92±30.70 (p=0.002) and for the nasal quadrant, it was increased from 47.91±19.30 to 54.47±20.11 (p=0.007). For the superior quadrant, RNFL thickness increased from 65.71±27.76 to 70.16±29.06, whereas for the overall quadrant RNFL thickness increased from 52.58±17.38 to 58.50±20.18 with p=0.0001. These results were consistent with the results by the studies of Keltner JL et al[6] in 2006 and Wessel JM et al[7] in 2013 where authors reported similar quadrant-wise changes following glaucoma filtration surgery.

The present study also evaluated age-related alteration in RNFL thickness. The study results showed that for age >50 years, visual field (dB) was decreased significantly from 7.21±2.33 to 6.76±2.29 (p< 0.0001), cusp disc ratio decreased significantly from 0.85±0.11 to 0.79±0.12 (p=0.0006), average RNFL increased from 55.72±19.62 to 63.53±20.85 ((p< 0.0001), and intraocular pressure also decreased from 25.85±6.51 to 10.78±3.21 (p=0.053). For age >50 years, visual field (dB) was decreased from 6.91±3.61 to 6.44±3.12 non-significantly (p< 0.312), cusp disc ratio decreased significantly from 0.87±0.12 to 0.83±0.17 (p=0.03), average RNFL increased from 49.98±15.19 to 53.37±19.01 ((p=0.023), and intraocular pressure also decreased from 27.81±4.22 to 14.52±5.71 (p< 0.0001). The RNFL thickness increased significantly for all age groups and intraocular pressure decreased significantly. These findings were comparable to the results by Chauhan BC et al[8] in 2013 and Enders P et al[9] in 2019 where authors showed comparable age-related RNFL thickness alterations as the present study.

In the present study, RNFL thickness was increased for both females and males with reduced intraocular pressure significantly. Based on genders, for females, the visual field increased from 6.89±3.26 to 7.03±2.59 non-significantly (p=0.8407) and the cusp disc ratio decreased from 0.86±0.12 to 0.82±0.14 non-significantly (p=0.0948). Average RNFL increased from 49.53±14.71 µm to 54.23±17.15 µm (p=0.0052) and intraocular pressure decreased from 27.27±6.88 to 14.19±6.11 mm Hg significantly (p< 0.0001). For males, the visual field decreased significantly from 7.19±2.92 to 6.25±2.85 (p=0.01), cusp field ratio also decreased significantly from 0.86±0.11 to 0.78±0.16 (p< 0.0001). Average RNFL increased from 52.29±19.33µm to 62.31±22.17µm significantly (p=0.001) and intraocular pressure decreased from 26.61±5.98 to 11.65±3.62 mm Hg significantly (p< 0.0001). These results were similar to the results by Gardiner SK et al[10] in 2015 and Reis ASC et al[11] in 2017 where authors reported comparable gender-related alterations in RNFL thickness following glaucoma filtration surgery as suggested by using optical coherence tomography.

Conclusion

Within its limitations, the present study concludes that RNFL thickness increase with a decrease in intraocular pressure following glaucoma filtration surgery. This increase in thickness was also seen with age and gender. However, the present study had few limitations including smaller sample size, geographical area biases, recall bias, and single-institution

nature. Hence, more longitudinal and prospective studies with larger sample sizes, and longer monitoring periods are needed to reach a definitive conclusion.

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S. No	Quadrant	Preoperative Retinal Nerve Fiber Layer Thickness (µm)	Preoperative Retinal Nerve Fiber Layer Thickness (µm)	p-value
1.	**Temporal**	43.45±14.07	46.73±16.69	0.067
2.	**Inferior**	53.39±25.77	60.92±30.70	0.002

3.	**Nasal**	47.91±19.30	54.47±20.11	0.007
4.	**Superior**	65.71±27.76	70.16±29.06	0.007
5.	**Overall**	52.58±17.38	58.50±20.18	0.0001

Table 1: Retinal Nerve Fiber Layer Thickness alteration before and after glaucoma filtration surgery

S. No	Parameter	Preoperative Retinal Nerve Fiber Layer Thickness (µm)	Preoperative Retinal Nerve Fiber Layer Thickness (µm)	p-value
1.	**Age less than 50 years**			
a)	Visual Field (dB)	7.21±2.33	6.76±2.29	< 0.0001
b)	Cup: Disc Ratio	0.85±0.11	0.79±0.12	0.0006
c)	Average RNFL (µm)	55.72±19.62	63.53±20.85	< 0.0001
d)	Intraocular Pressure (mm Hg)	25.85±6.51	10.78±3.21	0.053
2.	**Age more than 50 years**			
a)	Visual Field (dB)	6.91±3.61	6.44±3.12	0.312
b)	Cup: Disc Ratio	0.87±0.12	0.83±0.17	0.03
c)	Average RNFL (µm)	49.98±15.19	53.37±19.01	0.023
d)	Intraocular Pressure (mm Hg)	27.81±4.22	14.52±5.71	< 0.0001

Table 2: Retinal Nerve Fiber Layer Thickness alteration based on the age before and after glaucoma filtration surgery as assessed using Optical Coherence Tomography

S. No	Parameter	Preoperative Retinal Nerve Fiber Layer Thickness (µm)	Preoperative Retinal Nerve Fiber Layer Thickness (µm)	p-value
1.	**Females**			
a)	Visual Field (dB)	6.89±3.26	7.03±2.59	0.8407

b)	Cup: Disc Ratio	0.86±0.12	0.82±0.14	0.0948
c)	Average RNFL (µm)	49.53±14.71	54.23±17.15	0.0052
d)	Intraocular Pressure (mm Hg)	27.27±6.88	14.19±6.11	< 0.0001
2.	**Males**			
a)	Visual Field (dB)	7.19±2.92	6.25±2.85	0.01
b)	Cup: Disc Ratio	0.86±0.11	0.78±0.16	< 0.0001
c)	Average RNFL (µm)	52.29±19.33	62.31±22.17	0.001
d)	Intraocular Pressure (mm Hg)	26.61±5.98	11.65±3.62	< 0.0001

Table 3: Retinal Nerve Fiber Layer Thickness alteration based on the gender before and after glaucoma filtration surgery as assessed using Optical Coherence Tomography